ISSN: 1304-2947
e-ISSN: 1307-9948

TÜRK GERİATRİ DERNEĞİ
2003
TURKISH GERIATRICS SOCIETY

Turkish Journal of Geriatrics

Türk Geriatri Dergisi



17/2 2014

www.geriatri.org

The Official Scientific Journal of Turkish Geriatrics Society
Türk Geriatri Derneği'nin Bilimsel Yayın Organıdır

Türk Geriatri Dergisi / Turkish Journal of Geriatrics
17/2 2014

www.geriatri.org

ISSN: 1304-2947 • e-ISSN: 1307-9948

Türk Geriatri Derneği IAGG üyesidir

Member of IAGG

TÜRK GERİATRİ DERNEĞİ'nin bilimsel yayın organı ve yerel süreli yayındır.
(*The official scientific journal of Turkish Geriatrics Society)*

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Ayrıntı Basımevi - İvedik Organize Sanayi Bölgesi 28. Cad. 770 Sok. No: 105-A
Ostim/ANKARA
Telefon: (0312) 394 55 90 - 91 - 92
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"Turkish Journal of Geriatrics"; Science Citation Index Expanded (Sci Search), Journal Citation Reports/Science Edition, Social Sci Search, Journal Citation Reports/Social Sciences Edition, Index Copernicus Master List, EMBASE, SCOPUS, ELSEVIER, EBSCO, TÜBİTAK - ULAKBİM "TÜRK TIP DİZİNİ", Türk Medline ve Türkiye Atıf Dizini kapsamında yer almaktadır.

"Turkish Journal of Geriatrics" is indexed in: Science Citation Index Expanded (Sci Search), Journal Citation Reports/Science Edition, Social Sci Search, Journal Citation Reports/Social Sciences Edition, Index Copernicus Master List, EMBASE, SCOPUS, ELSEVIER, EBSCO and "Turkish Medical Index" of Turkish Academic Network and Information Center in The Scientific and Technological Research Council of Turkey (TÜBİTAK-ULAKBİM), Turk Medline and Turkey Citation Index.

Yılda dört kez (Mart, Haziran, Eylül, Aralık) yayınlanır.
[Published four times (March, June, September, December) a year]

İLETİŞİM *(Correspondance)*
Güneş Kitabevi Ltd. Şti.
M. Rauf İnan Sok. No. 3 06410
Sıhhiye/ANKARA
Tel: (0312) 435 11 91-92
Fax: (0312) 435 84 23
web: http://www.guneskitabevi.com
e-posta: geriatri@guneskitabevi.com

TÜRK GERİATRİ DERNEĞİ
Turkish Geriatrics Society
www.turkgeriatri.org
info@geriatri.org
www.geriatri.dergisi.org
editor@geriatri.dergisi.org

Basım Tarihi: 15 Haziran 2014

Turkish Journal of Geriatrics
Türk Geriatri Dergisi

2014
17/2

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Baş Editörden
(From The Editor In Chief)

Turkish Geriatrics Society's mission is promoting scientific researches and organizing pre and post graduate education programs for continuous medical education at both national and international levels.On this basis, education programs of Turkish Geriatrics Society are taking place continuously.

"**Geriatric Nursing Updating Course**" for nurses which was organized by Prof. Fethiye Erdil, Prof. Sevilay Senol Celik and Assist. Prof. Zahide Tuna was held in 4th, April, 2014 and "**Basic Geriatrics Updating Course**" for medical doctors which was organized by Prof. Dilek Aslan, M.D and Assist. Prof.Tolga Aydos, M.D. was held in 5th. April, 2014 in Ankara-Kavaklıdere Gordion Hotel were performed successfully. National trainers who are experienced in geriatrics and gerontology took part during the interactive courses.

The society also organizes programs and distributes books free of charge to increase the public awareness about "**Healthy and Active Aging**" in different parts of the country. "**National Elderly Week**" in every 18-24th of March and "**International Elderly Day**" in every 1st of October are selected for such public education organizations in collaboration basically with the non-governmental organizations or various municipalities.

The latest the public awareness activity was a symposium which was organized by Assoc. Prof. Asuman Dogan, M.D. and Aytug Balcıoglu, M.D. was held in Çankaya Municipality 100 age club in 19th March, 2014. The members of the 100 age club were informed about prevention of various diseases that are seen in advanced age.

The board of directors of Turkish Geriatric Society cordially thank the organizers.

Prof. Yesim GOKCE KUTSAL, M.D

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RESEARCH

EFFECT OF PROGNOSTIC FACTORS ON SURVIVAL IN ELDERLY PATIENTS WITH NON-SMALL CELL LUNG CANCER

ABSTRACT

Introduction: More than half of newly diagnosed non-small cell lung cancer cases are patients aged more than 65 years and therefore, it is an important health problem in elderly population. In this study, we aimed to investigate effect of various the prognostic factors on survival in non-small cell lung cancer patients aged more than 65 years.

Materials and Method: Ninety-seven non-small cell lung cancer patients aged ≥65 years were included in this study. Performance status was assessed as Eastern Cooperative Oncology Group 0-1 and 2-3. Lower than 12.0 (x 10^9/L) or higher than the value of white blood cell count were classified as normal or higher, respectively. Similarly, lower than 400 (x 109/L) or higher than the value of platelet count were classified as normal or higher, respectively. Mortality risk was analyzed using the multivariate Cox regression model including all the significant variables in the univariate analysis.

Results: Overall survival estimated by Kaplan–Meier test was 11.2 [95% confidence interval (7.55-14.85)] months. In univariate analysis, performance status, stage, white blood cell and platelet counts significantly affected overall survival (p <0.001, 0.001, 0.044, and 0.006, respectively). In multivariate analysis, performance status and platelet count significantly affected overall survival (p <0.001and 0.017, respectively).

Conclusion: Survival in elderly patients with non-small cell lung cancer is significantly influenced by performance status, stage, white blood cell and platelet count. In this patient group, not only age but also these factors should be kept in mind in the treatment planning of the patients.

Key Words: Carcinoma, Non-Small-Cell Lung; Aged; Thrombocytosis; Leukocyte Count; Survival Analysis.

ARAŞTIRMA

KÜÇÜK HÜCRELİ DIŞI AKCİĞER KANSERİ OLAN YAŞLI HASTALARDA PROGNOSTİK FAKTÖRLERİN SAĞKALIMA ETKİSİ

ÖZ

Giriş: Yeni tanı alan küçük hücreli dışı akciğer kanseri olan olguların yarısından fazlası 65 yaş üstü olgulardır ve bundan dolayı yaşlı nüfus için önemli bir sağlık sorunudur. Bu çalışmada biz küçük hücreli dışı akciğer kanseri olan 65 yaş ve üstü yaşlı hastalarda sağkalım üzerine çeşitli prognostik faktörlerin etkisini araştırmayı planladık.

Gereç ve Yöntem: Histopatolojik olarak küçük hücreli dışı akciğer kanseri tanısı konan 65 yaş ve üstü 97 olgu bu çalışmaya dahil edildi. Performans durumu, Eastern Cooperative Oncology Group 0-1 ve 2-3 olarak iki grupta ele alındı. Beyaz küre sayısı 12.0 (x 109/L)'den düşük ise normal, bu değerden fazla ise yüksek olarak sınıflandı. Benzer olarak, trombosit sayısı 400 (x 109/L)'den düşük ise normal, bu değerden fazla ise yüksek olarak sınıflandı. Mortalite riski, tek değişkenli analizde anlamlı olan tüm değişkenlerin dahil edildiği çok değişkenli Cox regresyon modeli kullanılarak analiz edildi.

Bulgular: Kaplan-Meier testi ile saptanan genel sağkalım süresi 11,2 [%95 Güven Aralığı (7.55-14.85)] aydı. Tek değişken analizde performans skoru, evre, beyaz küre ve trombosit sayısı genel sağkalımı anlamlı olarak etkiliyordu (sırasıyla p <0,001, 0,001, 0,044 ve 0,006). Çok değişkenli analizde genel sağkalım oranlarının performans skoru ve trombosit sayısı genel sağkalımı anlamlı olarak etkiliyordu (sırasıyla p <0,001 ve 0,017).

Sonuç: Küçük hücreli dışı akciğer kanseri olan yaşlı hastalarda sağkalım performans durumu, evre, beyaz küre ve trombosit sayıları tarafından anlamlı bir şekilde etkileniyordu. Bu hasta grubunda sadece yaş değil, bu faktörlerde bu hastaların tedavi planında göz önünde bulundurulmalıdır.

Anahtar Sözcükler: Küçük Hücreli Dışı Akciğer Kanseri; Yaşlı; Trombositoz; Lökosit Sayısı; Sağkalım.

İletişim *(Correspondance)*

Dilek ÜNAL
Kayseri Eğitim ve Araştırma Hastanesi, Radyasyon Onkolojisi Kliniği KAYSERİ

Tlf: 0352 437 75 25
e-posta: dilekunaldr@gmail.com

Geliş Tarihi: 04/10/2013
(Received)

Kabul Tarihi: 31/01/2014
(Accepted)

[1] Kayseri Eğitim ve Araştırma Hastanesi, Radyasyon Onkolojisi Kliniği KAYSERİ
[2] Kayseri Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği KAYSERİ
[3] Kayseri Eğitim ve Araştırma Hastanesi, Patoloji Kliniği KAYSERİ
[4] Erciyes Üniversitesi Tıp Fakültesi, Radyasyon Onkolojisi Kliniği KAYSERİ

Introduction

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related mortality in Western societies (1). NSCLC accounts for more than % 85 of all lung cancers (2). Patients often have advanced disease at the time of diagnosis. Incidence of lung cancer in elderly patients is rising due to the increased life expectancy (3). More than half of newly diagnosed patients with NSCLC are older than 65 years (4). Elderly patients are a complex group of patients with a lot of comorbidities and decreased functional capacity. NSCLC is an important public health problem in the elderly population. There is no standard treatment for this group patient with NSCLC. Moreover, limited information is available about survival and the factors associated with survival in this group of patients with NSCLC (5).

In this study, we aimed to investigate effect of various the prognostic factors on survival in NSCLC patients aged more than 65 years.

Materials and Method

Ninety-seven patients, histopathologically proven NSCLC, who are 65 years old or older, were included in this study. Impact of clinical and laboratory features on survival was analyzed retrospectively. The study was approved by the ethics committee of Kayseri Research and Education Hospital. International Union Aganist Cancer (UJCC) and American Joint Comitte on Cancer (AJCC) staging systems were used (6). Staging work-up included physical examination findings, chest plain radiographs, computed tomography (CT) scan of the chest and abdomen (in some cases abdominal ultrasonography), magnetic resonance imaging or CT of the brain, radionuclide bone scan, fiberoptic bronchoscopy, and mediastinoscopy. Data of stage, sites of metastasis, number of metastasis, performance status, routine blood tests (hemoglobin concentration, leucocyte and platelet count) were collected. Demographic data such as age, gender, smoking history, family history of cancer were also recorded.

Performance status was evaluated with the Eastern Cooperative Oncology Group (ECOG) performance status scale. Performance was graded as follows; 0: asymptomatic, 1: symptomatic, but completely ambulatory, 2: symptomatic, in bed for less than 50% of waking hours, 3: symptomatic, confined to bed or chair more than 50% of waking hours, 4: completely disabled, totally confined to bed or chair (7).

Survival was defined as the time between diagnosis and death.

Anemia was defined according to the WHO criteria, hemoglobin level below 13 g/dl in men, and 12 g/dl in women was regarded as anemia (8).

Statistical Analysis

Statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, Illinois, USA). Kolmogorov-Smirnov test was used to determine normality of distributions of variables. Continuous variables with normal distribution are presented as mean ± SD. Median value is used where normal distribution is absent. Qualitative variables are given as percent. Survival rates were estimated using the Kaplan-Meier method and the log-rank test was used for the comparison of outcomes. Mortality risks were analyzed using the multivariate Cox regression model in which we included (in a backward-wald manner) all the significant variables from the univariate analysis. A p value of <0.05 was considered significant.

Results

Table 1 shows characteristics of 97 patients with NSCLC. Mean age was 72.3±5.6 (range, 65-88) years and 81 (83.5%) of 97 patients were male. Most of the patients had a history of smoking. Approximately one-third of the patients had chronic obstructive pulmonary disease (COPD). More than half of the patients had epidermoid carcinoma. Most of the patients were diagnosed with bronchoscopic biopsy and trans-thoracic fine needle aspiration biopsy. Forty-seven (48.5%) of 97 patients had anemia. At the time of analysis just 24 (24.7%) of patients were alive. Only 2 patients could be treated with surgery. Twenty-six of 44 patients with stage III disease were given curative radiotherapy. Doses of radiotherapy were 60-66 Gy. Eighteen patients received the concomitant chemotherapy consisting of docetaxel and cisplatin whereas 5 patients were given the concomitant chemotherapy consisting paclitaxel and carboplatin. The number of concomitant chemotherapy was 2 to 7 cycles. Two of stage III disease patients receiving radiotherapy were given induction chemotherapy whereas 13 patients with stage III disease received maintenance chemotherapy, the number of which was 1 to 4 cycles. Twenty-five of 53 patients with stage IV disease received palliative chemotherapy, the number of which was 1 to 6 cycles, whereas 6 patients was given palliative radiotherapy due to cranial metastases in 3 patients, bone metastasis in 2 patients, and superior vena cava syndrome in 1 patient.

Table 1— Characteristics of the Patients with NSCLC.

Age (year)	72.3±5.6
Female (%)/Male (%)	16 (16.5)/81 (83.5)
Final status	
Living (%)	24 (24.7)
Exitus (%)	73 (75.3)
History of smoking (%)	77 (79.4)
Amount of smoking in patients with positive history (package/year)	48 (10-170)
Presence of chronic obstructive pulmonary disease (%)	34 (35.1)
Family history of cancer (%)	10 (10.3)
Performance status (ECOG)	
0 (%)	14 (14.4)
1 (%)	48 (49.5)
2 (%)	21 (21.6)
3 (%)	14 (14.4)
Histology	
Non-identified NSCLC (%)	16 (16.5)
Adenocarcinoma (%)	27 (27.8)
Epidermoid carcinoma (%)	54 (55.7)
Stage	
III (%)	44 (45.4)
IV (%)	53 (54.6)
Diagnostic procedure	
Bronchoscopic biopsy (%)	59 (60.8)
Trans-thoracic fine needle aspiration biopsy (%)	29 (29.9)
Biopsy of metastasis (%)	7 (7.2)
Mediastinoscopy (%)	2 (2.1)
Hemoglobin e (g/dL)	12.67±1.89
Presence of anemia (%)	47 (48.5)
White blood cell count (x 109/L)	9.8±3.0
Platelet count (x 109/L)	304±109
Treatment	
Surgery (%)	2 (2.1)
Stage III patients	
Curative radiotherapy (%)	26 (26.8)
Concomitant chemotherapy (%)	23 (23.7)
Induction chemotherapy (%)	2 (2.1)
Maintenance chemotherapy (%)	13 (13.4)
Stage IV patients	
Palliative chemotherapy (%)	25 (25.8)
Palliative radiotherapy (%)	6 (6.2)

NSCL: non-small cell lung cancer.

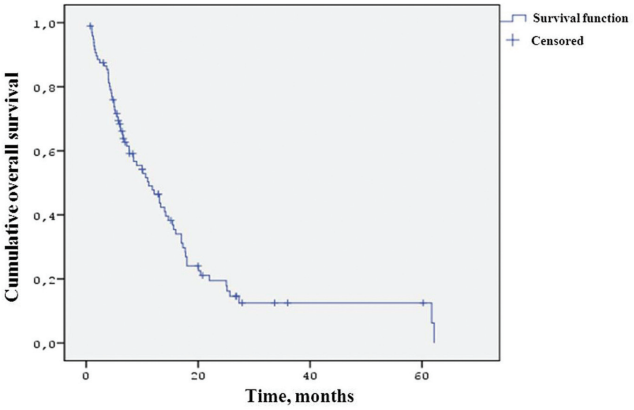


Figure 1— Overall survival by Kaplan-Meier analysis.

Table 2— Overall Survival and p Value According to Characteristics of Patients.

Factor	Overall Survival Months (95% confidence interval)	p
Gender		0.751
Female	8.5 (4.57-12.37)	
Male	11.8 (7.72-15.95)	
Stage		0.010
III	15.6 (12.17-19.03)	
IV	8.5 (4.63-12.31)	
Histology		0.490
Non-identified NSCLC (%)	6.1 (4.82-7.44)	
Adenocarcinoma (%)	12.1 (8.38-15.88)	
Epidermoid carcinoma (%)	11.8 (6.01-17.66)	
ECOG performance status		<0.001
0	17.8 (1.35-34.19)	
1	15.4 (13.04-17.76)	
2	4.6 (3.57-5.57)	
3	5.2 (1.52-8.88)	
Chronic obstructive pulmonary disease		0.735
Yes	10.1 (6.36-13.84)	
No	13.3 (4.14-22.47)	
Presence of anemia		0.276
Yes	11.0 (6.58-15.41)	
No	11.8 (4.55-19.11)	

NSCL: non-small cell lung cancer.

Overall survival was 11.2 months with Kaplan-Meier analysis (95% confidence interval 7.55-14.85) (Figure 1).

The overall survival rates according to characteristics of the patients are shown in Table 2. Stage and ECOG performance status were the characteristics that significantly influenced the overall survival (p=0.010 and p <0.001, respectively). On the other hand, gender, histology, presence of COPD and anemia did not associate with overall survival (p >0.05).

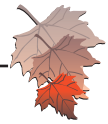


Table 3— Univariate Analysis of Risk Factors for the Overall Survival.

Risk Factor	Odds Ratio (95% confidence interval)	p
Age (year)	1.02 (0.98-1.06)	0.334
Sex (female/male)	1.11 (0.58-2.11)	0.751
Chronic obstructive pulmonary disease (yes/no)	1.09 (0.67-1.78)	0.736
History of smoking (yes/no)	1.12 (0.63-1.98)	0.699
ECOG performance score (0-1/2-3)	3.3 (2.00-5.53)	<0.001
Histology(adenocarcinoma/ epidermoid carcinoma)	1.11 (0.63-1.96)	0.726
Stage (III/IV)	1.85 (1.15-2.98)	0.011
Presence of anemia (yes/no)	1.29 (0.81-2.07)	0.279
White blood cell count (normal/high)	1.72 (1.02-2.94)	0.044
Platelet count (normal/high)	2.22 (1.26-3.91)	0.006

Univariate and multivariate analyses were performed to identify the risk factor(s) related to overall survival. Variables were classified as the most effective forms in the regression model. Patients were classified into two groups according to the performance score; ECOG 0-1 and ECOG 2-3. Histology was grouped as adenocarcinoma or epidermoid carcinoma. White blood cell (WBC) count was regarded as normal if it is lower than 12.0 (x 10^9/L), and as high if it is higher. Platelet count was regarded as normal if it is lower than 400 (x 10^9/L), and as high if it is higher. Table 3 shows the results regarding ten variables examined in univariate analysis as potential risk factors for overall survival. Four of the ten factors (ECOG performance status, stage, WBC and platelet counts) differed significantly between these groups ($p < 0.05$) in univariate analysis. All of these significant variables in the univariate analysis were included in the multivariate Cox regression to analyze mortality risk (Table 4). The multivariate Cox regression analysis identified that the overall survival rates were significantly associated with ECOG performance status (0-1 or 2-3) and platelet count (normal or high). Mortality risk was 3.21 times higher in patients with ECOG 2-3 compared to ECOG 0-1. Patients with high platelet counts had 2.01 folds higher mortality risk from those whose platelet counts were normal. In contrast, the overall survival rates were not significantly associated with stage and WBC count ($p > 0.05$).

Table 4— Multivariate Analysis of Factors Affecting on Overall Survival.

Risk Factor	Odds Ratio (95% confidence interval)	p
ECOG performance score (0-1/2-3)	3.21 (1.92-5.36)	<0.001
Stage (III/IV)	-	-
White blood cell count (normal/high)	-	-
Platelet count (normal/high)	2.01 (1.13-3.56)	0.017

Discussion

Elderly patients are a complex group of patients with a lot of comorbidities and decreased functional capacity. Cancer incidence can be different in elderly people compared with the young population, and prognosis may vary in many tumor types. For example lymphoma, over carcinoma and acute myeloid leukemia are more aggressive in elderly population while breast cancer is more indolent (9).

NSCLC is an important health problem in elder population. In this group of patient, limited information is available about survival and the factors associated with survival. In the present study we demonstrated that ECOG performance status and platelet count was associated with overall survival.

Platelets play an important role in many physiological pathways including hemostasis and inflammation. They are also closely associated with progression and prognosis of malignant tumors (10,11). Although the exact mechanism of the relationship between high platelet count and worse prognosis remains unknown, some possible mechanisms have been suggested. Thrombocytosis can promote tumor cell growth and angiogenesis (10). Thrombocytes secretes a variety of growth factors including transforming growth factor-beta (TGF-ß), vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF). These growth factors can promote tumor cell proliferation and adhesion (12,13). Likewise, it has been shown that platelet-derived soluble mediators can induce invasion in different cell lines. (14). These factors are also important targets of treatment. For example, bevacizumab, an anti-VEGF monoclonal antibody, is effective in the treatment of metastatic colorectal carcinoma (15). Platelets can influence metastasis by protecting the tumor cell from host's immune system (16). Several studies have been demonstrated that pre-treatment platelet count is a novel prognostic factor in patients with NSCLC. In their study with 510 operable NSCLC patients Yu et al. have reported that the 3-year cumulative overall survival probability was 75.3% for patients with normal platelet counts and 59.2% for patients with elevated platelet counts (10). Similarly Maraz et al. have

reported that overall 5 year survival was worse in lung cancer patients with thrombocytosis, and thrombocytosis was directly correlated with the stage of cancer. They observed that the frequency of thrombocytosis was 18.6%, 19.3%, 27.5 and 28.6% in patients with tumor stages I to IV, respectively (17). In our study, thrombocytosis was a negative prognostic factor in both univariate and multivariate analysis. So it seems that a relationship between thrombocytosis and cancer is also available in elderly population.

There is a well-known relationship between cancer and inflammation. Inflammation is an important factor in tumor proliferation and prognosis (18). On the other hand, the exact mechanism(s) mediating this relationship remains unresolved. Understanding of the cause-effect relationship between inflammation and cancer may lead to significant improvements in terms of diagnosis and treatment. Tumor cells produce various cytokines and chemokines, which attract leucocytes. The inflammatory component of a neoplasm may include different types of leucocytes such as neutrophils, dendritic cells, and macrophages. These cells can produce various cytokines, cytotoxic mediators such as reactive oxygen radicals, and mediators such as tumor necrosing factor-alpha (TNF-α) and interleukins. These cells contribute carcinogenesis in the beginning of neoplastic proliferation by creating a favorable environment for tumor growth, by facilitating genomic disorders, and by activating angiogenesis. On the other hand, inflammatory responses may also be anti-tumoral, but these anti-tumoral inflammatory responses are frequently defective in cancer patients (19). In several clinical studies, it has been shown that pre-treatment WBC count and neutrophil/lymphocyte ratio, which are an indicator of systemic inflammation, are associated with poor prognosis in various types of cancer, including NSCLC. Teremuaki et al. have reported that pre-treatment neutrophil count is an independent prognostic factor in patients with advanced NSCLC. They reported an overall survival of 19.3 months for the patients with low neutrophil count, and 10.2 months for the patients with high neutrophils (20). Cedres et al. have shown that high neutrophil/lymphocyte ratio is a predictor of poor prognosis in patients with NSCLC. They reported that patients with high neutrophil/lymphocyte ratio had an overall survival of 5.6 months while patients with low neutrophil/ lymphocyte ratio had an overall survival of 11.1 months (21). In our study high leucocyte count was associated with poor prognosis in univariate analysis. Just as the thrombocytes, the relationship between leucocyte count (i.e. inflammation) and cancer prognosis in elderly population is not different from general population.

Performance status is a measure of functional capacity. A number of methods have been developed to assess the performance state. Karnofsky and ECOG performance scales are the most commonly used methods. Performance status is usually poor in elderly population compared to younger groups (22). Performance status is a predictor of overall survival in cancer patients, and it is generally used to determine cancer treatment decisions (23). Similarly, in our study, ECOG performance status significantly affected overall survival in both univariate and multivariate analysis.

The relationship between cancer stage and survival is a well-known entity. So it is not surprising that stage of cancer was associated with overall survival in univariate analysis in the present study.

Anemia is a negative prognostic factor for many types of cancer in general population. It has been shown that in patients with NSCLC anemia have negative effects on quality of life, increased hospitalization, , as well as survival (24). On the other hand, in our study, anemia was not a prognostic factor associated with survival. We suggest that anemia is not a factor affecting prognosis in elderly population.

In general population, overall survival in advanced NSCLC is 10-23 months for stage 3, and 6-18 months for stage 4 cancer (25). In our study, overall survival was 15.6 months for patients with stage 3, and 8.5 months for patients with stage 4. We suggest that elderly patients with NSCLC have a similar overall survival in general population. Therefore, it should be to consider performance status and other parameters rather than age in the treatment decisions of patients with advanced NSCLC.

In conclusion, overall survival was associated with performance status, stage of cancer, leukocytosis, and thrombocytosis in elderly patients with NSCLC. In this group of NSCLC patients, these factors rather than age should be taken into consideration in treatment planning.

Conflict of Interest

The authors have no financial disclosures to declare and no conflicts of interest to report.

References

1. Parkin DM. Global cancer statistics in the year 2000. Lancet Oncol 2001;2(9):533-43. (PMID:11905707).
2. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: Analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006;24(28):4539-44. (PMID:17008692).

3. Pallis AG, Gridelli C, van Meerbeeck JP, et al. EORTC Elderly Task Force and Lung Cancer Group and International Society for Geriatric Oncology (SIOG) experts' opinion for the treatment of non-small-cell lung cancer in an elderly population. Ann Oncol 2010;21(4):692-706. (PMID:19717538).
4. Gridelli C, Perrone F, Monfardini S. Lung cancer in the elderly. Eur J Cancer 1997;33(14):2313-4. (PMID:9616273).
5. Kefeli U, Kaya S, Ustaalioglu BO, et al. Prognostic factors in elderly patients with non-small cell lung cancer: A two-center experience. Med Oncol 2011;28(3):661-6. (PMID:20354816).
6. Mountain CF. Revisions in the international system for staging lung cancer. Chest 1997;111(6):1710-7. (PMID:9187198).
7. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5(6):649-55. (PMID:7165009).
8. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser 1968;405:5-37. (PMID:4975372).
9. Arslan C, Kilickap S, Dede DS, et al. Frequency of cancer types in patients aged 65 and older: Results from cancer registry database of Hacettepe University Hospitals. Turk J Geriatr 2011;14(3):187-92. (in Turkish).
10. Yu D, Liu B, Zhang L, Du K. Platelet count predicts prognosis in operable non-small cell lung cancer. Exp Ther Med 2013;5(5):1351-4. (PMID:23737877).
11. Sasaki K, Kawai K, Tsuno NH, et al. Impact of preoperative thrombocytosis on the survival of patients with primary colorectal cancer. World J Surg. 2012;36(1):192-200. (PMID:22045447).
12. Stone RL, Nick AM, McNeish IA, et al. Paraneoplastic thrombocytosis in ovarian cancer. N Engl J Med 2012;366(7):610-8. (PMID:22335738).
13. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, et al. Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. J Gynecol Oncol 2012;23(4):265-73. (PMID:23094130).
14. Dineen SP, Roland CL, Toombs JE, et al. The acellular fraction of stored platelets promotes tumor cell invasion. J Surg Res 2009;153(1):132-7. (PMID:18541268).
15. Tol J, Punt CJ. Monoclonal antibodies in the treatment of metastatic colorectal cancer: A review. Clin Ther 2010;32(3):437-53. (PMID:20399983).
16. Placke T, Kopp HG, Salih HR. Modulation of natural killer cell anti-tumor reactivity by platelets. J Innate Immun 2011;3(4):374-82. (PMID:21411974).
17. Maráz A, Furák J, Varga Z, et al. Thrombocytosis has a negative prognostic value in lung cancer. Anticancer Res 2013;33(4):1725-9. (PMID:23564823).
18. Schmidt H, Bastholt L, Geertsen P, et al. Elevated neutrophil and monocyte counts in peripheral blood are associated with poor survival in patients with metastatic melanoma: A prognostic model. Br J Cancer 2005;93(3):273-8. (PMID:16052222).
19. Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420(6917):860-7. (PMID:12490959).
20. Teramukai S, Kitano T, Kishida Y, et al. Pretreatment neutrophil count as an independent prognostic factor in advanced non-small-cell lung cancer: an analysis of Japan Multinational Trial Organisation LC00-03. Eur J Cancer 2009;45(11):1950-8. (PMID:19231158).
21. Cedrés S, Torrejon D, Martínez A, et al. Neutrophil to lymphocyte ratio (NLR) as an indicator of poor prognosis in stage IV non-small cell lung cancer. Clin Transl Oncol 2012;14(11):864-9. (PMID:22855161).
22. Souhami RL, Bradbury I, Geddes DM, Spiro SG, Harper PG, Tobias JS. Prognostic significance of laboratory parameters measured at diagnosis in small cell carcinoma of the lung. Cancer Res 1985;45(6):2878-82. (PMID:2985256).
23. Inal A, Kaplan MA, Kucukoner M, et al. Prognostic factors in elderly patients with advanced non-small cell lung cancer treated with first-line cisplatin-based chemotherapy: A retrospective analysis of single institution. J BUON 2012;17(3):533-6. (PMID:23033295).
24. Gauthier I, Ding K, Winton T, Shepherd FA, Livingston R, Johnson DH, Rigas JR, Whitehead M, Graham B, Seymour L. Impact of hemoglobin levels on outcomes of adjuvant chemotherapy in resected non-small cell lung cancer: the JBR.10 trial experience. Lung Cancer 2007;55(3):357-63. (PMID:17141357).
25. Jabbari S, Hansen EK, Haas-Kogan DA. Non-small cell lung cancer. In: Eric K. Hansen, Mark Roqch (Eds). Handbook of Evidence Based Radiation Oncology. 2nd edition, Springer, New York, USA 2010, pp 221-47.

Turkish Journal of Geriatrics
2014; 17 (2) 119-124

Düriye Deniz DEMİRSEREN
Fadime KILINÇ
Selma EMRE
Ahmet METİN

RESEARCH

NAIL CHANGES AND DISEASES IN GERIATRIC AGE GROUP: ASSESSMENT OF 249 PATIENTS ADMITTED TO DERMATOLOGY OUTPATIENT CLINIC

ABSTRACT

Introduction: The increase in the geriatric population requires the maintenance of quality of life at an older age. Although nail diseasesdo not usually affect life expectancy, they are important in terms of quality of life and the morbidity that they may cause.

Materials and Method: For this study, we recruited a total of 249 patients aged 65 years and older who had presented to the dermatology outpatient clinic. The incidence of nail diseases, the age groups for these diseases, education levels, BMIs and the relationship with additional diseases were investigated.

Results: The most frequent nail color change was lunula loss, in 77.9% of participants, and the most frequent surface change was brittle nails, in 42.1%.The most common nail finding due to repetitive trauma was splinter hemorrhages, in 16.9%, followed by onychauxis in 8.4% and onychocryptosis in 7.6%. The most common contour change was pincer nail,in 5.6%, and the most common infection was onychomycosis,in 33.3%. Lunula loss and onychauxis were significantly more common in patients aged 75 or older, compared to younger patients (p=0.002, p=0.01, respectively). BMI was significantly higher in patients diagnosed with an ingrowing nail (p <0.001).

Conclusion: The most frequently observed color change in the geriatric age group is lunula loss; the most common surface change is brittle nail, and the most common nail infection is onychomycosis. Lunula loss and onychauxis development increase with age. It is quite important to know the common nail diseases in order to be able to detect age-specific nail changes and the clues they provide in the geriatric age group.

Key Words: Aged; Patient; Nail.

ARAŞTIRMA

GERİATRİ YAŞ GRUBUNDA TIRNAK DEĞİŞİKLİKLERİ VE HASTALIKLARI: DERMATOLOJİ POLİKLİNİĞİNE BAŞVURAN 249 HASTANIN DEĞERLENDİRİLMESİ

ÖZ

Giriş: Geriatik nüfusun artması, ileri yaşta nitelikli yaşam sürme gereksinimi beraberinde getirmektedir. Tırnak hastalıkları yaşam süresini etkilemiyor gibi görünse de, yaşam kalitesi açısından ve yol açabileceği morbiditeler açısından önemli yer tutmaktadır.

Gereç ve Yöntem: Araştırmaya dermatoloji polikliniğine başvuran 65 yaş ve üzeri 249 hasta dahil edildi. Hastalarda saptanan tırnak değişiklikleri ve lezyonlarının görülme sıklığı ile birlikte yaş grupları, öğrenim durumu, Beden kitle indeksi ve ek hastalıklar ile ilişkisi araştırıldı.

Bulgular: Hastalarda saptanan en sık renk değişikliği %77,9 ile lunula kaybı ve en sık yüzey (surface) değişikliği %42,1 ile kırılgan tırnak olarak tespit edildi. Tekrarlayan travmalara bağlı tırnak değişikliklerinde en sık rastlanan bulgular sırasıyla %16,9 ile splinter hemoraji, %8,4 ile onychauxis ve %7,6 ile onychocryptosis olarak gözlendi. En sık rastlanan kontur değişikliği %5,6 ile pincer nail iken en sık rastalanan enfeksiyon hastalığı da %33,3 ile onikomikoz idi. Yaş grupları ile korelasyona bakıldığında, 75 yaş ve üzeri hastalarda lunula kaybı ve onychauxis, 75 yaş altı hastalara göre anlamlı olarak yüksek saptandı (sırası ile p=0,002, p=0,01). Hastalıkların BMİ ile korelasyonu değerlendirildiğinde, tırnak batması saptanan hastalarda BMİ'in anlamlı olarak yüksek olduğu tespit edildi (p <0,001).

Sonuç: Geriatrik yaş grubunda en sık gözlenen renk değişkliği lunula kaybı, en sık rastlanan yüzey değişikliği kırılgan tırnak, en sık rastlanan enfeksiyon hastalığı onikomikozdur. Lunula kaybı ve onychauxis gelişimi yaş ile korele olarak artar. Tırnak hastalıklarının geriatrik yaş grubu hastalarındaki yaşa özel değişkiliklerini ve bize gösterdiği ipuçlarını görebilmek açısından sık gözlenen tırnak hastalıklarını bilmek oldukça önemlidir.

Anahtar Sözcükler: Yaşlı; Hasta; Tırnak.

İletişim *(Correspondance)*

Duriye Deniz DEMİRSEREN
Ankara Atatürk Eğitim ve Araştırma Hastanesi,
Dermatoloji Kliniği ANKARA

Tlf: 0312 2912525
e-posta: ddemirseren@yahoo.com

Geliş Tarihi: 20/01/2014
(Received)

Kabul Tarihi: 19/02/2014
(Accepted)

Ankara Atatürk Eğitim ve Araştırma Hastanesi, Dermatoloji Kliniği ANKARA

Introduction

The increase in the elderly population throughoutthe world and in our country requires the maintenance of quality of life at an advanced age. Although nail diseases do not usually affect life expectancy, they are important in terms of quality of life and the morbidity that they may cause. There are changes in nail color, thickness, shape, structure and surface with the degradation of nutrition in the nail bed and germinative matrix, as a natural result of aging. Factors such as joint restriction, visual problems, increased trauma and low motivation for personal care with advancing age may also contribute to the progression of problems by creating nail care difficulties (1-3).

A dermatology examination is not complete without a thorough nail examination. The changes in an elderly patient may be a natural process of aging, or may be modified by age although present for a long time. Some nail appearances may be a clue to systemic diseases or may lead to susceptibility to some conditions that may lead to much more serious problems in the future. Protection from nail diseases requires periodic nail care and an appropriate medical approach (1,4). It is therefore important to know the natural process and common diseases and approaches in geriatric patients.

In this study, we aimed to determine the prevalence of nail changes and diseases in patients aged 65 years or more, the distribution of these diseases by age group, and their correlation with additional diseases, body mass index and educational levels.

Materials and Method

For this study, we recruited a total of 249 patients aged 65 years or older who presented to the Ankara Ataturk Training and Researh Hospital dermatology outpatient clinic. The approval of the local ethics committee of our hospital was obtained before starting the study, and the study was conducted in accordance with the Helsinki Declaration. All patients participating in the study were informed about the study and signed an informed consent form. Demographic information and body mass index (BMI) of the patients were recorded. A dermatological examination including a detailed nail evaluation was performed by dermatologists. A native preparation was prepared for microscopy in patients who were suspected of suffering from onychomycosis. A biopsy was taken and a histopathological examination performed when necessary. The patients were divided into 2 age groups as 65-74, 75 years and over. The incidence of nail diseases, the age groups of these diseases, BMI and their relationship were investigated.

Table 1— Demographic and Clinical Characteristics of Patients.

Sex, n (%)	
Male	118 (47.4)
Female	131 (52.6)
Age.	
Min-max. (mean±sd)	65-97 (70.19±6.56)
65-75	206 (82.7)
75-85	33 (13.3)
>85	10 (4.0)
BMI	
≤30	147 (63.6)
>30	84 (36.4)
Nail disease duration (mean±sd)	1-560 (62.5±22.1)

Statistical analyses were performed using SPSS 16.0 (Chicago, IL, USA). Of the continuous variables, those with normal distributions were describedwith mean ± sd, while those that were not consistent with a normal distribution were described with medians, and categorical variables were described as numbers and percentages. Comparisons were made using Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables. A p value <0.05 was accepted as significant.

Results

A total of 131 (52.6%) females and 118 (47.4%) males participated in the study. The age range was 65 to 97 years and the mean age was 70.19±6.56 years. Patients'clinical and demographic data are summarized in Table 1. The most frequent nail color changes were lunula loss at 77.9% and dull nail at 41.7%. The most frequent surface change was brittle nails at 42.1%. The most frequent brittle nails group included onychorrhexis (38.6%) (Figure 1) and onychoschizia



Figure 1— Onychorrhexis on the toenail and superficial white onychomycosis on the second nail of 67-year-old male patient.



Figure 2— Onychoschizia and subungual hematoma on the big toenail of a 71-year-old male patient.



Figure 3— Onychogryphosis on the 1st, 2nd and 3rd toenails of a 75-year-old female patient.

Table 2— Skin Findings in the Geriatric Age Group and the Distribution of Disorders by Age Group.

	Total n=249	**65-74 n=206**	**≥75 n=43**
	n (%)	n (%)	n (%)
Alteration in nail color			
Lunula loss	194 (77.9)	163 (79.1)	31 (72.0)
Dull, pale discoloration	104 (41.7)	78 (37.8)	26 (60.5)
Leukonychia	12 (4.8)	11 (5.2)	1 (3.0)
Melanonychia	2 (0.8)	1 (0.5)	1 (3.0)
Alteration in nail surface texture			
Brittle nails	105 (42.1)	72 (34.95)	33 (76.7)
Onychorrhexis	96 (38.6)	75 (36.4)	21 (48.8)
Onychoschizia	60 (24.1)	50 (24.3)	10 (2.3)
Transverse splitting	23 (9.2)	21 (10.2)	2(4.6)
Triangular fragments at the free edge	20 (8.0)	17 (8.3)	2 (4.6)
Lamellar splitting	16 (6.4)	15 (7.3)	1 (2.3)
Pitting	7 (2.8)	5 (2.4)	2 (4.6)
Linked to repeated trauma			
Splinter hemorrhages	42 (16.9)	34 (16.5)	8 (18.6)
Onychauxis	21 (8.4)	15 (6.6)	6(13.9)
Onychocryptosis	19 (7.6)	19 (9.2)	- (-)
Pachyonychia	18 (7.2)	11 (5.3)	7 (16.2)
Subungual hematomas	11 (4.4)	9 (4.3)	2 (4.6)
Median nail dystrophy	8 (3.2)	7 (3.4)	1 (2.3)
Onycholysis	6 (2.4)	5 (2.4)	1(2.3)
Onychogryphosis	5 (2.0)	4 (1.9)	1 (2.3)
Onychoclavus	2 (0.8)	1 (0.5)	1 (2.3)
Nail biting	1 (0.4)	1 (0.5)	- (-)
Alteration in contour			
Pincer nail	14 (5.6)	13 (6.3)	1 (2.3)
Koilonychia	3 (1.2)	2 (0.9)	1(2.3)
Infections			
Onychomycosis	83 (33.3)	57 (27.66)	23 (53.5)
Paronychia	2 (0.8)	2 (0.9)	- (-)
Tumors			
Amelanotic malignant melanoma	1 (0.4)	- (-)	1 (2.3)
Myxoidpseudocyst	1 (0.4)	1 (0.5)	- (-)
Subungual exocytosis	1 (0.4)	1 (0.5)	- (-)

(24.1%) (Figure 2). Onychogryphosis was present in 2% of our patients (Figure 3). Skin findings and the distribution of the disorders by age group are summarized in Table 2. Among our patients with onychomycosis, 63.4% had distal lateral subungual onychomycosis (DLSO) , 12.9% had total dystrophic onychomycosis (TDO), and 7.5% had superficial white onychomycosis (SWO) (Figure 1). We did not find any patients with proximal subungual onychomycosis in our study. A myxoid pseudocyst was present in one patient. Regarding age groups, lunula loss and onychauxis weresignificantly more common in patients aged 75 years or over compared to younger patients (p=0.002, p=0.01, respectively). BMI was significantly higher in patients with an ingrowing toenail (p <0.001).

Discussion

Nail region problems in the elderly, who are gradually constituting a larger part of society, make up 10% of all dermatological disorders (2). Some nail changes are due to the natural aging process. Nail water and calcium concentrations decrease with aging, while magnesium increases and iron decreases. The size of the nail plate keratinocytes increases. The elastic tissue and blood vessels thicken with aging, causing the nail bed dermis and especially the section under the pink portion of the nail to thicken. Atherosclerosis also causes changes in the nails (1,5).

The nail plate color may show various changes with advancing age. Normally, the lunula area is white and the nail bed is pink. Lunula loss, in 77.9% of our patients, was the most frequent nail color change. The decrease in lunula visibility is considered a natural age-related change when detected at advanced ages (6). The significantly higher lunula loss rate in patients aged 75 and over in our study supports the correlation with age.The second most frequent color change in our patients was a pale and dull nail appearance. Rao et al. reported this finding at a rate of 69%, lower than in our patients, in astudy they conducted with 100 patients over the age of 60. The rate of leukonychia was 4.7% in our study. It can be in the form of real leukonychia, where the matrix is also included, or as total, subtotal, transverse, punctate or longitudinal leukonychia. Leukonychia is thought to be due to repetitive microtrauma and may also be due to cirrhosis, azotemia and hypoalbuminemia, oroccur without other disorders. Pseudoleuconychia can be present in onychomycosis and after enamel procedures, along with keratin granulation (2). The change is called ''Neapolitan nail" as it resembles Neapolitan ice cream and is characterized by the lack of the lunula and a color change that is white in the proximal nail plate, pink in the middle part and opaque in the distal section to make up 3 horizontal bands. Although a study has reportedthat a special color change is present in about 20% of people older than 70, we did not detect this in our study (7). Terry nail, another disorder considered to be the natural result of aging, is characterized by a white band at the proximal nail and a pink band at the distal section and was not found among our patients (8,9). Longitudinal melanonychia was present in 0.8% of our patients. It has been described as "frictional longitudinal melanonychia" due to repetitive trauma (1,10). The main disorders in the differential diagnosis of longitudinal melanonychia are nevi and fungal infections and distinguishing itfrommalignant melanoma is very important. Hutchinson's finding is pigmentation of the nail bed and around the matrix and indicates melanoma. When melanonychia is found in older patients, a careful history should be taken, samples for fungal infection should be taken, dermatoscopical examination should be performed and a biopsy should be obtained if necessary (11,12).

The normal nail surface is smooth and various irregularities can develop in the nail surface with advancing age. The fingernails are normally soft and fragile and are prone to longitudinal fissuring and splitting. Contrary to popular belief, the calcium content in the nail bed is as low as about 0.2%, and does not contribute to the hardness of the nail. (3,13-15). An age-dependent decrease in cholesterol sulphate levels is thought to contribute to these brittle nails (1). The most common surface change in our patients was brittle nails, at a rate of 42.1%. This ratio is higher than the ratio of 34% reported by Rao et al. (5). Brittle nails can appear as onychorrhexis, onychoschizia, lamellar and transverse splitting, and triangular fragments at the free edge. Onychorrhexis is longitudinal ridging in the nail surface. Aging is the most important reason for onychorrhexis (16). The onychorrhexis rate was 24.1% in our study and was reported as 85% by Rao et al. Onychorrhexis can be defined as transverse and lamellar splitting of the distal nail plate and free edge. Avoiding repeated wetting and drying, hydration of the nail with phospholipid-rich emollients, and the use of nail hardeners containing formaldehyde and biotin at 2.5 mg/day for 1.5-15 months are recommended for brittle nail treatment (2,3). The nail surface disorder of pitting was present in 2.8% of our patients. The most common reason is psoriasis, but it can also be found in alopecia areata and finger eczema (1,4).

In our study, the most common disorder due to repetitive trauma was splinter hemorrhage. Nail bed capillaries in people over the age of 70 often show distortion. These capillary distortions are thought to be responsible for the splinter he-

morrhages seen in the elderly (1). The most common cause in elderly patients is trauma (2).

Onychauxis was significantly more common in patients over the age of 75 in our study. Pachyonychia is hypertrophy of the whole nail plate, while onychauxis is local hypertrophy of the nail plate (17). Loss of transparency of the nail plate is characterized by color change and subungual hyperkeratosis. It may be idiopathic or age-related and is more commonly observed in the toes. The risk of onychomycosis is increased in these nails (1). The increased rate in our patients over the age of 75 supports the effect of advanced age and increasing trauma.

Onychocryptosis is an ingrowing or embedded toenail. Ingrowing toenails were found in 7.6% of our patients and were significantly more common in obese patients. Obesity is considered to contribute to a predisposition for onychocryptosis (18). Cutting the nails incorrectly due to limitation of movement and visual problems in the elderly contributes to this susceptibility Granulation tissue formation or secondary infection may be seen. Conservative treatment, regular nail care, proper footwear, and fighting infection in the elderly are important in prevention and treatment (1,2,18).

The rate of subungual hematoma in the elderly was 4% in our study. Rao et al. found subungual hematoma in three patients (5). The cause can be trauma, improper footwear, or walking long distances. Anticoagulant use also increases the likelihood of developing a hematoma. A color change progressing to the distal section and a gradually lighter color are important clues in distinguishing hematomas from nevi and melanomas. Evacuating the hematoma when it is first formed decreases the pain (1,2,4).

Onychogryphosis is also called oyster shell or ram's horn deformity. It was found in 5% of our patients and it develops as a result of hyperkeratotic tissue formation in the lateral nail folds or periungual folds due to onycholysis or the repeated minor trauma of improper footwear. Cutting the nail is very difficult because it is thickened. Periodic debridement of the thickened nail plate is therefore required. Electrical files and creams containing 40% or more urea can be useful. Chemical or surgical matricectomy should be used in recurrent and complicated cases (2).

Pincer nail was the most common contour change in our study and can affect only the big toenail or all toe nails. If mild, the inward turning of the nail can be prevented and nail plate pressure decreased by fixing the nail from the top with stainless steel wire and plastic supports for 6 months. The removal of the lateral matrix with phenol is the simplest, least painful and most effective treatment (1,19).

Other nail contour changes we observed were clubbing and spoon nail (koilonychia).Clubbing is a hyponychial angle (the angle between the skin and nail) over 180 degrees with softening in the nail bed and increased nail curvature. It may be observed together with lung neoplasms and infections, subacute bacterial endocarditis and cyanotic congenital heart diseases and hepatocarcinoma. Spoon nail may be associated with iron deficiency anemia, polycythemia, coronary diseases, and endocrine disorders such as diabetes and acromegaly (1).

The most common nail infection was onychomycosis, at 33.3% in our study. This rate was consistent with the 31.5% reported by Yalcin et al., who investigated skin diseases in 4099 geriatric patients, and lower than the 41.5% reported in a prospective analysis of skin diseases in 200 geriatric patients conducted in 2010 (20,21). Incidence of the subtypes of onychomycosis we found in our study is consistent with astudy of 108 patientsby Dias et al., where foot onychomycosis was investigated in the geriatric population. The DLSO, TDO and SWO rates were 63.4%, 12.9% and 7.5%, respectively, in our study and 59.3%, 24.1% and 4.6% in the Dias et al. study. Aging increases susceptibility to onychomycosis (22). The nails become discolored, brittle and thickened. (1,22). Exposure of the nails to microtrauma, improper shoes, and the spread of dermal fungal infection to the nails responsible in the etiology (23). The basic complaint is usually aesthetic, but tenderness can also be present and the thickened nails can lead to onychomycosis. Treatments used in young patients can also be provided to healthy elderly subjects. If systemic treatment is needed, other medications taken by the patient should be queried for drug interactions. 250 mg/day terbinafine or 100 mg/day itraconazole can be used for 6 weeks for fingernails and 12 weeks for toenails. Mechanical interventions, local treatments such asantifungal nail polishes, and chemical nail thinning using preparations with urea when there is no risk of ischemia are more suitable when oral treatment cannot be administered (1).

Paronychia is characterized by inflammation of the softnail tissue at the proximal part and lateral edge. We found this disorder at a rate 0.8% in our study. Acute paronychia is common in the elderly and causes secondary changes in the nail plate The disorder can be treated with abscess drainage, topical or systemic antibiotics. Chronic paronychia is characterized by nail plate changes in the form of erythematous and swollen nail folds, cuticle loss, and a large number of transverse ridges. Keeping the nail folds dry, and topical antifungal or antiseptic agents, are used in the treatment (2).

Mucous cyst, also known as myxoid pseudocyst, is the most common benign nail tumor. Mucous cysts are more

common in women and are most commonly found at the proximal nail fold of the fingers. (4).

The nail cancer incidence peaks in the 7th decade (2). Amelanotic malignant melanoma wast he only malignant tumor we found in our study. Amelanotic malignant melanoma is most commonly confused with pyogenic granuloma. Pyogenic granuloma and amelanotic malignant melanoma should be considered in hemorrhagic tumors that grow rapidly in geriatric patients and a biopsy should be obtained before starting treatment (24).

In conclusion, the most frequently observed color change was lunula loss, the most commonly found surface change was brittle nails, and the most commonly found infectious disease was onychomycosis in the geriatric age group. Knowing the common nail changes and diseases, the changes that should be considered normal, and the clues that can indicate dangerous disorders in the geriatric age group is very important in taking preventive measures and planning treatment.

References

1. Baran R. The nail in the elderly. Clin Dermatol 2011;29(1):54-60. (PMID:21146733).
2. Singh G, Haneef NS, Uday A. Nail changes and disorders among the elderly. Indian J Dermatol Venereol Leprol 2005;71(6):386-92. (PMID:16394478).
3. Abdullah L, Abbas O. Common nail changes and disorders in older people: diagnosis and management. Can Fam Physician 2011;57(2):173-81. (PMID:21321168).
4. Yazıcı A. The nail and hair changes in older people. Turkiye Klinikleri J Cosm Dermatol-Special Topics 2012;5(2):57-63.
5. Rao S, Banerjee S, Ghosh SK, Gangopadhyay DN, Jana S, Mridha K. Study of nail changes and nail disorders in the elderly. Indian J Dermatol 2011;56(5):603-6. (PMID:22121296).
6. Cohen PR. The lunula. J Am Acad Dermatol 1996;34(6):943-53. (PMID:8647987).
7. Horan MA, Puxty JA, Fox RA. The white nails of old age (Neapolitan nails). J Am Geriatr Soc 1982;30(12):734-7. (PMID:7142618).
8. Saraya T, Ariga M, Kurai D, Takeshita N, Honda K, Goto H. Terry's nails as apart of aging. Intern Med 2008;47(6):567-8. (PMID:18344651).
9. Aktaş A, Geçer E. Nail changes in elderly. Turkiye Klinikleri J Dermatol-Special Topics 2009;2(2):69-71.
10. Baran R. Frictional longitudinal melanonychia: a new entity. Dermatologica 1987;174(6):280-4. (PMID:3622879).
11. Di Chiacchio N, Ruben BS, Loureiro WR. Longitudinal melanonychias. Clin Dermatol 2013;31(5):594-601. (PMID:24079589).
12. Braun RP, Baran R, Le Gal FA, et al. Diagnosis and management of nail pigmentations. J Am Acad Dermatol 2007;56(5):835-47. (PMID:17320240).
13. Cohen PR, Scher RK. Geriatric nail disorders: Diagnosis and treatment. J Am Acad Dermatol 1992;26(4):521-3. (PMID:1597537).
14. van de Kerkhof PC, Pasch MC, Scher RK, et al. Brittle nail syndrome: a pathogenesis-based approach with a proposed grading system. J Am Acad Dermatol 2005;53(4):644-51. (PMID:16198786).
15. Scher RK, Fleckman P, Tulumbas B, McCollam L, Enfanto P. Brittle nail syndrome: Treatment options and the role of the nurse. Dermatol Nurs 2003;15(1):15-23. (PMID:12656000).
16. Holzberg M. Nail signs of systemic disease. In: Maria K. Hordinsky, Marty E. Sawaya, Richard K. Scher (Eds.). Atlas of hair and nails. Philadelphia, Churchill Livingstone, USA 2000, pp 59-70.
17. Cohen PR, Scher RK. The nails in older individuals. In: Richard K. Scher, C. Ralph Daniel (Eds). Nails: therapy, diagnosis, surgery, 3nd edition, Elsevier Saunders, Philadelphia, USA 2005, pp 245-64.
18. Ikard RW. Onychocryptosis. J Am Coll Surg 1998;187(1):96-102. (PMID:9660032).
19. Koçyiğit P. Treatment options for ingrowing nail. Turkiye Klinikleri J Cosm Dermatol-Special Topics 2013;6(3):18-23.
20. Yalçın B, Tamer E, Toy GG, Oztaş P, Hayran M, Alli N. The prevalence of skin diseases in the elderly: Analysis of 4099 geriatric patients. Int J Dermatol 2006;45(6):672-6. (PMID:1676625).
21. Demirseren DD, Emre S, Ateşkan Ü, Metin A. Prospective analysis of skin findings of patients admitted to a geriatric outpatient clinic. Turk J Geriatrics 2010;13(1):87-91 (in Turkish).
22. Dias N, Santos C, Portela M, Lima N. Toenail onychomycosis in a Portuguese geriatric population. Mycopathologia 2011;172(1):55-61. (PMID:21365319).
23. Scher RK, Rich P, Pariser D, L Elewski B. B. The epidemiology, etiology, and pathophysiology of onychomycosis. Semin Cutan Med Surg 2013 Jun; (2 Suppl 1):S2-4 Review. (PMID:24156160).
24. Tosti A, Piraccini BM. Nail disorders. In: Jean Bolognia, Joseph Jorizzo, Julie Schaffer (Eds). Dermatology. 2nd edition, China, Elsevier Saunders 2008, pp 1019-38.

Turkish Journal of Geriatrics
2014; 17 (2) 125-133

Yonca SÖNMEZ[1]
Halil AŞCI[2]
Gülşen OLGUN İZMİRLİ[3]
Duru GÜNDOĞAR[4]
Fatma Nihan CANKARA[2]
Şükriye YEŞİLOT[2]

RESEARCH

EVALUATION OF POTENTIALLY INAPPROPRIATE DRUG USE AND MEDICAL NON-ADHERENCE IN A COMMUNITY-DWELLING ELDERLY POPULATION: A CROSS-SECTIONAL STUDY

ABSTRACT

Introduction: The objectives of the study were to evaluate potentially inappropriate drug use and medical non-adherence and to determine the risk factors for potentially inappropriate drug use and medical non-adherence in the elderly dwelling in a community health center service area.

Materials and Method: The cross-sectional study included all individuals aged 65 years and older (n=687) dwelling in the area of a community health center in Isparta, Turkey. The dependent variables of the study were potentially inappropriate drug use and medical non-adherence. The structured questionnaire, comprising both dependent and independent variables, was administered to elderly people by conducting face-to-face interviews at home. Chi-square, independent samples t-test, and logistic regression were used for data analysis.

Results: Among the elderly using at least one drug per day, 17.6% were using at least one potentially inappropriate medication. Non-steroidal anti-inflammatory drugs and digoxin (in doses >0.125 mg/day) were the most common drugs that were used inappropriately. Medical non-adherence was determined in 40.6% of the elderly. The most common non-adherent behavior was "forgetting to take the medication." In the multivariate analysis, polymorbidity (p=0.001) and polypharmacy (p=0.016) were risk factors for potentially inappropriate drug use. The only risk factor for medical non-adherence was "not knowing most of the side effects of the drug" (p=0.018).

Conclusion: In this study, lower prevalence rates than those for most previous studies were found for both potentially inappropriate drug use and medical non-adherence. Since polymorbidity and polypharmacy were risk factors for potentially inappropriate drug use, physicians should be cautious in the selection of drugs for elderly patients with polymorbidity.

Key Words: Aged, Inappropriate Prescribing; Medication Adherence.

ARAŞTIRMA

TOPLUMDA YAŞLILARDA UYGUNSUZ İLAÇ KULLANMA OLASILIĞI VE İLAÇ UYUMSUZLUĞUNUN DEĞERLENDİRİLMESİ, KESİTSEL BİR ÇALIŞMA

ÖZ

Giriş: Bu çalışmada bir toplum sağlığı hizmet bölgesinde yaşayan yaşlıların uygunsuz ilaç kullanma olasılığının ve ilaç uyumsuzluğunun değerlendirilmesi ile potansiyel uygunsuz ilaç kullanımı ve ilaç uyumsuzluğu için risk faktörlerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Kesitsel tipteki çalışma Türkiye'nin İsparta ilindeki bir Toplum Sağlığı Bölgesinde yaşayan 65 yaş üzeri 687 yaşlı bireyi kapsamaktadır. Araştırmanın bağımlı değişkenleri uygunsuz ilaç kullanma olasılığı ve ilaç uyumsuzluğudur. Araştırmanın bağımlı ve bağımsız değişkenlerini içeren yapılandırılmış anket, yaşlılara evlerinde yüz-yüze görüşme yöntemiyle uygulanmıştır. Veri analizinde ki-kare, bağımsız gruplarda t-testi ve lojistik regresyon kullanılmıştır.

Bulgular: Her gün en az bir ilaç kullanan yaşlıların %17,6'sı en az bir adet uygunsuz ilaç kullanım olasılığını tanımlamışlardır. Non-steroid anti-inflamatuar ilaçlar ve digoxin (>0,125 mg/gün) en sık uygunsuz kullanılan ilaçlardı. Yaşlıların %40,6'sında ilaç uyumsuzluğu saptandı. İlaç uyumsuzluğunu belirleyen davranışlar içinde "ilaç içmeyi unutma" en sık görüldü. Çok değişkenli analizlerde polimorbidite (p=0,001) ve polifarmasi (p=0,016) uygunsuz ilaç kullanma olasılığı için risk faktörleriydi. İlaç uyumsuzluğu için tek risk faktörü "kullanılan ilaçların çoğu yan etkisini bilmemek"ti (p=0,018).

Sonuç: Bu çalışmada uygunsuz ilaç kullanma olasılığı ve ilaç uyumsuzluğu sıklığı diğer çalışmaların çoğundan daha düşüktü. Polifarmasi ve polimorbiditenin uygunsuz ilaç kullanma olasılığı için risk faktörleri olması nedeniyle hekimler polimorbiditesi olan yaşlı hastalarda ilaç seçiminde dikkatli olmalıdır.

Anahtar Sözcükler: Yaşlı; Uygunsuz İlaç Kullanımı; İlaç Uyumu.

İletişim *(Correspondance)*

Yonca SÖNMEZ
Süleyman Demirel Üniversitesi Tıp Fakültesi, Halk Sağlığı Anabilim Dalı ISPARTA

Tlf: 0246 211 36 53
e-posta: yoncasonmez@yahoo.com

Geliş Tarihi: 13/01/2014
(Received)

Kabul Tarihi: 15/02/2014
(Accepted)

[1] Süleyman Demirel Üniversitesi Tıp Fakültesi, Halk Sağlığı Anabilim Dalı ISPARTA
[2] Süleyman Demirel Üniversitesi Tıp Fakültesi, Farmakoloji Anabilim Dalı ISPARTA
[3] Gönen Toplum Sağlığı Merkezi ISPARTA
[4] Süleyman Demirel Üniversitesi Tıp Fakültesi, Psikiyatri Anabilim Dalı ISPARTA

Introduction

With increasing age, physiological variations occur in the absorption, distribution, metabolism and excretion of drugs from the body, and the sensitivity of receptors. Moreover, multiple chronic diseases and related polypharmacy are frequently present in the elderly. Therefore, elderly people are more liable to medication-related problems including adverse drug reactions, and drug-drug and drug-disease interactions (1,2). Many medications involve special risks when used by the elderly and are considered potentially inappropriate for this population. Potentially inappropriate drug use (PIDU) in older adults is a major health concern. Previous studies have demonstrated that PIDU is related to increased number of hospitalizations and mortality (3) and causes a poorer health status (4). Leading authorities have proposed different screening tools for determining the potentially inappropriate drugs that should be avoided in the elderly. Among these tools, the Beers criteria are the most frequently used ones. The Beers Criteria were developed in 1991 and revised and modified three times in 1997, 2003 and 2012 (5,6). According to Gallagher et al.'s review based on the Beers criteria, PIDU prevalence in the elderly varies from 12% in the community-dwelling elderly to 40% in nursing home residents (7).

The frequency of chronic diseases, cognitive and physical deficiencies and the number of drugs utilized increase with older age and this causes medical non-adherence (MN) as well as PIDU to become a major health issue. Medication adherence is defined as the degree to which a patient's or caregiver's behavior regarding medication administration coincides with medical advice (8). Adherence to treatments is essential to the well-being of elderly patients, and is thus a critically important component of care. In the elderly, failure to adhere to medical recommendations and treatment has been found to increase the likelihood of therapeutic failure (9,10). Non-compliance or non-adherence with drug therapy in older patient populations ranges from 21 to 55 percent (11).

In this study we aimed to evaluate potentially inappropriate drug use and medication non-adherence and to determine the risk factors for PIDU and MN in the elderly dwelling in a community health center service area.

Materials and Method

Study Design and Study Population

This cross-sectional survey was conducted in October 2013. The study population consisted of 687 individuals aged 65 years and older dwelling in the catchment area of the Community Health Center of the Gonen District of Isparta, Turkey. Gonen is a rural district comprising a center, a town, and six villages with a population of 7800 people. Since we aimed to reach the whole population, we did not select a sample. By the end of the study 563 elder individuals had been reached (response rate 82.0%). People who could not be found at home (85 subjects, *12.4%)* and who rejected participation (39 subjects, 5.6%) were not included.

Dependent and Independent Variables

The dependent variables of the study were PIDU and **MN.** PIDU was determined by the Beers criteria, which were updated in 2012 (6). The Beers criteria comprise three categories. The first category consists of drugs that should be avoided independent of the disease; the second category consists of drugs that should be avoided in the presence of certain diseases or syndromes; and the third category consists of drugs that should be used with caution (6). In this study PIDU was evaluated concerning the first two categories. Accordingly, PIDU was accepted to be present if there was at least one inappropriate drug use by the elderly. The presence of MN was evaluated using the scale developed by Morisky and colleagues, consisting of four closed-ended yes/no questions (12): 1) Do you ever forget to take your medicine? 2) Are you careless at times about taking your medicine? 3) When you feel better do you sometimes stop taking your medicine? and 4) Sometimes if you feel worse when you take the medicine, do you stop taking it? MN was evaluated to be present with a "yes" answer to at least one of these questions (13,14).

Age, sex, marital status, presence of health insurance, regular income, living alone/with others, area of residence, receiving health care in the last six months, health perception, polymorbidity, polypharmacy, knowing the aim of the use of the drugs, knowing most of the adverse effects of the drugs, presence of depressive symptoms, dependence during basic daily living activities, and problems of vision and hearing were investigated as independent variables. Utilization of five or more drugs was accepted as polypharmacy, while the presence of three or more chronic diseases was accepted as polymorbidity. In order to evaluate the presence of depressive symptoms the Geriatric Depression Scale (GDS) was used. This scale was developed by Yesavage and colleagues. It comprises 30 items and the validity and reliability of the Turkish version has been established by Ertan and Eker (15). The scale was scored between 0 and 30, and higher scores indicate the presence of more depressive symptoms. Dependence in basic

daily living activities was evaluated using the Barthel Index. The maximum score obtained from the scale is 100 and it indicates complete independence. People scoring 90 points or less were accepted as being dependent (16).

Data Collection

The structured questionnaire comprising the dependent and independent variables was administered to the elderly people in the study by conducting face-to-face interviews at home. Subjects who could not be found at home in the first trial were re-visited twice. In the case of a communication problem (hearing, speech and/or mental problem) the questionnaire was administered to the primary caregiver. Drug utilization data consisted of the names and durations of the drugs used daily. To minimize underreporting, boxes and/or the prescriptions for the drugs were asked for, and the brand names of the drugs were recorded. During data analysis drugs were categorized according to the Anatomical Therapeutic Chemical (ATC) Classification (17). Data on doses and duration of drugs were also collected. Chronic diseases and syndromes were investigated in detail.

Ethical Issues

The study was approved by the Ethical Committee for Clinical Studies of Siileyman Demirel University School of Medicine (Registration Number: 187). Verbal informed consents were obtained from participants following a brief explanation of the aim of the study.

Data Analysis

The data were analyzed using the SPSS 18.0 for Windows program. Variables were presented as frequencies, percentages, or mean±±standard deviations. The groups were compared by using chi-square and independent samples t-test for univariate analyses and logistic regression for multivariate analyses. Two logistic regression models were built in order to determine the risk factors affecting PIDU and MN. The factors that were determined to be significant in the univariate analyses were included in the models. One-tailed p-values were used and $p<0.05$ was set as the value for significance.

RESULTS

Descriptive Characteristics of the Study Population

The mean age of the study group was 74.9±±7.0 years (range 65-100), of which 29.1% were 80 years old and above (Table 1). Other descriptive data are shown in Table 1. Most participants (87.4%) had been admitted to a health institution in the last six months (Table 1). The mean admission frequency in the last six months was 2.8±±2.4 (range 0-13), and the most frequently admitted institutions were family health centers (n=355, 72.2%), state hospitals (n=225, 45.7%), and university hospitals (n=42, 8.6%).

Of the elderly, 53.6% (n=302) reported problems with their vision, while 41.9% (n=236) reported problems with hearing. The mean basic daily living activity score was 95.7±±12.0 (range 5-100), and 16.5 % (n=93) were evaluated as "being dependent". The mean GDS score was 8.5±±7.4 (range 0-30).

Table 1— Characteristics of the Study Population (N=563).

Characteristic	Value
Age, year, mean±sd (range)	74.9±7.0 (65-100)
Age groups, n (%)	
65-69	141 (25.0)
70-74	137 (24.3)
75-79	121 (21.5)
>80	164 (29.1)
Sex, n (%)	
Female	340 (60.4)
Male	223 (39.6)
Education level, n (%)	
Illiterate	164 (29.1)
Just literate	114 (20.2)
Primary school	265 (47.1)
Secondary school or above	20 (3.6)
Marital status, n (%)	
Married	345 (61.3)
Widowed/Divorced/Single	218 (38.7)
Area of residence, n (%)	
District center	214 (38.0)
Town	124 (22.0)
Village	225 (40.0)
Living alone, n (%)	157 (27.9)
Regular income, n(%)	490 (87.0)
Health coverage, n (%)	508 (90.2)
Health perception, n (%)*	
Very good	12 (2.2)
Good	273 (50.2)
Fair	201 (36.9)
Poor	54 (9.9)
Very poor	4 (0.7)
Use of health service in the last six months, n (%)	492 (87.4)

*Health perception was evaluated using data involving 544 subjects since data concerning 19 older adults were.

Table 2— Characteristics of the Study Group Concerning Chronic Diseases and Drug Use (N= 563).

Characteristic	Value
Presence of chronic disease(s), n (%)	429 (76.2)
The number of chronic disease(s), mean±SD (range)*	1.9±.1.1 (1-8)
Presence of polymorbidity, n (%)	106(18.8)
Chronic disease(s), n (%)*	
Hypertension	254 (45.1)
Heart failure	107(19.0)
Diabetes mellitus	83 (14.7)
Joint diseases	48 (8,5)
Chronic obstructive pulmonary disease/asthma	45 (8.0)
Osteoporosis	38 (6.7)
Depression	21 (3.7)
Use of at least one drug per day, n (%)	409 (72.6)
Total number of drugs used per day, mean±SD (range)*	3.1±1.9 (1-11)
Presence of polypharmacy, n (%)	80(14.2)
Drugs used per day (According to ATC), n (%)§	
Cardiovascular system	487 (38.5)
Alimentary tract and metabolism	255 (20.2)
Nervous system	208 (16.4)
Respiratory system	73 (5.8)
Musculoskeletal system	72 (5.7)
Blood and blood forming organs	39 (3.1)
Other systems	131 (10.4)
Presence of medical non-adherence*	166 (40.6)
Components of medical non-adherence[1]	
Forgetting to take the drug	114(27.9)
Carelessness in taking the drug on time	87 (21.2)
Stopping the drug when feeling better	66 (16.1)
Stopping the drug when feeling worse	59 (14.4)

*429 subjects with at least one disease were evaluated.
*The most frequent seven diseases were listed.
*409 subjects who used at least one drug per day were evaluated. §A total of 1265 drugs used by 409 subjects were evaluated.
[1]The same subject may have more than one non-adherence components simultaneously.

Of the participants, 76.2% had at least one chronic disease. The prevalence of polymorbidity was 18.8%). Hypertension was the most common chronic disease (45.1%). Approximately three-quarters of the group (72.6%) was using at least one drug daily. The mean number of drugs used was 3.1±±1.9 (range 1-11), cardiovascular system drugs being the most frequent (38.5%). Polypharmacy prevalence was 14.2% (Table 2). All the participants reported drug use on the advice of a physician. Of our group, 81.4% (n=333) reported that they knew the aim of the drug use, while only 19.3% (n=79) reported they knew most of the side effects of the drugs.

Medical Non-adherence and Potentially Inappropriate Drug Usage

Medical non-adherence was present in 40.6% (n=166) of the elderly. When the components of MN were evaluated, the most important problem was determined to be forgetting to take the drug (27.9%) (Table 2).

Of the elderly, 17.6% (n=72) had at least one PIDU (Table 3). Of the elderly with PIDU, 90.3% (n=65) had one drug utilization, 8.3% (n=6) had two, and 1.4% (n=l) had three inappropriate drug utilizations.

The most frequently used inappropriate drugs were non-steroidal anti-inflammatory drugs (NSAIDs) (n=30, 7.3%) and digoxin >0.125 mg/day (n=12, 2.9%) independent of the disease. Related to the disease or syndrome, the most frequently used inappropriate drugs were NSAIDs (n=10, 2.4%>) and non-dihydropyridine group calcium-channel blockers (n=9, 2.2%) in patients with heart failure (Table 3). When the drugs that are not accepted as inappropriate but recommended to be used with caution in the elderly were investigated, it was determined that the study group most frequently used aspirin (5.6%) and selective serotonin re-uptake inhibitors (SSRIs) (5.6%) (Table 3).

Factors Associated With Potentially Inappropriate Drug Use and Medical Non-adherence

We found that sociodemographic factors such as age, sex, education level, marital status and living alone were not significantly related to PIDU and MN (for all factors p>0.05) (Table 4). There were no significant relationships between PIDU and MN and regular income, presence of health coverage, area of residence, and admission to a health institute in the last six months (for all of the factors p>0.05). Hearing and vision problems, dependence in daily living activities and health perception did not affect PIDU and MN significantly (for all factors p>0.05) (Table 4).

There were no significant differences between the subjects with PIDU (9.1±±7.4) and without PIDU (9.2±±7.8) in terms of GDS score (p=0.873). Similarly, the GDS scores of the subjects with MN (9.1±±7.9) and without MN (9.3±±7.6) were not significantly different (p=0.795). According to the univariate analysis results, PIDU was significantly higher in subjects with polymorbidity (34.9% vs

Table 3— Potentially Inappropriate Drug Use and Drugs Recommended to Be Used With Caution in Community-dwelling Elderly (N=409)*.

Characteristic	Value
At least one inappropriate drug use	72(17.6)*
Inappropriately used drugs independent from disease	
First generation antihistamines	
Hydroxyzine	2 (0.5)
Clemastine	1 (0.2)
Antithrombotics	
Dipyridamole	4(1,0)
Alphai blockers	
Doxazosin	5(1.2)
Anti-arrhythmic drugs	
Amiodarone	1 (0.2)
Digoxin (>0.125 mg/d)	12 (2.9)
Nifedipine	1 (0.2)
Benzodiazepines	
Alprazolam	1 (0.2)
Non-steroidal anti-inflammatory drugs*	
Diclofenac	14 (3.4)
Ibuprofen	1 (0.2)
Ketoprofen	3 (0.7)
Meloxicam	4(1,0)
Naproxen	3 (0.7)
Indomethacin	5(1.2)
Inappropriately used drugs related to disease or syndrome	
Heart failure	
Non-steroidal anti-inflammatory drugs	10 (2.4)
Diltiazem	8 (2.0)
Verapamil	1 (0.2)
Dementia	
Antipsychotics	2 (0.5)
Chronic constipation	
Solifenacin	1 (0.2)
Trospium	1 (0.2)
History of gastric or duodenal ulcers	
Non-Cox-2 selective non-steroidal anti-inflammatory drugs	3 (0.7)
Drugs recommended to be used with caution in elderly	
Aspirin for primary prevention of cardiac events§	23 (5.6)
Antipsychotics	1 (0.2)
Carbamazepine	2 (0.5)
Mirtazapine	3 (0.7)
Selective serotonin re-uptake inhibitors	23 (5.6)
Vasodilators	3 (0.7)

*409 subjects who used at least one drug per day were evaluated.
*Some of the older subjects may use more than one inappropriate drug independent from disease and a drug may be inappropriately used both independent from the disease and with respect to disease/syndrome
*Subjects using Non-steroidal anti-inflammatory drugs without a proton pump inhibitor or misoprostol for more than 3 months.
§Subjects aged 80 or older using aspirin independent from dose.

11.6%), polypharmacy (36.3% vs 13.1%), and in subjects who did not know the aim of the drug use (26.3% vs 15.6%) (for all factors $p<0.05$) (Table 4). These three variables were included in the logistic regression model that revealed only polymorbidity and polypharmacy to be significant risk factors. PIDU was associated with an odds ratio of 2.84 (95% CI=1.55-5.20) for polymorbidity and 2.21 (95% CI=1.16-4.19) for polypharmacy (Table 5). Univariate analyses revealed that MN was more frequent in the subjects who knew neither the aim of their drug usage nor most of the side effects of the drugs ($p<0.05$) (Table 4). In the logistic regression model that included these two variables, "not knowing most of the side effects of the drug" was a significant risk factor for MN (OR=1.96, 95% CI =1.12-3.41) (Table 5).

Discussion

In this study PIDU and MN, which are two important problems related to drug utilization, were evaluated in elderly people with a relatively lower education level living in the rural area of Isparta city.

Potentially Inappropriate Drug Usage

According to the results of our study, PIDU prevalence was estimated as 17.6% in community-dwelling older adults. The most frequent inappropriately used drugs were NSAIDs and digoxin. According to the Beers criteria, NSAIDs increase the risk of peptic ulcer disease and gastrointestinal system bleeding in high-risk groups aged >75 years and taking oral/parenteral corticosteroids, anticoagulants or antiplatelet agents. Upper gastrointestinal system ulcers, gross bleeding and perforation risk are present in 1% of subjects who have been using NSAIDs for 3-6 months, and in 2% of subjects who have been using NSAIDs for 1 year (6). In our study 18 subjects had been using NSAIDs for more than 6 months, and 12 subjects had been using NSAIDs for 3-6 months. Three subjects were using two different NSAIDs concomitantly. Using >0.125 mg/day digoxin, which has a narrow therapeutic index, does not confer an additional benefit in patients with heart failure and increases the risk of serious side effects and toxicity signs related to decreased renal clearance (6).

It was supposed that in patients with heart failure, drugs such as NSAIDs, diltiazem and verapamil might increase fluid retention and exacerbate heart failure symptoms (6). In our study among the heart failure patients, 10 were using NSAIDs, 8 were using diltiazem and 1 was using verapamil. Therefore, the physicians' knowledge, particularly about the

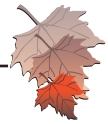


Table 4— Distribution of Potentially inappropriate Drug Use and Medical Non-adherence Concerning Some Variables (n=409)*.

Variable	Potentially Inappropriate Drug Use		Medical Non-adherence	
	n (%)f	P*	n (%)f	P*
Age groups				
65-74 (n=206)				
>75(n=203)	32(15.5) 40 (19.7)	0.268	88 (42.7) 78 (38.4)	0.377
Sex				
Female (n=258)	45 (17.4)	0.910	100 (38.8)	0.325
Male (n=151)	27(17.9)		66 (43.7)	
Education level				
Illiterate (n=127)	23 (18.1)	0.792	56 (44.1)	0.431
Just literate (n=80)	12(15.0)		28 (35.0)	
Primary school or above (n=202)	37(18.3)		82 (40.6)	
Marital status				
Married (n=241)	41 (17.0)	0.707	99 (41.1)	0.808
Other (n= 168)	31 (18.5)		67 (39.9)	
People lived with				
Living alone (n=125)	20(16.0)	0.572	57 (45.6)	0.171
Living with family (n=284)	52(18.3)		109 (38.4)	
Vision problems				
Present (n=227)	34(15.0)	0.119	95 (41.9)	0.561
Absent (n= 182)	38 (20.9)		71 (39.0)	
Hearing problems				
Present (n=176)	30(17.0)	0.797	80 (45.5)	0.081
Absent (n=233)	42(18.0)		86 (36.9)	
Dependence in basic daily living activities				
Dependent (n=69)	13 (18.8)	0.767	34 (49.3)	0.107
Independent (n=340)	59 (17.4)		132 (38.8)	
Health perception				
Very good/good (n=199)	40 (20.1)	0.197	83 (41.7)	0.653
Fair/poor/very poor (n=210)	32(15.2)		210 (39.5)	
Polymorbidity				
No (n=303)	35 (11.6)	**<0.001**	129 (42.6)	0.166
Yes (n=106)	37 (34.9)		37 (34.9)	
Polypharmacy				
No (n=329)	43 (13.1)	**<0.001**	131 (39.8)	0.521
Yes (n=80)	29 (36.3)		35 (43.8)	
Know aim of drug use				
Yes (n=333)	52(15.6)	**0.027**	126 (37.8)	**0.018**
No (n=76)	20 (26.3)		40 (52.6)	
Know most of the side effects				
Yes (n=79)	13 (16.5)	0.765	21 (26.6)	**0.005**
No (n=330)	59(17.9)		145 (43.9)	

409 subjects who used at least one drug per day were evaluated, f Row percentage, Chi-square test

Table 5— Factors Affecting Potentially Inappropriate Drug Use and Medical Non-adherence Concerning Logistic Regression Analysis.

Variables	Potentially Inappropriate Drug Use			Medical Non-adherence	
	OR*	95% CI	p	OR*	95% CI p
Polymorbidity					
No	**1**				
Yes	**2.84**	**1.55-5.20**	**0.001**		
Polypharmacy					
No	**1**				
Yes	**2.21**	**1.16-4.19**	**0.016**		
Know aim of drug usage					
Yes	1			1	
No	1.72	0.92-3.20	0.089	1.59	0.95-2.67 0.076
Know most of the side effects					
Yes				**1**	
No				**1.96**	**1.12-3.41 0.018**

*Odds Ratio, the groups indicated as 1 signify the reference groups, CI indicates confidence interval.

usage of NSAIDs, digoxin and non-dihydropyridine group calcium-channel blockers in older adults seems deficient. It has been reported that there is a lack of evidence showing benefit versus risk for using aspirin in adults >80 years of age and that SSRIs should be used with caution since they can cause hyponatremia (6). In our study, these two drugs were the most frequently used ones within the group of drugs that should be used with caution.

In a study in which the drug usage tendencies of a group of elderly people dwelling in a district in Izmir were investigated, PIDU prevalence was found to be 21.3%, with the most frequent inappropriately used drugs reported as digoxin and doxazosin (18). In a large scale study conducted by using electronic records in England and Wales, PIDU was 21.4% in the community subjects and 33.0% in the care home subjects (19). In the same study (19), the most frequent inappropriately used drugs were diazepam (4.2%), anticholinergic antihistamines (3.6%), and fluoxetine (3.4%). In the Three-City study conducted in France in which a modified form of the Beers criteria were used, 38.7% of the elderly had at least one potentially inappropriate drug usage and the most frequently (23.4%) used drug was cerebral vasodilators (20). Benzodiazepines (9.4%) were the second most frequent, and drugs with anticholinergic properties like tricyclic antidepressants (6.4%) were the third most frequently used drugs (20). In a study conducted in Poland, PIDU prevalence was 28.2% and the most frequently used drugs were chlordiazepoxide and diazepam (10.0%), long-acting benzodiazepines (7.7%) and indomethacin *(2.5%)* (21). According to a study by Roth and Ivey in 2002 involving older adults registered in the North Carolina Eldercare program, the prevalence of PIDU was 34% (13). Blalock and colleagues conducted another study in the rural part of the same area between 2002 and 2004, and found that 26.6% of older adults had at least one inappropriately used drug (22). The most frequently inappropriately used drugs were propoxyphene, NSAIDs, muscle relaxants and antispasmodics, anticholinergics, and antihistamines (22).

The PIDU prevalence in our study was lower than those found in the other studies. However it should be kept in mind that some of the studies used data from electronic health records (19). In our study we used information obtained from the older adults themselves, and the data was limited by underreporting by the subjects and recall and information bias. The differences in the results may also be related to the differences in the criteria used to determine inappropriate drug use. For example, in some studies the researchers added some items to the criteria (20) or inquired about certain drugs that were omitted from the updated version of the Beers criteria that we used (i.e. ferrous sulfate in dosages >325 mg/d, propoxyphene, fluoxetine) (18-20,22). Nevertheless, when our study is compared with the other studies, it is clear that the utilization of psychotropic drugs and anticholinergic drugs is much less frequent.

We determined that polypharmacy and polymorbidity were risk factors for PIDU. In parallel with our study, sever-



al other studies in the literature revealed that as the number of drugs used increases, the number of inappropriately used drugs also increases (19,20,22). Shah et al. (19) found that the number of comorbid conditions did not affect PIDU. On the other hand, Blalock et al. (22) found that a history of major depression, hypertension, osteoarthritis, and back problems were found to be risk factors for PIDU. Lechevallier-Michel and colleagues (20) determined that older age, being female, lower socioeconomic level, lower household income and poor health perception were risk factors for PIDU; however, we did not find any relationships with these variables. In the same study, the authors detected a significant relationship between the presence of depressive symptoms and PIDU, and explained this relationship by the fact that psychotropic drugs occupy an important portion of inappropriately used drugs (20). In our study the inappropriate use of psychotropic drugs was less than that reported in the literature. This may explain the absence of a relationship between PIDU and depressive symptoms in our group.

Medical Non-adherence

In our study the prevalence of MN was 40.6%. We determined that the most common nonadherent behavior components were "forgetting to take the medication" and carelessness in taking the drug on time. In two different studies conducted in USA in which the same scale was used, MN prevalence was found to be 53% by Roth and Ivey and 41% by Sirey et al. (13,14). Consistent with our study, in Sirey et al.'s study (14) the most common non-adherent behavior was also "forgetting to take medication" (33%).

Solmaz and Akin (23) investigated adherence to medication dosage in addition to the MN criteria. They determined MN in the elderly living at home as 77% (23). In the same study, the most common components of non-adherence were "stopping to take the medication when feeling better" (72.0%) and "forgetting to take medication" (70.7%) (23).

In our study the only risk factor for MN was determined to be "not knowing most of the side effects of the drug". Similarly, "not knowing the side effects of the drug" was also determined as a risk factor in Solmaz and Akin's study (23). In that study the other risk factors were "being 75 years of age and above", not having a caregiver to help with taking the medication, having moderate-severe cognitive deficits, and "not finding the information given about the drug adequate" (23). Consistent with our study, Sirey et al. (14) found that sociodemographic factors such as age, sex, education level, number of chronic diseases, presence of depression and disability, and problems with vision did not affect MN. However, difficulty in opening the medication bottle was reported as a tangible barrier (14).

In conclusion, lower prevalence rates than in most of the previous studies were detected for both PIDU and MN. Nonetheless, about one-fifth of the elderly comprising the study sample were using drugs inappropriately and about half of the sample had medication non-adherence. Older adults received health care mostly from family health centers. Therefore, physicians practicing in primary health care institutions have a particularly important responsibility for rational medication utilization in the elderly. All physicians, especially primary care physicians, should be informed about rational drug utilization during undergraduate education and post-graduate in-service training. During this training, it should be emphasized that polypharmacy should be avoided in older adults with polymorbidity; additional drugs should not be given for non-specific symptoms like drug side-effects. The drugs that are accepted as inappropriate should also be underlined. Moreover, physicians should be warned about inappropriately used drugs through electronic prescription systems. The national health care database of primary, secondary, and tertiary healthcare institutions should be integrated, so that coordinated dataflow within the health system can be achieved. By this means, all healthcare providers can reach all the information concerning the diagnosis and treatment process of the patient. Additionally, in order to decrease MN, patient-doctor communication should be enhanced and the purposes of drug utilization and particularly the possible side effects of the prescribed drugs should be explained to the patient and/or the caregiver. Elderly patients should be evaluated in regular follow-up visits to investigate the effectiveness and side effects of the drugs.

References

1. Cornelius C. Drug use in the elderly: Risk or protection? Curr Opin Psychiatry 2004;17(6):443-7.
2. The Merck Manual for Health Care Professionals. Drug-Related Problems in the Elderly. [Internet] Available from: http://www.merckmanuals.com/professional/geriatrics/drug_therapy_in_the_elderly/drug-related_problems_in_the_elderly.html#vl 133525. Accessed: 9.9.2013.
3. Lau DT, Kasper JD, Potter DE, Lyles A, Bennett RG. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Arch Intern Med 2005;165(l):68-74. (PMID:15642877).

4. Fu AZ, Liu GG, Christensen DB. Inappropriate medication use and health outcomes in the elderly. J Am Geriatr Soc 2004;52(11):1934-9. (PMID:15507075).
5. Resnick B, Pacala JT. 2012 Beers Criteria. J Am Geriatr Soc 2012;60(4):612-3. (PMID:22375952).
6. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. AGS updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60(4):616-31. (PMID:22376048).
7. Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. J Clin Pharm Ther 2007;32(2):113-21. (PMID:17381661).
8. MacLaughlin EJ, Raehl CL, Treadway AK, Sterling TL, Zoller DP, Bond CA. Assessing medication adherence in the elderly: which tools to use in clinical practice? Drugs Aging 2005;22(3):231-55. (PMID:15813656).
9. World Health Organization. Adherence to long-term therapies-Evidence for action, 2003. [Internet] Available from: http://whqlibdoc.who.int/publications/2003/9241545992.pdf. Accessed: 5.9.2013.
10. Hughes CM. Medication non-adherence in the elderly. How Big is the problem? Drugs Aging 2004;21(12):793-811. (PMID:15382959).
11. Williams CM. Using medications appropriately in older adults. Am Fam Physician 2002;66(10):1917-25. (PMID:12469968).
12. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24(l):67-74. (PMID:3945130).
13. Roth MT, Ivey JL. Self-reported medication use in community-residing older adults: A pilot study. Am J Geriatr Pharmacother 2005;3(3):196-204. (PMID:16257822).
14. Sirey JA, Greenfield A, Weinberger MI, Bruce ML. Medication beliefs and self-reported adherence among community-dwelling older adults. Clin Ther 2013;35(2):153-60. (PMID:23357585).
15. Ertan T, Eker E. Reliability, validity, and factor structure of the geriatric depression scale in Turkish elderly: Are there different factor structures for different cultures? Int Psychogeriatr 2000;12(2):163-72. (PMID:10937537).
16. Gama EV, Damian JE, Perez de Molino J, Lopez MR, Lopez Perez M, Gavira Iglesias FJ. Association of individual activities of daily living with self-rated health in older people. Age Ageing 2000;29(3):267-70. (PMID:10855912).
17. The Anatomical Therapeutic Chemical Classification System with Defined Daily doses (ATC/DDD) Index 2013. [Internet] Available from: http://www.whocc.no/atc_ddd_index/. Accessed: 4.11.2013.
18. Sonmez Y, Konakci SK, Duksal T, Ucku R. The characteristics of drug use in the elderly in the community STED 2008;17(11):149-54. (in Turkish).
19. Shah SM, Carey IM, Harris T, DeWilde S, Cook DG. Quality of prescribing in care homes and the community in England and Wales. Br J Gen Pract 2012:62(598):e329-36. (PMID:22546592).
20. Lechevallier-Michel N, Gautier-Bertrand M, Alperovitch A, et al. Frequency and risk factors of potentially inappropriate medication use in a community-dwelling elderly population: results from the 3C Study. Eur J Clin Pharmacol 2005;60(11):813-9. (PMID:15599504).
21. Rajska-Neumann A, Wieczorowska-Tobis K. Polypharmacy and potential inappropriateness of pharmaco-logical treatment among community-dwelling elderly patients. Arch Gerontol Geriatr 2007;44(1):303-9. (PMID:17317466).
22. Blalock SJ, Byrd JE, Hansen RA, et al. Factors associated with potentially inappropriate drug utilization in a sample of rural community-dwelling older adults. Am J Geriatr Pharmacother 2005;3(3):168-79. (PMID:16257819).
23. Solmaz T, Akin B. Medication use and ability of self-medication use in elderly living at home. Turkish Journal of Geriatrics 2009;12(2):72-81. (in Turkish).

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2014; 17 (2) 134-137

Pervin HÜRMÜZ[1]
Gökhan ÖZYİĞİT[1]
Mustafa CENGİZ[1]
Deniz YÜCE[2]
Melis GÜLTEKİN[1]
Gözde YAZICI[1]
Gülnihan EREN[1]
Murat GÜRKAYNAK[1]
Faruk ZORLU[1]

RESEARCH

RADIOTHERAPY IN THE TREATMENT OF ELDERLY GLIOBLASTOMA PATIENTS

ABSTRACT

Introduction: The incidence of glioblastoma increases with advancing age. In this study we evaluated our therapeutic results in elderly patients with glioblastoma.

Materials and Method: The charts of 65 patients age ≥65 and treated between January 2002 and December 2011 in our department were assessed. Forty-five patients were male and the median age was 70 years (range, 65-84 years). Karnofsky performance status was ≥70 in 82% of the patients. Gross tumor resection was performed in 32 patients. The radiotherapy field was localized to the tumor (or tumor bed) in 59 patients and to the whole brain±localized field in the rest. The median treatment dose was 60 Gy(range, 20-60 Gy). Thirty-one patients received concomitant and 17 patients received adjuvant temozolomide.

Results: The median follow-up time was 5 months (range, 1-44 months). One and two-year survival rates for the whole group were 38.9% and 11.7%, respectively. Median survival times according to treatment fields were: 9 months in the localized group, 3 months in the whole brain group and 18 months in the whole brain+localized field group (p=0.04). Gender, performance status, radiotherapy dose, and the type of surgery did not significantly affect survival rates. Patients with midline tumors had poorer outcomes compared to other locations (p=0.01). Patients receiving adjuvant temozolomide had better overall survival (p=0.02).

Conclusion: Radiotherapy seems to be a feasible treatment strategy in elderly patients with glioblastoma. Although the patient number is small, the patients who received whole brain+localized field radiotherapy or adjuvant temozolomide had better survival in the current study.

Key Words: Glioblastoma; Radiotherapy; Temozolomide; Aged.

ARAŞTIRMA

YAŞLI GLİOBLASTOM HASTALARININ TEDAVİSİNDE RADYOTERAPİ

ÖZ

Giriş: Glioblastom insidansı yaşla artmaktadır. Bu çalışmada yaşlı glioblastom tanılı olguların radyoterapi sonuçları değerlendirilmiştir.

Gereç ve Yöntem: Haziran 2002 ve Aralık 2011 tarihleri arasında tedavi uygulanan 65 yaş ve üzeri 65 olgunun verileri değerlendirildi. Hastaların ortanca yaşı 70 olup (65-84 yaş) 45'i erkektir. Karnofsky performans durumu hastaların %82'sinde ≥70'tir. Otuz iki hastada gros tümör rezeksiyonu yapılmıştır. Radyoterapi 59 hastada lokalize alana (tümör/ tümör yatağı), 6 hastada tüm beyin ve lokalize alana yönelik uygulanmıştır. Tedavi dozu medyan 60 Gy'dir (20-60 Gy). Otuz bir hasta eşzamanlı, 17 hasta adjuvan temozolomide almıştır.

Bulgular: Ortanca izlem süresi 5 aydır (1-44 ay). Bir ve iki yıllık genel sağkalım oranları sırasıyla %38,9 ve %11,7'dir. Tedavi alanlarına göre bakıldığında ortanca sağkalım lokalize radyoterapi alan grupta 9 ay (7-11 ay), tüm beyin radyoterapisi alanlarda 3 ay (1-6 ay) ve tüm beyin ve lokalize alana yönelik radyoterapi alanlarda 18 aydır (3-18 ay) (p=0,04). Cinsiyet, performans durumu, radyoterapi dozu ve cerrahi tipi sağkalım oranlarını anlamlı olarak etkilememiştir. Orta hat yerleşimli tümörlerde diğer yerleşimli tümörlere göre hastalık daha kötü seyretmektedir (p=0,01). Adjuvan temozolamide alanlarda sağkalım daha iyi bulunmuştur (p=0,02).

Sonuç: Glioblastom tanılı yaşlı hastalarda radyoterapi uygun bir tedavi yaklaşımıdır. Bu çalışmada gruplarda hasta sayısı az olmakla birlikte tüm beyin ve lokalize radyoterapi alanlarda ve adjuvan temozolamide alan hastalarda sağkalım daha iyi bulunmuştur.

Anahtar Sözcükler: Glioblastom; Radyoterapi; Temozolomid; Yaşlı.

İletişim *(Correspondance)*

Pervin HÜRMÜZ
Hacettepe Üniversitesi Tıp Fakültesi, Radyasyon Onkolojisi Anabilim Dalı ANKARA

Tlf: 0312 305 29 00
e-posta: phurmuz@yahoo.com

Geliş Tarihi: 03/02/2014
(Received)

Kabul Tarihi: 26/02/2014
(Accepted)

[1] Hacettepe Üniversitesi Tıp Fakültesi, Radyasyon Onkolojisi Anabilim Dalı ANKARA
[2] Hacettepe Üniversitesi Tıp Fakültesi, Prevantif Onkoloji ANKARA

Introduction

Glioblastomas (GB) account for 16% of all primary brain tumors. The incidence increases with advancing age, with the highest rates in those 75 to 84 years old. It is expected that in a few years, more than half of patients with GB will be over 65 years old (1). The current standard of care is surgery plus adjuvant concomitant temozolomide (TMZ) and radiotherapy (RT) followed by 6 cycles of adjuvant TMZ (2). It is known that age and performance status are the most important prognostic factors for GB (3-5). Furthermore, elderly patients generally have poor performance status and co-morbidities that interfere with their continuation with standard treatment. However, data related to the optimal management of elderly GB patients are still lacking. It has also been suggested that age alone should not disqualify patients from aggressive therapy with surgical resection, RT, and chemotherapy (6). To address the rarity of available data on elderly GB patients, we evaluated our therapeutic results in patients with GB older than 65 years, and assessed potential prognostic factors that impact on survival.

Materials and Method

The patient charts of all GB patients treated between January 2002 and December 2011 were assessed. Eligibility criteria were age older than or equal to 65 years, and confirmed histopathological or radiological diagnosis of GB. Patients who did not receive planned concurrent or adjuvant TMZ were included in the study. However, the patients who did not complete their planned RT sessions were excluded from the current study.

RT treatment field was localized to the tumor (or tumor bed) in 59 patients and to the whole brain (WB) ± localized field in the rest. The localized field involves the gross tumor volume (GTV) plus a margin for clinical target volume (CTV). For patients receiving 60 Gy localized RT, GTV was delineated using T1 contrast enhanced image sequences and CTV_{46Gy} was delineated using T2 or FLAIR sequences plus 2 cm on MRI. Subsequently, a 14 Gy additional dose was prescribed to GTV plus 1 cm (CTV_{60Gy}). The median treatment dose was 60 Gy (range, 20-60 Gy). In 6 patients, RT to the WB was delivered in 10 fractions to a total dose of 30 Gy. Three of these patients received an additional 15 Gy in 5 fractions as a booster dose to the tumor plus 1 cm. Thirty-one patients (31%) received concomitant TMZ and 6 patients received adjuvant TMZ. The concomitant TMZ dose was 75mg/m^2/day starting with the first day of RT. Adjuvant TMZ was delivered at 150 mg/m^2/day for 5 days in every 28-day period. Treatment characteristics are shown in Table 1.

Table 1— Treatment Characteristics of the Patients.

Characteristics	Patient Number = 65
Median (range) RT dose (Gy)	60 (20-60)
Treatment field	
Localized	59 (90.8%)
WB	3 (4.6%)
WB+ boost dose to tumor	3 (4.6%)
Concomitant TMZ	
Yes	31 (52%)
No	33 (48%)

Abbreviations: WB= Whole brain, TMZ= Temozolomide.

Overall survival was computed using the Kaplan-Meier method and compared using the log-rank test. All statistical analyses were performed using SPSS 15.0 software (SPSS Inc., Chicago, IL).

Results

The data of 65 eligible GB patients formed the body of current analysis. The median age of the patients was 70 (range, 65-84 years). Forty-five (69%) of the patients were male and the Karnofsky performance status (KPS) was ≥70 in 82% of the cases. Gross tumor resection (GTR) was performed in 32 patients. Patients' characteristics are shown in Table 2.

Table 2— Characteristics of the Patients.

Characteristics	Patient Number= 65
Mean (range) age (years)	70 (65-84)
Median (range) tumor size (cm)	5 (3-8)
Gender	
Female	20 (31%)
Male	45 (69%)
KPS	
≥70	58 (90%)
<70	7 (10%)
Number of lesions	
Single	60 (92%)
Multiple	5 (8%)
Resection	
Complete	32 (49%)
Partial	19 (29%)
Biopsy	2 (3.0%)
No	12 (18%)

Abbreviations: KPS= Karnofsky performance status.

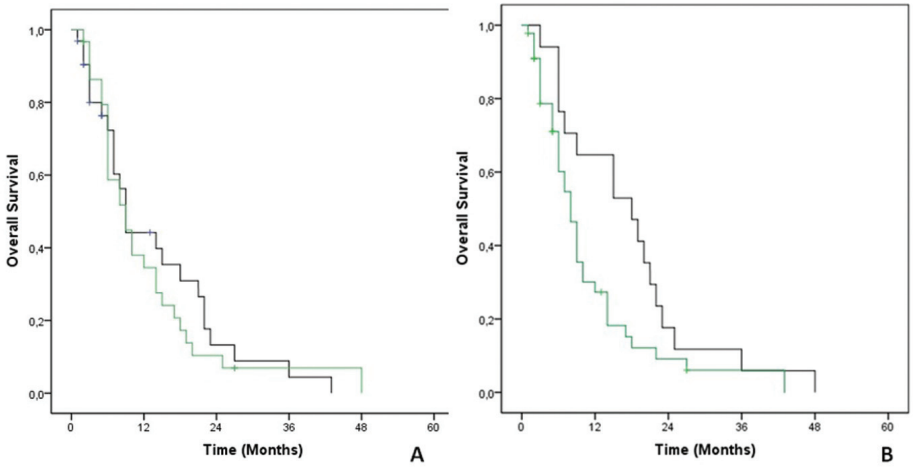


Figure 2— The effect of concomitant temozolomide (**A**), and adjuvant temozolomide (**B**) on survival (blue=with temozolomide, green=without temozolomide).

The median follow-up time was 5 months (range, 0-44 months). The tumor was unifocal in 60 patients (92%). Three patients had tumors located on the midline. KPS was ≥70 in 82% of the cases.

One and two year survival rates for the whole group were 38.9% and 11.7%, respectively. Median survival times according to treatment fields were: 9 months (range, 7-11 months) in the localized group, 3 months (range, 0-6 months) in the WB group and 18 months (range, 3-18 months) in the WB+ localized field group (p=0.04).

Gender, KPS, RT dose, number of tumors and the type of surgery did not significantly affect survival rates. Patients with midline tumors had poorer outcomes compared to other locations (p=0.01). Concomitant TMZ had no significant impact on survival; however, patients who received adjuvant TMZ had better survival (p=0.02) (Figure 1).

Discussion

In the current study we evaluated our treatment results in patients with GBM ≥65 years old and found that WB + localized field RT and adjuvant TMZ had a positive impact on survival; however, the addition of concurrent TMZ had no impact on survival.

It has been shown that older age and poor performance status are associated with poorer survival in patients with high grade glial tumors (3-5,7). However several studies have shown improved survival with treatment in elderly patients with GBM.

Iwamoto et al. reported their treatment results in 394 patients ≥65 years old. Approximately 82% of the patients underwent tumor resection; 81% received RT, and 43% received adjuvant chemotherapy. The median overall survival was 8.6 months. In the multivariate analysis, younger age, good KPS, single tumor, and surgical resection were found to affect survival. One hundred three patients who received adjuvant chemotherapy had a 55% decrease in the risk of death, compared with patients who had no additional treatment after RT (p<0.0001). They concluded that age alone should not disqualify patients from aggressive therapy with surgical resection, RT, and chemotherapy (6). Keime-Guibert et al. conducted a randomized trial comparing RT with supportive care alone for the management of GBM in patients 70 years of age or older (8). RT was delivered as a 1.8 Gy fraction dose to a total dose of 50 Gy. After 21 weeks of follow-up, the median survival for the 39 patients who received RT plus supportive care was 29.1 weeks, as compared with 16.9 weeks for the 42 patients who received supportive care alone (p=0.002). They concluded that RT improves survival without reducing the quality of life or cognition, in elderly patients with GBM. Scott et al. evaluated the role of RT in the treatment of GB in 2836 patients >70 years old from the SEER database. Multivariate analysis showed that RT improved CSS and OS, compared to patients who did not receive it (9). These studies have shown that RT should be delivered to elderly patients with GB, but they did not make any suggestions about the RT fields and doses.

Roa et al. randomized 100 patients with GBM, age 60 years or older, after surgery to receive either standard RT (60 Gy in 30 fractions over 6 weeks) or a shorter course of RT (40 Gy in 15 fractions over 3 weeks) (10). They found no difference in survival between the two RT arms. Median survival rates for the short and long course RT were 5.6 months and 5.1 months, respectively (p=0.63). There was an increase in post-radiotherapy steroids in the long course group. Malmström et al. randomized 291 patients who were over 60 years of age to receive TMZ (200 mg/m^2) on days 1-5 of every 28 days for up to six cycles, hypofractionated RT (34·0 Gy administered in 3·4 Gy fractions over 2 weeks), or standard RT (60·0 Gy administered in 2·0 Gy fractions over 6 weeks). For patients over 70 years of age, survival was better with TMZ and with hypofractionated RT than with standard RT (11).

In our study, 59 patients received the standard RT of 60 Gy in 30 fractions. However three patients who received a 30 Gy WB RT+ 15 Gy booster dose to the tumor had better survival. Although our patient group is too small to make a firm conclusion, hypofractionated RT might be a valid option for elderly patients with poor performance status. Concomitant TMZ did not affect the survival; however, 17 patients who received adjuvant TMZ had better survival. Iwamoto et al. also showed better survival in patients who received aggressive therapy including surgery, RT and chemotherapy. Furthermore, in the subgroup analysis of an EORTC/NCIC trial, patients older than 65 years had relatively diminishing benefits from the addition of TMZ to RT (12). It should also be kept in mind that those who received adjuvant chemotherapy were the ones with good performance status. Thus, this might be the reason for the long survival in this group of patients.

The retrospective nature of our study and the small number of patients in RT groups are both limitations of our study. However the number of elderly patients is increasing, leading to a challenge in making the proper treatment decisions. Prospective randomized studies should be carried out to form a guideline for this group of patients.

References

1. Dolecek TA, Propp JM, Stroup NE, et al. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2005-2009. Neuro Oncol 2012;14 Suppl 5:v1-49. (PMID:23095881).
2. Stupp R, Hegi ME, Mason WP, et al. European Organisation for Research and Treatment of Cancer Brain Tumour and Radiation Oncology Groups; National Cancer Institute of Canada Clinical Trials Group. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Lancet Oncol 2009;10(5):459-66. (PMID:19269895).
3. Iwamoto FM, Reiner AS, Panageas KS, Elkin EB, Abrey LE. Patterns of care in elderly glioblastoma patients. Ann Neurol 2008;64:628–34. (PMID:19107984).
4. Kita D, Ciernik IF, Vaccarella S, et al. Age as a predictive factor in glioblastomas: Population-based study. Neuroepidemiology 2009;33:17–22. (PMID:19325245).
5. Paszat L, Laperriere N, Groome P, et al. A population-based study of glioblastoma multiforme. Int J Radiat Oncol Biol Phys 2001;51:100–107. (PMID:11516858).
6. Iwamoto FM, Cooper AR, Reiner AS, Nayak L, Abrey LE. Glioblastoma in the elderly: The Memorial Sloan-Kettering Cancer Center Experience (1997-2007). Cancer 2009;115(16):3758-66. (PMID:19484785).
7. Buckner JC. Factors influencing survival in high-grade gliomas. Semin Oncol 2003;30(6 Suppl 19):10-4. (PMID:14765378).
8. Keime-Guibert F, Chinot O, Taillandier L, et al. Association of French-Speaking Neuro-Oncologists. Radiotherapy for glioblastoma in the elderly. N Engl J Med 2007;356(15):1527. (PMID:17429084).
9. Scott J, Tsai YY, Chinnaiyan P, Yu HH. Effectiveness of radiotherapy for elderly patients with glioblastoma. Int J Radiat Oncol Biol Phys 2011;81(1):206-10. (PMID:20675068).
10. Roa W, Brasher PM,Bauman G, et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: A prospective randomized clinical trial. J Clin Oncol 2004;22(9):1583. (PMID:15051755).
11. Malmström A, Grønberg BH, Marosi C, et al. Nordic Clinical Brain Tumour Study Group (NCBTSG). Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial. Lancet Oncol 2012(9):916-26. (PMID:22877848).
12. Laperriere N, Weller M, Stupp R, et al. Optimal management of elderly patients with glioblastoma. Cancer Treat Rev 2013;39(4):350-7. (PMID:22722053).

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2014; 17 (2) 138-142

Ferhat İÇME[1]
Sinan BECEL[1]
Asliddin AHMEDALİ[1]
Akkan AVCI[2]
Haldun AKOĞLU[3]
Salim SATAR[2]

RESEARCH

THE USE OF TRAUMA SCORING SYSTEMS IN ELDERLY PATIENTS WHO ARE ADMITTED TO THE EMERGENCY DEPARTMENT DUE TO FALLS

ABSTRACT

Introduction: The aim of our study is to review demographic characteristics, management in concordance with trauma scoring systems, and the significance of trauma scoring systems in predicting the duration of hospital stay in geriatric patients who are admitted to the emergency department because of falling.

Materials and Method: This retrospective study reviewed the records of 1086 patients who were admitted to our emergency department because of falling, between February 1, 2011 and January 31, 2012. Age, gender, date and time of the admission, type of fall, diagnosis related to fall, requisition for radiological tests, requisition for consultations, and end treatment status were recorded for each patient. Glasgow Coma Score, Revised Trauma Score and Injury Severity Score were calculated.

Results: Fourteen point five percent of all patients were geriatric patients. The number of hospitalized patients was 248 (22.8%) and the hospitalization period was 6.9±4.6 days. Comparison of patients according to their outcome of treatment in the emergency department (discharge or admission) showed a significantly higher mean Revised Trauma Score and significantly lower mean Injury Severity Score in the of discharged patients subgroup.

Conclusion: Our results suggest that anatomic scoring systems (Injury Severity Score) are more accurate than physiological scoring systems (Revised Trauma Score, Glasgow Coma Score) in predicting the duration of hospitalization in patients with trauma due to falling. But these results may require to support by further prospective studies.

Key Words: Fall; Geriatrics; Severity of Illness Index; Predictive Value of Tests.

ARAŞTIRMA

ACİL SERVİSE DÜŞME ŞİKAYETİYLE BAŞVURAN YAŞLI HASTALARDA TRAVMA SKORLAMA SİSTEMLERİNİN KULLANIMI

ÖZ

Giriş: Bu çalışmada, acil servise düşme nedeniyle başvuran geriatrik yaş grubundaki hastaların demografik özelliklerinin, travma skorlama sistemleri eşliğinde yönetiminin ve hastaneye yatırılan hastalarda travma skorlama sistemlerinin hastanede kalış sürelerini tahmin etmedeki yerinin gözden geçirilmesi amaçlanmıştır.

Gereç ve Yöntem: Geriye dönük olarak planlanan bu çalışmaya acil servise 1 Şubat 2011 ile 31 Ocak 2012 tarihleri arasında düşme şikayetiyle başvuran 1086 hasta alındı. Çalışmaya alınan hastalar için düzenlenen formlarda, yaş, cinsiyet, acil servise geliş şekli, başvuru tarihi ve saati, düşme şekli, düşme sonrası gelişen tanıları, radyolojik tetkik istenip istenmemesi, istenilen konsültasyon(lar), ve hastanın işlemler sonundaki nihai durumu kayıt altına alındı. Glasgow Koma Skoru, Revize Travma Skoru ve Yaralanma Şiddet Skoru hesaplandı.

Bulgular: Geriatrik yaş grubundaki hastalar toplam hasta sayısının %14.5'i idi. Hastaların 248'i (%22.8) hastaneye yatırılırken yatış süresi 6.9±4.6 gün idi. Hastalar acil serviste sonlandırılmalarına göre (taburculuk ya da yatış) karşılaştırıldığında Revize Travma Skoru anlamlı olarak daha yüksekken, taburcu edilen hastaların Yaralanma Şiddet Skoru anlamlı olarak daha düşüktü.

Sonuç: Düşme gibi sıklıkla anatomik bozukluk yaratan hasta gruplarında hastaneye yatış ve hastaneye yatırılan hastalarda hastanede kalış süresinin uzunluğunu tahmin etmede anatomik skorlama sistemlerinin (Yaralanma Şiddet Skoru), fizyolojik skorlama sistemlerinden (Revize Travma Skoru, Glasgow Koma Skoru) daha ön planda kullanılması gerektiği kanısındayız. Fakat bu sonuçların prospektif çalışmalarla desteklenmesi gerekebilir.

Anahtar Sözcükler: Düşme; Geriatri; Travma Skorlama Sistemleri.

İletişim *(Correspondance)*

FERHAT İÇME
Ankara Atatürk Eğitim ve Araştırma Hastanesi
Acil Servis, Bilkent ANKARA

Tlf: 0312 291 25 25
e-posta: ferhaticme@gmail.com

Geliş Tarihi: 14/05/2013
(Received)

Kabul Tarihi: 03/12/2013
(Accepted)

[1] Ankara Atatürk Eğitim ve Araştırma Hastanesi Acil Servis, Bilkent ANKARA
[2] Adana Numune Eğitim ve Araştırma Hastanesi Acil Aervis, Seyhan ADANA
[3] Marmara Üniversitesi Tıp Fakültesi Acil Anabilim Dalı İSTANBUL

Introduction

In the world's population, the ratio of the population aged 65 and older to the general population has been rapidly increasing due to the increase in life expectancy. The ratio of the elderly population is also increasing in our country. it is expected to be approximately 17.6% in the year 2050, whereas it was 5.7% in 2005 (1). Elderly people are at increased risk of trauma because of anatomical, physiological and endocrine changes due to old age. Falls are the most important causes of trauma and in the geriatric age group they are among the most frequently encountered causes of admissions to emergency departments (2). Falls are also important causes of morbidity and mortality for this age group (3).

Various trauma scoring systems, including physiologic scoring systems such as RTS and GCS and anatomical scoring systems such as ISS, were developed in order to evaluate, compare and define the severity of traumas. In these trauma scoring systems, Although calculation of the RTS is too complicate to use in the emergency room, calculation of the GCS is a little easier. But also, Although calculation of the ISS is relatively easy, must be know Abbreviated Injury Scale (AIS) score. These trauma scoring systems are utilized in evaluating multiple trauma cases for their ability to predict prognosis and especially mortality rates.

In our study we reviewed demographic characteristics, management according to trauma scoring systems and the significance of trauma scoring systems in predicting the duration of hospitalization in geriatric patients.

Materials and Method

In this retrospectively cross sectional planned study we enrolled 1086 patients who were admitted to the Ankara Atatürk Training and Research Hospital Emergency Department between February 1, 2011 and January 31, 2012 because of trauma due to falls in patients over the age of 65. Ethical approval was obtained from the hospital ethics committee. Data was collected from the automated hospital information system, emergency department patient cards and hospitalization files and included age, gender, method of presentation to emergency department (via emergency ambulance system or outpatient), the date and time of admission, type of fall (falling from a height, falling at ground level, falling due to syncope, etc.), diagnosis related to falling, requisition for radiological tests, requisition for consultations, and the treatment status of the patients in the emergency department (discharge, hospitalization or death). All patients admitted to the emergency department were included in the study.

The physiological scoring systems GCS and RTS and the anatomical scoring system ISS were calculated according to the results of the first examination in the Emergency Department. The calculation of the RTS was performed according to the formula defined by Champion et al. "Weighted RTS" [RTS= (0.9368xGCS) + (0.7326xSystolic blood pressure) + (0.2908xRespiratory rate)] (4). On the GCS results, 14-15 points were accepted as mild, 9-13 points as moderate and 3-8 points as severe. (5). The AIS is a dictionary in which 1 (minor) to 6 (fatal) points are given to trauma. When calculating the ISS the body is divided into 6 regions (head and neck, face, thorax, abdomen, extremities, and other), and sum of the squares of the AIS scores from the three most seriously injured regions is calculated as the ISS score. ISS scores range from 1 to 75 and scores of 16 and above indicate major trauma (6).

Statistical Analysis

Analyses of the data were performed using the SPSS for Windows Version 20.0 package program. The categorical variables were displayed as number and percentage and the numeric variables were summarized as mean±standard deviation, median and min-max. Normally distributed continuous variables were reported as the means and were compared using the Student's t test. Categorical data were assessed using Fisher's exact test. Normality analysis of the continuous variables were performed using the Kolmogorov-Smirnov and Shapiro-Wilks tests and Q-Q plots. If the variables were not normally distributed, the data were transformed (if applicable) or nonparametric tests were performed. To compare continious variables and determine the significance between the subgroups of nominal and ordinal variables, t-test or Mann–Whitney U test were used. The point biserial correlation coefficient (r^{pb}) was calculated for the quantification of the relationship between the nominal and scale variables. Otherwise, Pearson and Spearman coefficients were used as applicable. In this study, the maximum type I error was 0.05, and the level of significance was accepted as $p<0.05$.

Results

A total of 115,445 patients were admitted to Emergency Department of our hospital during the one year period between February 1, 2011 and January 31, 2012; 16759

Table 1— Demographic Characteristics of the Patients.

Age (mean)	77.5±7.9	
male	76.7±7.4	
female	78.1±8.1	
Gender	n	%
male	405	37.3
female	681	62.7
Method of arrival to emergency department		
By emergency ambulance system	429	39.5
By their on facilities	503	46.3
Unknown	154	14.2

n: the number of the patients.

Table 2— Radiological Examination.

	n	%
Direct radiography	679	62.5
Computed tomographies	104	9.6
Direct radiography + Computed tomographies	270	24.9
Other	33	3.0

n: the number of the patients.

(14.5%) of these patients were in the geriatric age group. A total of 1086 of these geriatric patients were admitted to the emergency department because of trauma due to falls. Four hundred and five patients (37.3%) were male, 681 (62.7%) patients were female and mean age was 77.5±7.9 (min: 65, max: 103). The number of the women was significantly greater than the men ($p < 0.01$) (Table 1).

The majority of the patients (84.4%) had fallen at ground level because of stumbling, whereas 86 patients (7.9%) had fallen from a height and 16 patients had fallen because of syncope. When falling types, RTS, and ISS scores were compared by gender, no statistically significant difference was detected ($p > 0.05$).

With respect to the location of traumas evaluated, the most affected parts of the body were the extremities (245 patients, 22.5%). At least one radiographic examination was requested for every patient. The most requested examination was direct radiography for 949 patients (87.4%), and no pathology was found in 646 patients (59.5%) (Table 2).

Pathologies were identified in 440 patients (40.5%) and the most common pathology was femoral fracture for 168 patients (15.5%) (Table 3).

The most frequently consulted department was orthopedics with 420 patients (40%). While 249 patients (22.9%) were hospitalized for treatment, the mean duration of hospitalization was 6.9±4.5 days (min=1 max=32). The most common hospitalizations were in the orthopedics department, with 212 (19.5%) patients (Table 4).

In the first examination in the Emergency Department, the GCS was calculated as 15 for 1005 patients (92.5%), between 13-14 in 64 patients (5.9%), and below 12 in 17 patients (1.6%). The RTS was calculated as 7.84 in 1042 patients (95.9%), 7.10 in 24 patients (2.2%), 6.90 in 10 patients (0.9%) and 6:12 in 9 patients (0.8%). Descriptive

Table 3— Defined Pathologies Due to Falling.

FRACTURES								
Femur	Tibia	Fibula	Patella	Foot Bones	Humerus	Radius	Ulna	Hand Bones
168 (15.5%)	15 (1.4%)	3 (0.3%)	3 (0.3%)	4 (0.4%)	15 (1.4%)	32 (2.9%)	3 (0.3%)	2 (0.2%)
Clavicle	Pelvis	Skull	Spine	Nasal	Blowout	Costa		
2 (0.2%)	14 (1.3%)	8 (0.7%)	18 (1.7%)	7 (0.6%)	3 (0.3%)	15 (1.4%)		
DISLOCATIONS								
Shoulder	Hip	Patella	Finger					
8 (0.7%)	7 (0.6%)	1 (0.1%)	1 (0.1%)					
OTHER								
Intracerebra Hemorrhage	Subarachnoid l Hemorrhage	Epidural Hemorrhage	Subdural Hemorrhage	Hemothorax	Hydrocephalus			
5 (0.5%)	8 (0.7%)	1 (0.1%)	5 (0.5%)	1 (0.1%)	1 (0.1%)			
Cerebro Vascular Disease	Cerebral Mass							
4 (0.4%)	2 (0.2%)							

Table 4— Consultations and Hospitalized Departments.

	Consultation		Hospitalization	
	n	%	n	%
Orthopedics	453	41.8	212	19.5
Brain surgery	65	6	16	1.5
General surgery	20	1.8	-	-
Ear, nose and throat diseases	14	1.3	-	-
Neurology	10	1	6	0.6
Other	41	3.7	3	0.3
Intensive care	-	-	11	1.0

n: the number of the patients.

statistical values of RTS are as follows: Mean: 7,802±0,208 (95% CI: 7,789-7,814); median 7,841 (range: 6,120-7,841). The ISS were calculated as ≥16 in 28 (2.5%) patients, between 4-16 in 213 (19.6%) patients and 1 in 845 (77.8%) patients. Descriptive statistical values of ISS are as follows: Mean: 2.92±4.015 (95% CI: 2.68-3.16); median 1 (range: 1-25). Comparison of patients according to their outcome of treatment in the emergency department (discharge or admission) showed a significantly higher mean RTS score (Admitted: 7.7250±0.3735 vs Discharged: 7.8244±0.1129; p<0.001; 95%CI of difference 0.099-0.024) and significantly lower mean ISS score (Admitted: 9.3468±4.0862 vs Discharged: 1.0131±0.2950; p<0.001; %95CI of difference: 7.8222-8.8451) in the of discharged patients subgroup.

A total of 248 patients (22.8%) were hospitalized and 838 (77.2%) patients were discharged as outpatients. Of the hospitalized patients, 237 (21.8%) were hospitalized in clinics and 11 (1%) were hospitalized in the intensive care unit. The general mean duration of hospitalization was 6.9±4.6 days. The mean duration of hospitalization was 6.4±3.7 days for patients who were hospitalized in clinics and 16.7±5.9 for patients who were hospitalized in the intensive care unit. Duration of hospitalization was significantly longer in patients who were hospitalized in the intensive care unit (p<0.01). No deaths occurred.

Discussion

Today, the increasing rate of growth in the elderly population necessitates the need for dealing more effectively with health problems of the elderly as well as the need for developing more specific approaches for every single problem, and using parameters specific to this approach.

In recent studies the reported rate of elderly patients admitted to emergency departments ranges between 12.3 and 15.4%, and the rate of falls in these admissions range between 5 and 7.3% (2,3,7,8). The results of our study are also in accordance with the literature, witk a rate of elderly patients admitted to the emergency department of 14.5% and the rate of falls among these patients of 6.5%. In addition, 38.3% of these admissions were made via the emergency ambulance system. This ratio was higher than the average for our country (9). We attribute this difference to the distant location of our hospital, which is difficult to reach through personal means of transportation.

Recent studies reveal that approximately 1/3 of elderly patients fall at least once a year and most of these falls occur at ground level (2,10). In our study, consistently, the majority of falls was also caused by stumbling at ground level (84.4%).

The use of auxiliary modalities by doctors is 50% higher in elderly patients when compared to young patients because of conditions such as atypical course of the disease, symptoms occurring late, and probable emergence of serious problems under mild symptoms in elderly patients (11). In our study, at least one radiographic examination was requested for each patient and for 37.5% of the patients additional advanced imaging techniques were utilized.

No pathology was detected in 59.5% of the radiological examinations. The most frequently diagnosed pathologies were extremity fractures which were followed by head injuries. These results were consistent with the literature (2,12). In addition, consistent with the literature, we found that the most common extremity fracture was femoral fracture (2). Due to high rates of extremity injuries the number of consultations (41.8%) and hospitalization (19.5%) to the orthopedics clinic were high in our study.

The more complex clinical conditions in elderly patients and the need for consuming more resources makes the duration of treatment in the emergency department and hospitalization to be longer when compared to younger patients (13). The length of 6.9 days hospitalization is consistent with the literature (8,2). In addition hospitalization of 6 patients in the neurology clinic suggests the importance of differentiating whether the fall occurred due to syncope, or whether syncope occurred due to the fall in these patients.

In our study, we found a lower mortality rate than reported in the literature (7,8,12). This is because we excluded highly fatal causes of injury such as traffic accidents and penetrating injuries.

Various trauma scoring systems, as well as intensive care scoring systems, are used for the evaluation of patients with multiple trauma. In spite of some shortcomings these scoring

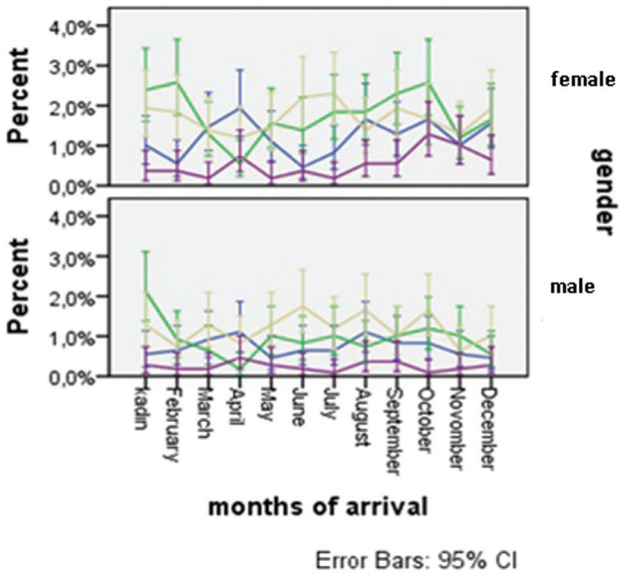


Figure 1— Comparison-of-hours-of-arrival-by-months.

systems are preferred particularly for their ability to predict the prognosis and mortality rates. However, the results of the studies evaluating trauma scoring systems in terms of predicting mortality in elderly trauma patients seems inconsistent. Güneytepe et. al. concluded that all of the systems (ISS, RTS, and GCS) are statistically significant in predicting mortality in elderly trauma patients. Osler and colleagues suggested that GCS is more effective in the elderly (14,15). In another study, ISS is suggested to be the most accurate scoring system for predicting mortality (16). In a study examining the significance of ISS in all age groups significant differences between the ISS scores and discharge from emergency department or hospital were found (12). In our study, Comparison of patients according to their outcome of treatment in the emergency department (discharge or admission) showed a significantly higher mean RTS score and significantly lower mean ISS score in the of discharged patients subgroup.

Consequently, we consider that for predicting prognosis and duration of hospitalization in cases of falls, which often cause anatomical disorders, anatomical scoring systems (such as ISS) could be preferred to physiologic scoring systems (e.g., RTS, GCS). But these results may require to support by further prospective studies.

Financial Disclosure: None declared

Funding Support: None declared

References

1. TurkStat. Elderly Statistics, Ankara, 2013. Publication number: 4158. [Internet] Available from: http://www.tuik.gov.tr/Kitap.do?metod=KitapDetay&KT_ID=11&KITAP_ID=265. Accessed: 21.12.2013.
2. Atilla ÖD, Tür FÇ, Aksay E, Doğan T, Eyler Y, Akın Ş. Clinical factors in geriatric blunt trauma. Tr J Emerg Med 2012;12(3):123-8.
3. Kandiş H, Karakuş A, Katırcı Y, Karapolat S, Kara İH. Geriatric population and forensic traumas. Turkish Journal of Geriatrics 2011;14(3):193-8. (in Turkish).
4. Champion HR, Sacco WJ, Copes WS, Gann DS, Gennarelli TA, Flanagan ME. A revision of the Trauma Score. J Trauma 1989;29(5):623-9. (PMID:2657085).
5. Centers for Disease Control and Prevention: Vital Statistics. [Internet] Available from: http://www.cdc.gov/nchs/vitalstats.htm. Accessed: 22.11.2012.
6. Osler T. Injury severity scoring: Perspectives in development and future directions. The American Journal of Surgery 1993;165(2A Suppl):43-51. (PMID:8438999).
7. Satar S, Sebe A, Avcı A, Karakuş A, İçme F. Emergency department and the elderly patient. Ç.Ü. Tıp Fakültesi Dergisi 2004;29(2):43-50.
8. Taymaz T. Examination of geriatric patients hospitalized from the emergency department. The Journal of Academic Geriatrics 2010;2(3):167-75. (in Turkish).
9. Şahin S, Boydak B, Savaş S, Yalçın MA, Akçiçek F. Characteristics of patients aged 65 and over in the emergency department. The Journal of Academic Geriatrics 2011;3(1):41-6. (in Turkish).
10. Masud T, Morris RO. Epidemiology of falls. Age Aging 2001;30:3-7. (PMID:11769786).
11. Kunt MM. Urgent problems in old age. Basic Geriatrice for the Primary Health. 1st press, Algı Tanıtım, Ankara 2012, pp 66-73 (in Turkish).
12. Erdur B, Türkçüer İ, Ergin A, Kabay B, Serinken M, Yüksel A. A cohort analysis of Pamukkale University Medical Faculty Emergency Department trauma cases. Turk J Emerg Med 2007;7(1):25-30.
13. Yim VW, Graham CA, Rainer TH. A comparison of emergency department utilization by elderly and younger adult patients presenting to three hospitals in Hong Kong. Int J Emerg Med 2009;2(1):19-24. (PMID:19390913).
14. Güneytepe Üİ, Aydın ŞA, Gökgöz Ş, Özgüç H, Ocakoğlu G, Aktaş H. The factors influencing the mortality in elderly trauma patients and scoring system. Uludag Medical Journal 2008;34(1):15-9 (in Turkish).
15. Osler T, Hales K, Baack B, et al. Trauma in the elderly. Am J Surg 1988;156(6):537-43. (PMID:3202269).
16. Knudson MM, Lieberman J, Morris JA, Cushing BM, Stubbs HA. Mortality factors in geriatric blunt trauma patients. Arch Surg 1994;129(4):448-53. (PMID:8154972).

Turkish Journal of Geriatrics
2014; 17 (2) 143-151

Pınar KURT[1]
Pembe KESKİNOĞLU[2]
Erdem YAKA[3]
Reyhan UÇKU[4]
Görsev YENER[3]

RESEARCH

A COMPOSITE SCORE FOR DOKUZ EYLUL COGNITIVE STATE NEUROCOGNITIVETEST BATTERY: A DOOR-TO-DOOR SURVEY STUDY WITH ILLITERATE, LOW AND HIGH EDUCATED ELDERLY IN TURKEY

ABSTRACT

Introduction: This study aimed to develop a composite score for the Turkish neuropsychological test battery named Dokuz Eylul Cognitive State for a large well educated and less educated elderly population, including those with mild cognitive impairment and dementia.

Materials and Method: Dokuz Eylul Cognitive State total scores were obtained by summing scores acquired from individual Dokuz Eylul Cognitive State subtests to establish a total composite score. Control participants (n=363) were dwelling in the community and tested by means of a door-to-door survey. The utility of the total score was further tested in independent samples of dementia patients with various etiologic backgrounds (n=53) or mild cognitive impairment (n=53) participants.

Results: Areas under the receiver operating characteristics curve in well and less educated dementia patients and healthy participants were found to be 0.931 and 0.954, respectively. A cut-off point of 72/73 of Dokuz Eylul Cognitive State for the well educated elderly had the highest sensitivity (83.8) and specificity (90.3), whereas a cut-off point of 49/50 for the less educated elderly had the highest sensitivity (91.2) and specificity (88.6). The Cronbach's · values of the Dokuz Eylul Cognitive State for well educated and less educated elderly were higher than 0.8.

Conclusion: These results support the validity of the Dokuz Eylul Cognitive State total score for the purpose of detecting and monitoring the progression of receiver operating characteristics and dementia in patients with different levels of education in clinical and research settings.

Key Words: Dementia; Mild Cognitive Impairment; Questionnaire.

ARAŞTIRMA

DOKUZ EYLÜL KOGNİTİF DURUM TEST BATARYASI İÇİN BİLEŞİK PUAN: TÜRKİYE'DEKİ EĞİTİMSİZ, DÜŞÜK VE YÜKSEK EĞİTİMLİ YAŞLILARLA ALAN ARAŞTIRMASI

ÖZ

Giriş: Bu çalışma yüksek ve düşük eğitimli hafif kognitif bozukluk ve demans hastalarını da içeren geniş bir yaşlı popülasyonu için Dokuz Eylül Kognitif Durum olarak adlandırılan Türkçe nöropsikolojik test bataryasının bileşik skorunu geliştirmeyi amaçlamıştır.

Gereç ve Yöntem: Bileşik skoru oluşturmak için Dokuz Eylül Kognitif Durum alt testlerinin toplamından elde edilen Dokuz Eylül Kognitif Durum toplam puanı kullanılmıştır. Kontrol grubu (n=363) toplum içinde yaşayan yetişkin bireylerdi ve testleri hane araştırması yoluyla yapıldı. Toplam skor daha sonra hafif kognitif bozukluk (n=53) ya da farklı etiyolojilere sahip demans (n=53) hastalarından oluşan bağımsız örneklemde test edildi.

Bulgular: Yüksek ve düşük eğitimli demans hastaları ve sağlıklı bireylerde alıcı işletim karakteristiği eğirisi altında kalan alan sırasıyla 0,931 ve 0,954 olarak bulundu. Yüksek eğitimli yaşlılarda 72/73 kesme değeri en yüksek duyarlılık (83,8) ve özgüllük (90,3) değerine sahipken; düşük eğitimli yaşlılarda 49/50 kesme değeri en yüksek duyarlılık (91,2) ve özgüllüğe (88,6) sahipti. Dokuz Eylül Kognitif Durum'un Cronbach · değerleri düşük ve yüksek eğitimliler için 0,8'den yüksek bulunmuştur.

Sonuç: Bu sonuçlar Dokuz Eylül Kognitif Durum toplam skorunun klinik ve araştırma alanlarında, farklı düzeylerde eğitime sahip hafif kognitif bozukluk ve demans hastalarının taranması ve ilerlemenin gözlenmesinde geçerliliğini desteklemektedir.

Anahtar Sözcükler: Demans; Hafif Kognitif Bozukluk; Kognitif Tarama Testi.

İletişim *(Correspondance)*

Pınar KURT
İstanbul Arel Üniversitesi, Psikoloji İSTANBUL

Tlf: 0212 867 25 00
e-posta: pinarkurt@arel.edu.tr

Geliş Tarihi: 23/12/2013
(Received)

Kabul Tarihi: 12/02/2014
(Accepted)

[1] İstanbul Arel Üniversitesi, Psikoloji İSTANBUL
[2] Dokuz Eylül Üniversitesi Tıp Fakültesi, Biyoistatistik ve Tıbbi Bilişim Anabilim Dalı İZMİR
[3] Dokuz Eylül Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı İZMİR
[4] Dokuz Eylül Üniversitesi Tıp Fakültesi, Halk Sağlığı Anabilim Dalı İZMİR

Introduction

Dementia is a prevalent disease among the elderly and neuropsychological assessment may play a key role in its diagnosis by providing objective information about cognitive deficits and changes (1). The Delphi consensus study reported that 60% of people with dementia live in developing countries and it is predicted that by 2040, this percentage will reach 71% (2). In almost all cognitive assessment tools, the level of education significantly influences the participant's performance on the test (3). Low education is considered to be associated with dementia, possibly due to the cerebral reserve hypothesis (4). The American Psychological Association (APA) has stated that only highly educated, normative majority samples have been used for many neuropsychological tests (5). The validated cognitive tests that are frequently used in Western countries do not reflect the actual cognitive performance of individuals who live in developing countries, and may lead to misdiagnosis of dementia mainly due to the literacy or reasonable level of education requirements of such tests (6). It is, therefore, necessary to define education-specific cut-off scores derived from population-based studies to avoid flooring effects among the low education group (3).

According to a 2013 report by the Turkish Statistical Institution (TUIK), the illiteracy or low level of education rate is 4% among the elderly, which is equivalent to over 5.5 million people in Turkey's population (7). Considering that the prevalence of dementia among people over 65 in Turkey is about 13%, there is a strong need for a valid test in Turkey, which involves gathering data from an epidemiological study of both educated and illiterate people. Our objective was to develop a composite score for a newly developed neuropsychological test named "Dokuz Eylül Kognitif Degerlendirme/Dokuz Eylul Cognitive Assessment" (DEKOD) for use with both well educated and less educated population groups in Turkey. By means of this battery, a profile of cognitive impairment can be described using multiple data points across cognitive domains.

We aimed to develop a total score for the Turkish DEKOD neuropsychological battery that would provide a normative-based summary score of global cognitive performance that could also be used to identify level of cognitive impairment. We hypothesized that this score can be helpful in differentiating dementia, mild cognitive impairment (MCI), and normal aging.

Materials and Method

Participants

Four hundred ninety community dwelling participants, 65 years old or above, were screened for dementia in a door-to-door type epidemiological study. Addresses to be surveyed were assigned by TUIK according to socio-economic and cultural backgrounds of the residents. The Narlıdere area in Izmir province in western Turkey was chosen by TUIK as an examplary pilot area for the Turkish population. A detailed random sampling method has been described elsewhere (8). Oral informed consent was obtained from all participants or their relatives living in the same house. The study was approved by the ethics committee of the Faculty of Medicine of Dokuz Eylul University.

Cognitive testing, which included the DEKOD, the rMMSE-T (revised Mini Mental State Examination-Turkish), the GDS (Geriatric Depression Scale), the IADLs (Instrumental Activities of Daily Living Scale) and the CDR (Clinical Dementia Rating Scale) was administered by a neuropsychologist. An intrarater retest was administered to 17 elderly participants after a period of 2-7 days. An interrater retest was administered to 14 elderly participants after a period of between 3-15 days by two neurologists. Clinical diagnosis was made by a senior neurologist according to the dementia and MCI diagnosis criteria mentioned in the following section. A total of 46 participants with severe dementia, other neuropsychiatric illnesses or hearing loss were excluded from the sample. Also, a few control participants with a native language other than Turkish were excluded. Overall, a total of 444 (338 healthy elderly, 53 with dementia and 53 with MCI) participants were included to the study. Two groups were identified according to education: Less educated (0-4 years of education) and well educated (5 or more years of education).

Diagnostic Criteria for Dementia and Mild Cognitive Impairment

The clinical diagnosis of dementia was assessed by a senior neurologist according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4rd Edition (DSM IV). Alzheimer's Disease (AD) and Vascular Dementia (VaD) participants in the dementia group were diagnosed as probable/possible AD or probable/possible VaD, using National Institute of Neurological and Communication Disorders and Stroke/AD and Related Disorders Association (NINCDS-ARDRA) and National Institute of Neurological Disorders and Stroke-Association Internationale pour la

Recherche et L'Enseignement en Neurosciences (NINDS-AIREN) criteria. The diagnosis of MCI subjects was conducted according to the following criteria established by Petersen et al. (1999): (a) Subjective memory complaint, (b) normal activities of daily living, (c) normal general cognitive function, (d) abnormal memory functioning determined for age [neuropsychological tests reveal 1.5 standard deviations (SD) below normative values], and (e) not demented.

Development of DEKOD

Although the prevalence of elderly people in Turkey who are illiterate or have little formal education is about 63% (8), the current validated neuropsychological test batteries which are routinely used in dementia clinics usually address subjects with at least 5 years of education. Therefore, there is a need for a neurocognitive testing battery for all illiterate, less and well educated people older than 65. We suggested the DEKOD as an easily administered neurocognitive test for which participants do not need to use pen or paper.

Description of Subtests of the DEKOD

The DEKOD is composed of attention, calculation and judgment, naming, verbal category fluency, and memory subtests, taking 30 minutes to administer in total.

- Attention (10 points): A short version of the Digit Span (forward and backward) subtest of the Wecshler Memory Scale-Revised (WMS-R, Wechsler, 1981) is used to assess attention. The participant is asked to repeat the numbers in the same order as they were presented (digits forward), then asked to repeat another series of numbers in reverse order (digits backward). The test begins with three numbers, increasing to seven digits until the participant makes two consecutive errors.
- Calculation (5 points): The participant is asked to calculate five simple (5+3= ; 21-8= ; 13x5= ;39÷13=) arithmetic operations.
- Abstract Thinking / Judgment (3 points): Three common proverbs in Turkish are given.
- Language (Verbal/Category Fluency, Boston Naming Test) (32 points): 12 items from the 15-item version Boston Naming Test (BNT) used by the Consortium To Establish a Registry for Alzheimer's Disease (CERAD) is used to assess naming ability and an animal list is used to assess verbal/category fluency.
- Immediate memory (30 items, 20 points): A list of ten frequent, concrete words (oil, arm, building, letter, ticket, cat, engine, gras, stick, shore) from Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog) is given to the participant to encode. The list is repeated three times with the same words in a random order. The sum of immediate recalled words is recorded after each trial.
- Memory (free recall) (10 points): After approximately 20 minutes of immediate memory, the participant is asked to recall the words from the given list of ten words. One point was scored for each correct word.
- Memory (recognition) (20 points): This is a recognition test of the words from the immediate memory subtest with ten true words and ten false words. The participant is asked to say "yes" when the examiner reads a word from the immediate memory subtest and "no" when the examiner reads a false word. One point was scored for each true word from the immediate memory list and false word that was not from the given list.

Statistical Analysis

A receiver operating characteristics (ROC) analysis was performed to establish the cut-off points of the DEKOD for MCI and dementia screening. The highest sensitivity and specificity of cut-off points of the test were selected. Correlations between test-retest and Kappa analyses were evaluated in order to determine the reliability of the DEKOD. Cronbach's · coefficients were calculated for internal consistency of the test.

Results

Demographic and Cognitive Characteristics

The study was conducted with 338 healthy elderly (183 male and 261 female, 70.7±5.4 years of age), 53 dementia (11 male, 42 female 74±7.8 years of age) and 53 MCI (23 male, 30 female 71.7±5.6 years of age) participants. The demographic and cognitive characteristics of participants are summarized in Table 1. When compared by age, less educated healthy elderly (70.7±5.3) and MCI participants (71.2±4.9) were significantly younger than participants with dementia (78.7±7.7). All three groups – healthy elderly, MCI and dementia – differed significantly from each other in their DEKOD and rMMSE-T scores (Table 1).

The DEKOD total score was inversely correlated with age (r=-0.59, p=0.00) and clinical stage [CDR (r=-0.65, p=0.00) and GDS (r=-0.44, p=0.00)]. A strong positive correlation was observed between the DEKOD and the rMMSE-T (r=0.78, p=0.00) and the IADLs (r=0.72, p=0.00).

Table 1— Demographic Characteristics and Test Scores of the Healthy Elderly, MCI and Dementia Subjects.

	Healthy Elderly n= 338		MCI n= 53		Dementia n= 53	
	0-4 Years of Education n= 150	5 Years or More Education n= 188	0-4 Years of Education n=31	5 Years or More Education n= 22	0-4 Years of Education n=43	5 Years or More Education n= 10
Age Mean (SD)	70.7 (5.3)*	70.6 (5.5)	71.2 (4.9)*	72.6 (5.8)	78.7 (7.7)	71.9 (6.0)
Gender (M/F)	37/113	112/76	11/20	12/10	6/37	5/5
DEKOD Meanscore (SD)	66.3 (12.6)	83.5 (10.7) ++	57.7 (9.7) **	69.1 (8.1) **	29.9 (17.3)	49.8 (25.1)
MMSE Meanscore (SD)	24.2 (3.4)	26.7 (2.1) ++	23.6 (3.3) **	23.2 (3.3) **	14.8 (6.0)	16.4 (7.2)
GDS Meanscore (SD)	4.5 (3.5)	2.3 (2.6)	4.5 (3.3) *	3.3 (2.7) **	6.9 (3.6)	7.0 (3.8)
IADL Meanscore (SD)	21.4 (2.3)	21.3 (2.0)	20.0 (3.1) **	22.0 (1.4) **	7.3 (6.0)	12.5 (7.4)
CDR Meanscore (SD)	0**†	0**††	0.4 (0.3)**	0.3 (0.3)**	1.22 (0.7)	0.81 (0.65)

SD: StandardDeviation, M: Male, F: Female, MCI: Mild Cognitive Impairment, DEKOD: Dokuz Eylul Cognitive Assessment Test, MMSE: Mini Mental State Examination, GDS: Geriatric Depression Scale, IADL: Instrumental Activities of Daily Living, CDR, Clinical Dementia Rating Scale, *significantly different from dementia group (p<0.05), **significantly different from dementia group (p<0.005), †significantly different from MCI group (p<0.05), ††significantly different from MCI group (p<0.005).

Table 2— Comparison of DEKOD and rMMSE-T in Dementia and MCI Groups.

		DEKOD						rMMSE-T					
		Cut-Off	Sensitivity	Specifity	AUC	PPV	NPV	Cut-Off	Sensitivity	Specifity	AUC	PPV	NPV
High Educated	Dementia	72/73	84%	90%	0.93	0.28	0.99	22/23	98%	90%	0.96	0.80	0.98
(5 years or more)	MCI	75/76	80%	79%	0.86	0.05	0.90	26/27	61%	85%	0.83	0.09	0.90
Low-Educated	Dementia	49/50	91%	90%	0.95	0.76	0.95	17/18	95%	83%	0.91	0.76	0.91
(0-4 years)	MCI	60/61	70%	65%	0.72	0.24	0.86	22/23	67°%	55%	0.56	0.22	0.83

AUC: Area Under the Curve; PPV: Positive Predictive Value; NPV; Negative Predictive Value.

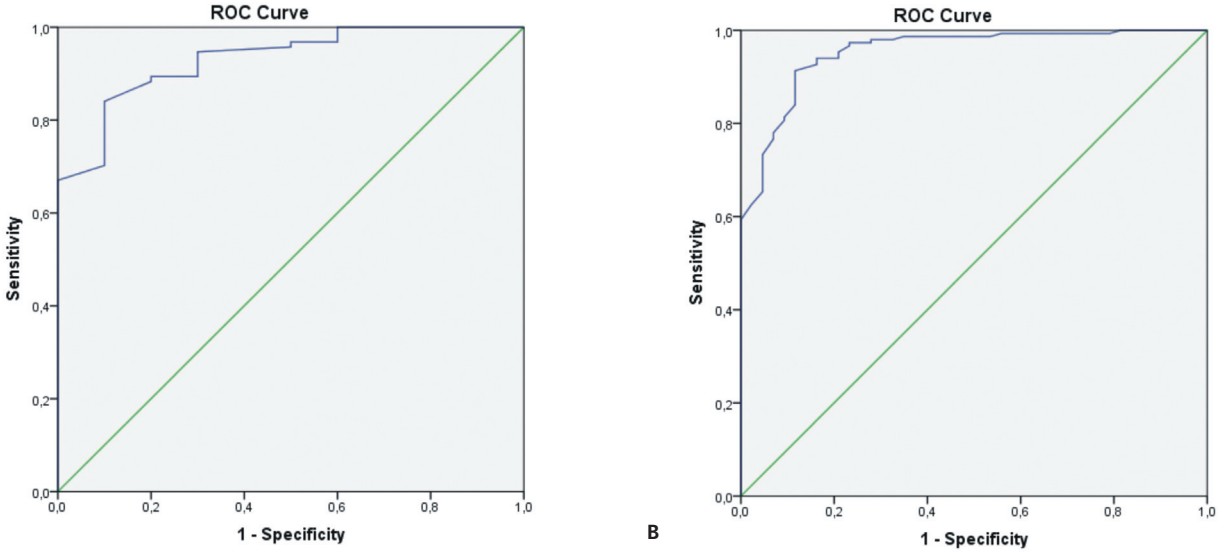


Figure 1— A. Receiver operating characteristic (ROC) curve for educated healtly elderly versus dementia subjects. Area under ROC curve = .931 (Standart error (SE) = 0.032; 95% confidence interval (CI) = 0.870-0.993. **B.** ROC curve for less educated healthy elderly versus dementia subjects. Area under ROC curve= .954 (SE= 0.016; 95% CI= 0.922-0.985)

Validity of DEKOD

We found that the DEKOD is a valid cognitive test for the Turkish speaking population, based on a door-to-door type epidemiological study. The sensitivity and specificity rates for differentiating dementia patients from healthy control participants were over 80% in the educated, illiterate and less educated population groups. The comparison of DEKOD and rMMSE-T values in dementia and MCI groups are shown in Table 2.

The DEKOD was also efficient in differentiating MCI from HC in the educated group, but was less effective in differentiating the less educated MCI from the less educated HC.

Healthy Elderly Versus Dementia

In the ROC curve for the DEKOD in educated healthy elderly compared to dementia participants, the area under the curve (AUC) was found to be 0.931 (Figure 1A). A cut-off point of 72/73 had the highest sensitivity (84%) and specificity (90%). The positive predictive value (PPV) was found to be 27.6%. Likewise, negative predictive value (NPV) was 99% when the disease prevalence was 5%. When the positive likelihood ratio (+LR) and negative likelihood ratio (-LR) were calculated, they were found to be 8.3 and 0.2, respectively.

In the ROC curve for the DEKOD in the less educated healthy elderly versus dementia participants, the AUC was found to be 0.954 (Figure 1B). A cut-off point of 49/50 had the highest sensitivity (91%) and specificity (89%). The PPV was 76.5% and the NPV was 95%. When +LR and -LR were calculated, they were found to be 8.27 and 0.1, respectively.

Healthy Elderly Versus MCI Participants

In the ROC curve for the DEKOD in educated healthy elderly versus MCI participants, the AUC was found to be 0.862 (Figure 2A). A cut-off point of 75/76 had the highest sensitivity (80%) and specificity (79%). The PPV was 0.5% and the NPV was 90%. Additionally, +LR and -LR were calculated to be 3.8 and 0.25, respectively.

In the ROC curve for the DEKOD in less educated healthy elderly versus MCI participants, the AUC was found to be 0.719 (Figure 2B). A cut-off point of 60/61 had the highest sensitivity (70%) and specificity (65%). The PPV was found to be 24.5% and the NPV was 85.9%. +LR and -LR were calculated to be 20 and 0.46, respectively.

Reliability of the DEKOD

An internal consistency analysis was performed for both educated and less educated elderly participants in terms of total score and items of the DEKOD. Correlations and Kappa

values for intrarater and interrater test-retest reliability of the DEKOD were also calculated.

The Cronbach's α values of the DEKOD for educated and less educated elderly participants were higher than 0.86, indicating good internal consistency. Strong and statistically significant correlations between intrarater and interrater test-retest scores of elderly participants were observed [0.781 ($p<0.01$); 0.756 ($p<0.01$), respectively] when a Kappa analysis was performed.

Discussion

The purpose of this study was to examine the validity and reliability of a brief cognitive assessment test, the DEKOD, to differentiate illiterate or less educated demented and MCI participants from healthy elderly control (HC) participants in the Turkish speaking population. The results of the study revealed that the DEKOD is a useful cognitive screening tool for detecting dementia, regardless of educational level, with a high reliability and validity in the population above 65 years of age. The main advantage of the DEKOD is that it provides a tool that does not require reading and writing, therefore is easily administered to illiterate individuals. The test also has good sensitivity and specificity when applied to educated MCI participants. However, the test seems not to be sensitive enough to differentiate MCI participants from HC in the less educated population. The clinical diagnosis of dementia does not only include the assessment of cognitive impairment but also impairment in daily living activities. In the current study, the IADLs was used to assess functional status of the participants. In line with previous studies (9), we found that impairment of IADLs significantly correlated with DEKOD scores. Therefore, combined use of the DEKOD and IADLs would help to improve the sensitivity for detecting MCI in the less educated population.

DEKOD Test in Dementia

It is well known that better educated participants outperform illiterate or less educated participants on cognitive tests (10). The cut-off scores used in the cognitive assessment of educated participants may lead to incorrect evaluations of the cognitive state of illiterate or less educated participants in terms of the diagnosis of mild cognitive impairment or dementia. We have developed the DEKOD to address the assessment challenges involved in cognitive screening of illiterate or less educated dementia and/or MCI participants, and evaluated its validity by means of a trial with the community-dwelling elderly. Recently, Babacan-Yıldız et al. (10) have developed the COST (Cognitive State Test), which

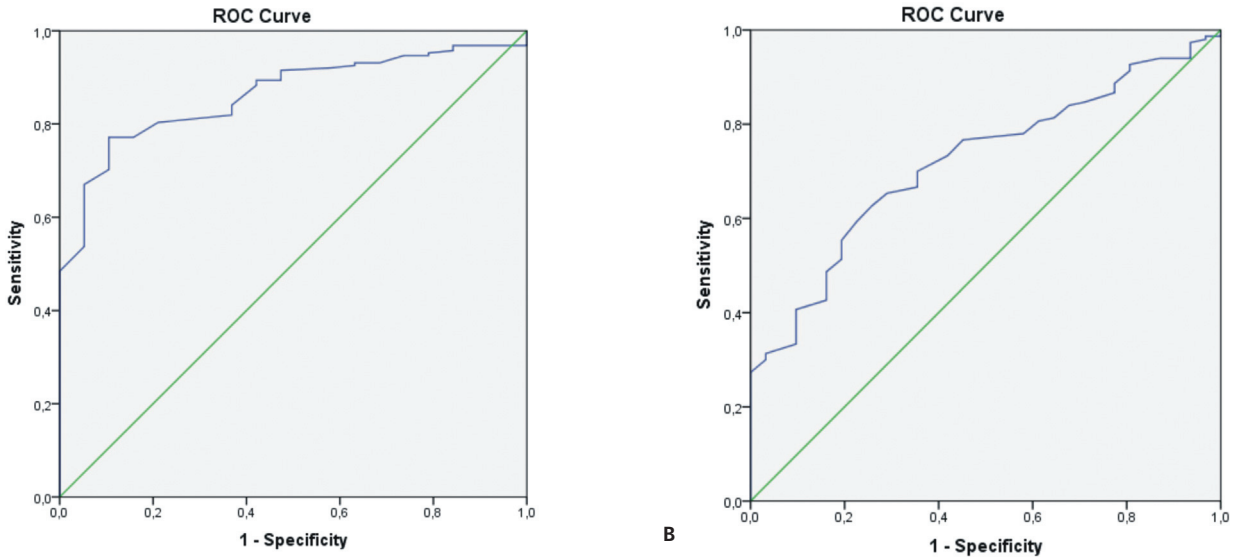


Figure 2— A. Receiver operating characteristic (ROC) curve for educated healthy elderly versus MCI subjects. Area under ROC curve= .862 (SE= 0.032; 95% CI= 0.799-0.925). **B.** ROC curve for less educated healthy elderly versus MCI subjects. Area under ROC curve= .719 (SE= 0.044; 95% CI= 0.633-0.804)

serves the same purpose in the Turkish speaking population. The COST was administered only to enrolled AD patients among those who were referred to an outpatient clinic, along with a relatively small sample size of healthy controls (n=114), and cannot be extrapolated to the general population of Turkey. The main strength of the present study is that data collection for the DEKOD was based on a door-to-door survey that involved a representative sample of elderly people living in the community.

The Montreal Cognitive Assessment (MoCA) has been suggested as a cognitive screening tool for the detection of MCI (11). Selekler et al. (12) reported that the MoCA provides an efficient way to discriminate Turkish MCI and AD patients from the healthy elderly. However, the sample size of their study is very small (MCI, n=20; AD, n=20; healthy participants, n=165) and the mean education level is approximately ten years of schooling in the targeted population. Therefore the test cannot be generalized to the Turkish population and the MoCA needs to be validated on a large sample group before being recommended for use in clinical practice.

In Turkey, one of the most commonly used screening tools is the Mini Mental State Examination (MMSE) (13). The first Turkish version of the MMSE (MMSE-T) was validated with an elderly group of participants who had received at least five years of education (14). Thus, it did not reflect the cognitive properties of the community-dwelling elderly. In their community-based study, Keskinoğlu et al. (8) revised the MMSE-T (rMMSE-T) and suggested a cut-off score as 22/23, with 91% sensitivity, 97% specificity, 59% positive predictive value and 99.6% negative predictive value. The rMMSE-T is a brief screening tool that assess orientation, registration, attention and calculation, recall, naming, repetition, comprehension, reading, writing and drawing abilities of both literate and illiterate elderly.

Still, in clinical settings it was observed that a more comprehensive assessment of memory encoding, retrieval and recognition, as well as naming, verbal fluency and calculation abilities, was needed. Therefore, the aim of developing the DEKOD was to detect the abnormalities in these cognitive domains. Although the cognitive domains that have been assessed by rMMSE-T and DEKOD are similar to each other, DEKOD offers a relatively more detailed evaluation of the above mentioned skills than rMMSE-T does. Furthermore, DEKOD includes the subtests that assess verbal fluency and judgment which are two considerable components of executive functions. In terms of the DEKOD's validity, the study was conducted on a large scale elderly population, including demented patients with various etiologies and MCI participants. The DEKOD total score showed a good positive correlation with rMMSE-T and IADLs and a weak negative correlation with CDR and GDS scores. These results suggest that the DEKOD can distinguish severe stages of dementia. Aside from the subtests of the DEKOD that assess memory, calculation and naming, its subitems that include verbal fluency, abstract thinking and attention also allow screening for frontal lobe disturbance appearing in frontotemporal or Lewy-body dementia.

The high sensitivity and specificity values of the DEKOD suggest its usefulness as a diagnostic tool in screening educated and less educated dementia patients. The PPV indicates the probability that the disease is present when the test is positive. The PPV of the DEKOD obtained from educated and less educated elderly show that the test is good at diagnosing dementia in the less educated group, but not in educated participants. Because the predictive value is affected by the prevalence (8), the low PPV value was foreseen because of the relatively low disease prevalence among these participants. The negative predictive values of the DEKOD are high for both educated and less educated groups, indicating that if a participant has a higher score than the cut-off values, no dementia is present.

DEKOD Test in MCI

MCI is defined as a transitional state from normal aging to dementia (15). MCI patients may convert to Alzheimer's Disease, VaD or other types of dementia. The cumulative conversion rate of MCI to dementia was found to be about 21.9% in community-based studies, with an annual conversion rate of 3% (9).

In the present study, the DEKOD showed relatively good sensitivity (80%) and specifity (79%) for the educated MCI group. The mean scores of healthy elderly participants were significantly higher than those of MCI participants, regardless of education level (Table 1). However the sensitivity (70%), specificity (65%) and positive predictive value (24.5%) tests showed that the DEKOD did not serve so well to differentiate between the cognitive states of less educated MCI and healthy elderly participants. This result may be explained by the difficulty in providing operational criteria that distinguish MCI from normal cognitive aging (16), and because cognitive impairment due to age may be mainly affected by the low level of education. Cognitive tests specially designed to screen

for MCI such as the MoCA (11), or Memory Alteration Test (M@T) (17) have not been studied to assess the effect of educational level on the cognitive performance of MCI and healthy elderly participants. Therefore, it is suggested that the validity and reliability of the above mentioned tests, together with the DEKOD, for use with the MCI and healthy elderly participants with low levels of education, should be examined thoroughly.

Although the diagnostic criteria for MCI require normal activities of daily living (15), recent studies have reported that there is a significant association between MCI and IADL impairment (18). In the present study, the IADLs did not show any differences between either educated or less educated subgroups of MCI and healthy control participants. However, illiterate or less educated MCI participants performed lower on the DEKOD test when compared to age-matched healthy elderly participants. The combined use of the DEKOD along with a functional abilities assessment scale is suggested in order to distinguish in less educated MCI participants from healthy controls.

The main limitation of our study is the heterogeneity of the studied population, including both probable/possible AD or probable/possible VaD participants in dementia group and amnestic and non-amnestic MCI participants in MCI group. DEKOD must be administered in a larger and defined subgroups of dementia and MCI populations. In order to determine DEKOD's ability to distinguish these subgroups of dementia and MCI, further studies are needed to be conducted in clinical settings.

We believe a test like the DEKOD that examines cognitive domains such as memory, attention, calculation, verbal fluency, naming and abstract thinking, without requiring writing or reading skills, is a valid test in differentiating those with dementia from the healthy elderly, regardless of education. Moreover, it has still high sensitivity for distinguishing MCI participants from healthy elderly in the community-dwelling population with an education level of 5 years or more. In the less educated population, the DEKOD should be interpreted more cautiously or should be used together with functionality scales for better evaluation.

Conflict of Interest: None.

Description of Authors' Roles

P. Kurt was responsible for data collection and wrote the paper. P. Keskinoglu designed the study, and supervised the data collection. E. Yaka was responsible for data collection and clinical diagnosis. R. Ucku was responsible for study design. G. Yener was responsible for study design, test preparation, data collection and clinical diagnosis.

Acknowledgements

This study has been founded by the Scientific and Technological Research Council of Turkey (Project No: SBAG-HD-145(106S131).

References

1. Sano M. Neuropsychological testing in the diagnosis of dementia. J Geriatr Psychiatry Neurol 2006;19:155-9. (PMID:16880357).
2. Ferri CP, Prince M, Brayne C, et al, Alzheimer's Disease International. Global prevalence of dementia: A Delphi consensus study. Lancet 2005;366(9503):2112–7. (PMID:16360788).
3. Mathew R, Mathuranath PS. Issues in evaluation of cognition in the elderly in developing countries. Ann Indian Acad Neurol 2008;11(2):82–8. (PMID:19893644).
4. Meng X, D'Arcy C. Education and dementia in the context of the cognitive reserve hypothesis: A systematic review with meta analyses and qualitative analyses. PlosOne 2012;7(6), e38268. DOI: 10.1371.
5. American Psychological Association. Guidelines for the evaluation of dementia and age-related cognitive change. American Psychologist 2012;67(1):1–9. (PMID:21842971).
6. Jitapunkul S, Lailert C, Worakul P, et al. Chula mental test: A screening test for elderly people in less developed countries. International Journal of Geriatric Psychiatry 1996;11(8):715-20.
7. Turkish Statistical Institute. Prime Ministry Republic of Turkey, Turkish Government Statistical Institute. Address based population registration system results 2012. [Internet] Available from: http://www.turkstat.gov.tr. Accessed: 27 August 2013.
8. Keskinoğlu P, Uçku R, Yener G, et al. Reliability and validity of revised Turkish version of Mini Mental State Examination (rMMSE-T) in community-dwelling educated and uneducated elderly. Int J Geriatr Psychiatry 2009;24(11):1242-50. (PMID:19337986).
9. Tomaszewski-Farias S, Mungas D, Reed BR, et al. Progression of mild cognitive impairment to dementia in clinic- vs community-based cohorts. Arch Neurol 2009;66(9):1151-7. (PMID:19752306).
10. Babacan-Yildiz G, Isik AT, Aydemir E, et al. COST: Cognitive State Test, a brief screening battery for Alzheimer disease in illiterate and literate patients. International Psychogeriatrics 2013;25(3):402-13. (PMID:23137551).
11. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695-9. (PMID:15817019).

12. Selekler K, Cangoz B, Uluç S. Power of discrimination of Montreal Cognitive Assessment (MOCA) scale in Turkish patients with mild cognitive impairment and Alzheimer's disease. Turkish Journal of Geriatrics 2010;13(3):166-71 (in Turkish).
13. Folstein MF, Folstein S, Mc Hugh PR. "Mini Mental State"º A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98. (PMID:1202204).
14. Güngen C, Ertan T, Eker E, et al. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. Turkish Psychiatry Index 2002;13:273–81. (PMID:12794644).
15. Petersen RC, Smith GE, Waring SC, et al. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56(3):303-8. (PMID:10190820).
16. Morris JC. Revised criteria for mild cognitive impairment may compromise the diagnosis of Alzheimer disease dementia. Arch Neurol 2012;69(6):700–8. (PMID:22312163).
17. Rami L, Molinuevo JL, Sanchez-Valle R, et al.Screening for amnestic mild cognitive impairment and early Alzheimer's disease with M@T (Memory Alteration Test) in the primary care population. Int J Geriatr Psychiatry 2007;22: 294–304. (PMID:16998781).
18. Luck T, Luppa M, Angermeyer MC, et al. Impact of impairment in instrumental activities of daily living and mild cognitive impairment on time to incident dementia: Results of the Leipzig Longitudinal Study of the Aged. Clin Neuropsychol 2009;23(3):446–61. (PMID:20667169).

Turkish Journal of Geriatrics
2014; 17 (2) 152-156

RESEARCH

EFFECTS OF HEARING AIDS ON TINNITUS IN GERIATRIC PATIENTS WITH AGE-RELATED HEARING LOSS

Aydın ACAR[1]
Hasan ŞAHİN[2]
Rauf Oğuzhan KUM[1]
Zeynel ÖZTÜRK[3]
Melih ÇAYÖNÜ[4]
Fulya EKER[1]
Celil GÖÇER[5]

ABSTRACT

Introduction: The aim of this study was to evaluate the effects of hearing aids on tinnitus in elderly patients with presbycusis using the Tinnitus Handicap Inventory.

Materials and Method: Twenty-four elderly patients who were diagnosed with presbycusis and subjective tinnitus between September 2013 and January 2014 were included in this study. The tinnitus handicap inventory questionnaire was completed before a hearing aid was prescribed and then 3 months after using the hearing aid. The effects of the use of hearing aid on tinnitus were assessed by comparing the scores.

Results: A total of 24 patients, 10 females and 14 males were included in the study. Their ages ranged from 65 to 74 years, with a mean of 67.04±2.95. With respect to tinnitus handicap inventory scores, before using hearing aid the mean score was 60.08±11.86, and after 3 months it decreased to 42.33±13.48. This difference was found to be highly significant (p=0.001). For all degrees of hearing loss, the decrease in patients' tinnitus handicap inventory scores after the use of hearing aid was found to be statistically significant (26-40 dB; p=0.007, 41-55 dB; p = 0.018, ≥56 dB; p=0.011).

Conclusion: Among elderly patients with tinnitus and presbycusis, a significant difference was observed in the severity of tinnitus after 3 months of hearing aid use. The results of this study confirm the effectiveness and benefit of fitting hearing aids for tinnitus in elderly patients with presbycusis.

Key Words: Aged; Hearing Aids; Tinnitus; Presbycusis.

ARAŞTIRMA

YAŞA BAĞLI İŞİTME KAYBI OLAN GERİATRİK HASTALARDA İŞİTME CİHAZI KULLANIMININ TİNNİTUS ÜZERİNE OLAN ETKİLERİ

ÖZ

Giriş: Bu çalışmanın amacı yaşa bağlı işitme kaybı olan geriatrik hastalarda işitme cihazı kullanımının tinnitus üzerine olan etkilerini tinnitus engellilik anketi ile araştırmaktır.

Gereç ve Yöntem: Çalışmaya Eylül 2013 Ocak 2014 tarihleri arasında presbiakuzi ve subjektif tinnitus tanısı alan 24 yaşlı hasta alındı. Çalışma prospektif olarak tasarlandı. İşitme cihazı verilmeden önce ve cihaz verildikten 3 ay sonra tinnitus engellilik anketi uygulandı ve sonuçlar karşılaştırıldı. İşitme cihazının tinnitus üzerine olan etkileri araştırıldı.

Bulgular: Çalışmaya katılan hasta sayısı, 10'u kadın ve 14'ü erkek olmak üzere toplam 24 kişidir. Hastaların ortalama yaşı 65-74 aralığında olmak üzere 67,04±2,95 yıldı. İşitme cihazı kullanmadan önce tinnitus engellilik anketi skor ortalaması 60,08±11,86 (aralık 40-80) idi ve işitme cihazı kullandıktan sonra tinnitus engellilik anketi skor ortalaması 42,33±13,48 (aralık 20-66) ye düştü. Tinnitus engellilik anketi skorundaki 17,75 birimlik düşüş, diğer bir ifadeyle düzelme istatiksel olarak ileri derecede anlamlı bulundu (p=0,001). İşitme kaybı derecesine göre işitme cihazı kullandıktan sonra tinnitus engellilik anketi skorlarındaki düşüş istatiksel olarak anlamlı bulundu (26-40 dB; p=0,007, 41-55 dB; p=0,018, ≥ 56 dB; p=0,011).

Sonuç: Tinnitus ve presbiakuzisi olan yaşlı hastalarda 3 ay işitme cihazı kullanımı sonrası tinnitusun olumsuz etkilerinde belirgin azalma izlendi. Bu çalışmanın sonuçları presbiakuzisi olan yaşlı hastalarda işitme cihazı kullanımının tinnitus üzerine etkinliğini kanıtlamıştır. Tinnitus ve işitme kaybı şikayeti olan yaşlı hastalar işitme cihazından fayda görebilir.

Anahtar Sözcükler: Yaşlı; İşitme Cihazı; Tinnitus; Presbiakuzi.

İletişim *(Correspondance)*

Aydın ACAR
Ankara Numune Eğitim ve Araştırma Hastanesi, Kulak Burun Boğaz Kliniği ANKARA

Tlf: 0532 431 36 21
e-posta: acaraydin66@gmail.com

Geliş Tarihi: 18/03/2014
(Received)

Kabul Tarihi: 24/03/2014
(Accepted)

[1] Ankara Numune Eğitim ve Araştırma Hastanesi, Kulak Burun Boğaz Kliniği ANKARA
[2] Ankara Numune Eğitim ve Araştırma Hastanesi, Odyoloji, Kliniği ANKARA
[3] Nişantaşı Üniversitesi Meslek Yüksekokulu, Odyoloji Kliniği İSTANBUL
[4] Amasya Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Anabilim Dalı AMASYA
[5] Lokman Hekim Sincan Hastanesi, Kulak Burun Boğaz Kliniği ANKARA

Introduction

Tinnitus describes the perception of an auditory sensation in the absence of a corresponding external stimulus; it is experienced by approximately 10% of adults in various countries (1). There are several causes of tinnitus, and presbycusis underlies the majority of tinnitus cases (2). Presbycusis can be defined as the hearing loss associated with aging, reflecting the loss of auditory sensitivity.

With improvements in quality of life (QoL) and health care, aging of the population has become a worldwide reality, and therefore presbycusis is increasing and is quite common in the elderly population. Presbycusis and tinnitus not only cause auditory problems, but also affect QoL. Due to the frequent co-existence of tinnitus and hearing loss in the elderly population, there is a need to understand its causes in order to improve prevention and develop appropriate treatments (3,4).

Surgical or medical treatment may be an option for some patients, but there is no certain treatment modality for an individual with hearing loss and tinnitus, so hearing aids (HA) are commonly used for tinnitus management and to help these patients increase their QoL (5).

Several health questionnaires are available that assess the effects of tinnitus, of which the Tinnitus Handicap Inventory (THI) is the most commonly used (6).

The aim of the present study was to evaluate the effects of hearing aids on tinnitus in elderly patients with presbycusis, using the THI.

Materials and Method

Between September 2013 and January 2014, a total of 24 patients who were diagnosed with tinnitus and bilateral symmetrical or asymmetrical sensorineural hearing loss, or mixed hearing loss with sensorineural dominance, through audiometric tests were included in this study. This study was designed prospectively. All patients in this study had sufficient hearing loss to warrant the use of HA, but their primary presenting complaint was tinnitus, rather than hearing loss. All of the patients had had subjective tinnitus for at least 1 year. Patients were not allowed to begin any new medication or other treatments during the study that might have altered progress in either a positive or negative direction. None of the patients had used an HA before. All of the participants were over the age of 65 years. All of them were otherwise healthy and were examined by the same audiologist, and similar hearing aids were recommended to all. The HA was given to the ear with a better speech discrimination score (SDS). In cases of the same SDS scores with both ears, the HA was given to the ear that had a greater conductive hearing loss component. Patients who were diagnosed with Ménière's disease or otosclerosis, or who had objective tinnitus or any mental, neurological, or psychological pathology, were excluded from the study. Twenty-seven patients were enrolled, with 24 completing the study. One patient died during the study, one patient lost his HA and the other patient did not want to continue the study. These patients were excluded from the data analysis.

Patients with average hearing loss had more than a 30 dB loss. Pure-tone audiometric (PTA) evaluation was performed using an AC-40 clinical audiometer (Inter acoustics, Denmark). The SDS test was done using monosyllable phonetically balanced word lists (FD-300). In the audiometric tests, PTA thresholds at 500, 1000, 2000 and 4000 Hz frequencies, and an HA fitting process were applied. The patients were divided into 3 groups (26-40 dB, 41-55 dB and ≥ 56 dB) according to degree of hearing loss (7).

Subjective tinnitus severity was assessed using a standardized outcome measure, the validated Turkish version of the THI (8). The THI is a scale consisting of 25 items requiring an answer of yes (4 points), sometimes (2 points), or no (0 point). Thus, scoring can range from 0 to 100 points. In the original definition, THI scores of 18–36 correspond to "mild handicap", THI scores of 38–56 correspond to "moderate handicap", THI scores of 58–76 correspond to "severe handicap", and THI scores of 78–100 correspond to "catastrophic handicap"(9). The THI questionnaire was completed before an HA was prescribed and also 3 months after using the hearing aid, and the scores were compared to assess the effects of use of HA on tinnitus.

The study was approved by the Local Ethical Committee, No: 2013/691. All participants gave their informed consent prior to their inclusion in the study.

For the statistical analysis, NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) programs were used. Descriptive statistical used were mean, standard deviation, median, frequency, ratio, minimum, and maximum. To compare quantitative data and two groups of parameters that did not show a normal distribution, the Mann Whitney U test was used; to compare three or more groups the Kruskal-Wallis test was used, and to detect the source of differences between groups the Mann Whitney U test was used. The Paired Sample T test was used for within-group comparisons of

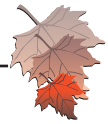


Table 1— Demographic and Descriptive Characteristics of the Patients.

	Min-Max	Mean±sd
Age (years)	65-74	67.04 ± 2.95
Level of Hearing Loss (dB)	34-64	46.79 ± 8.85
		n
Gender	Male	14
	Female	10
Degree of Hearing Loss (dB)	26-40	9
	41-55	7
	≥ 56	8

normally distributed variables, and the Wilcoxon Signed Ranks test for parameters that do not show a normal distribution. The significance level was set at $p<0.01$ for the Wilcoxon Signed Ranks test and paired sample t tests, and at $p<0.05$ for the Mann Whitney U test.

Results

A total of 24 patients, 10 females and 14 males were included in the study. Their age ranged from 65 to 74 years, with a mean of 67.04±2.95 years. General group characteristics and demographic results are given in Table 1. The patients were divided into 3 groups according to their degree of hearing loss: for 26-40 dB, n=9; for 41-55 dB, n=7; for ≥56 dB, n=8. The average degree of hearing loss, averaged over both ears, was 46.79±8.85 dB (range 34-64). With respect to THI scores, before using HA the mean score was 60.08±11.86 (range 40-80), and after 3 months it decreased to 42.33±13.48 (range 20-66). The decrease in THI scores after the use of HA was 17.75 units, which was highly statistically significant (p=0.001) (Table 2).

Though many of the patients localized their tinnitus bilaterally (20 patients), it was localized on the left side in 2 patients and on the right side in 2 patients.

Differences in THI scores before the use of HA varied significantly according to the degree of hearing loss ($p = 0.002$) (Table 3). According to the paired comparisons, the THI scores of patients with a hearing loss ≥ 56 dB were significantly higher than those of patients with a hearing loss of 26-40 dB and 41-55 dB ($p = 0.001$, $p = 0.019$, respectively). There was no significant difference in THI scores between patients with hearing losses of 26-40 dB and 41-55 dB before the use of HA ($p = 0.099$).

Differences in THI scores after the use of HA varied significantly according to the degree of hearing loss ($p=0.001$) (Table 3). According to the paired comparisons, the THI scores of patients with a hearing loss ≥ 56 dB were significantly higher than those of patients with a hearing loss 26-40 dB and 41-55 dB ($p=0.001$, $p = 0.015$, respectively). There was no significant difference in THI scores between patients with hearing losses 26-40 dB and 41-55 dB, after the use of HA ($p = 0.210$).

According to the degree of hearing loss, the decrease in THI scores of patients after the use of HA was found to be statistically significant (26-40 dB, $p=0.007$; 41-55 dB, $p=0.018$; ≥ 56 dB, $p=0.011$) (Table 3).

There was no statistically significant difference between the degree of hearing loss groups (26-40 dB, 41-55 dB, ≥ 56 dB) in THI score changes after the use of HA ($p=0.538$) (Table 3).

There was no statistically significant difference between male and female patients with respect to THI score changes after the use of HA ($p=0.461$).

Discussion

The main findings of this study were that use of HAs for three months led to a significant reduction in tinnitus handicap as measured by the THI, and that HAs can significantly reduce the negative impact of tinnitus on QoL.

Table 2— Assessment of Tinnitus Handicap Inventory (THI) Scores.

		Before Hearing Aid (n=24)	After Hearing Aid (n=24)	p
THI Scores	**18-36 (Mild handicap)**	–	11	
	38-56 (Moderate handicap)	9	8	
	58-100 (Severe handicap)	15	5	
	Min-Max	40-80	20-66	**0.001****
	Mean±sd	60.08 ± 11.86	42.33 ± 13.48	

Paired Sample t Test, **p<0.01.

Table 3— Assessment of Tinnitus Handicap Inventory (THI) Scores According to Degree of Hearing Loss.

		Degree of Hearing Loss			
		26-40 dB (n=9) Mean±sd (Median)	41-55 dB (n=7) Mean±sd (Median)	≥56 dB (n=8) Mean±sd (Median)	[a]p
THI Scores	Before Hearing Aid	50.89±8.55 (48.0)	58.86±9.99 (64.0)	71.50±5.83 (72.0)	**0.002****
	After Hearing Aid	32.22±4.94 (34.0)	39.71±13.03 (44.0)	56.00±8.48 (58.0)	**0.001****
	[b]p	**0.007****	**0.018***	**0.011***	
THI Scores Changes		18.67±7.42 (24.0)	19.14±7.47 (22.0)	15.50±7.15 (14.0)	**0.538**

[a]Kruskal Wallis Test, [b]Wilcoxon Signed Ranks Test, **p<0.01, *p<0.05.

Sensorineural hearing loss and tinnitus in elderly patients result from similar pathological processes (degeneration of nerve fibers in the cochlear ganglion and the cochlear nuclei, atrophy of hair cells in the organ of Corti, impaired blood supply of the spiral ligament and the vascular stripe, atrophy of the spiral ligament and rupture of the cochlear duct) (10). The relationship between tinnitus and hearing loss has been previously demonstrated (11). Some 11% of patients with presbycusis complain of annoying tinnitus (12) and many patients with chronic tinnitus show at least some degree of hearing loss (13). Tinnitus and presbycusis are considered to begin at age 45-55 years, reaching a peak in the mid-60s (14). Tinnitus and presbycusis are difficult therapeutic problems for patients. Tinnitus usually occurs in the poorer hearing ear, and these patients have a significant reduction in communication skills (14). Tinnitus symptoms create distress and negatively affect the quality of life in approximately 4% of the population (15).

Several management procedures have demonstrated relief for tinnitus sufferers, such as HAs (16), tinnitus retraining therapy (17), masking with acoustic stimulation (15) and neuromonics acoustic desensitization (18).

A number of studies have demonstrated relief provided by amplification, and HAs are widely used as part of the clinical treatment of tinnitus (4,11,19). HAs may affect tinnitus audibility through many mechanisms such as auditory signals that can mask or mingle with tinnitus, making it less perceptible, reducing attention towards hearing loss and tinnitus which in turn reduces associated stress and down-regulating central gain by increasing auditory nerve activity (20).

The THI is a reliable test, used to determine the severity of symptoms in patients with tinnitus and for patient follow-up (17). In a recent review of the role of HAs for tinnitus, measures used in the studies included the THI, Tinnitus Handicap Questionnaire and others. The analysis found that a large number of studies support the use of HAs although many of them provide a low level of evidence for the benefits of HA use for tinnitus (4). Surr et al. administered the THI prior to and after the HA fitting and demonstrated a statistically significant reduction in THI scores six weeks post-fitting, stating that some 90% of tinnitus patients may benefit from HA amplification (21). A recent study compared HA use to sound generator use, and the estimated effect on change in tinnitus loudness or severity as measured by the THI score was compatible with benefits for both HAs and sound generators, but no significant difference was found between the two treatments (22). In our study, the mean THI score decreased (improved) from 60.08 to 42.33 after 3 months of using an HA (Table 2). Although a recent study reported that if an HA is programmed for tinnitus it is more beneficial for patients who suffer from tinnitus (23), in our study, HAs were programmed for presbycusis rather than tinnitus and an appropriate improvement was detected in tinnitus with elderly patients who had presbycusis. In addition, some authors have reported that in patients with unilateral sensorineural hearing loss and tinnitus, fitting the impaired ear exclusively was effective, and individuals with bilateral complaints required bilateral fitting (11). However, in our study the patients were fitted only with a unilateral HA. In our study benefit was observed after 3 months of HA use, unlike many other studies which observed maximum benefit after 6 to 12 months of HA use (19).

One of the major risk factors for tinnitus is high-frequency hearing loss (2). Tinnitus usually occurs in the poorer hearing ear, and these patients have a significant reduction in communication skills (14). Some authors reported no correlation between the degree of hearing loss and tinnitus (24). We found a correlation between the degree of hearing loss, as me-

asured with audiometry, and tinnitus. Patients whose level of hearing loss was ≥56 dB, had higher THI scores than patients whose hearing loss was 26-40 dB or 41-55 dB. However, improvement in THI scores at all hearing loss levels was similar, and no significant differences were observed (Table 3). This indicates that with an increase in hearing loss, the QoL of elderly patients with tinnitus decreases, and HAs have similar effects on tinnitus for all levels of hearing loss.

In conclusion, among elderly patients with tinnitus and hearing loss, a significant difference was observed in the severity of tinnitus after 3 months of HA use. Tinnitus sufferers could benefit from HA, and the results of this study confirm the effectiveness of fitting HAs for tinnitus in elderly patients with presbycusis.

Conflict of Interest: The authors declare that they have no conflict of interest.

Acknowledgments: None.

REFERENCES

1. Lockwood AH, Salvi RJ, Burkard RF. Tinnitus. N Engl J Med 2002;347(12):904-10. (PMID:12239260).
2. Hoffman HJ, Reed GW. Epidemiology of tinnitus, In: Snow JB (Ed). Tinnitus: Theory and Management. BC Decker, Ontario 2004, pp 16-41.
3. Henry JA, Dennis KC, Schechter MA. General review of tinnitus: prevalence, mechanisms, effects, and management. J Speech Lang Hear Res 2005;48(5):1204-35. (PMID:16411806).
4. Shekhawat GS, Searchfield GD, Stinear CM. Role of hearing AIDS in tinnitus intervention: a scoping review. J Am Acad Audiol 2013;24(8):747-62. (PMID:24131610).
5. Saltzman M, Ersner MS. A hearing aid for the relief of tinnitus aurium. Laryngoscope 1947;57(5):358-66. (PMID:20241853).
6. Newman CW, Jacobson GP, Spitzer JB. Development of the Tinnitus Handicap Inventory. Arch Otolaryngol Head Neck Surg 1996;122(2):143-8. (PMID:8630207).
7. Clark JG. Uses and abuses of hearing loss classification. Asha 1981;23(7):493-500. (PMID:7052898).
8. Aksoy S, Firat Y, Alpar R. The Tinnitus Handicap Inventory: A study of validity and reliability. Int Tinnitus J 2007;13(2):94-8. (PMID:18229787).
9. Newman CW, Sandridge SA, Jacobson GP. Psychometric adequacy of the Tinnitus Handicap Inventory (THI) for evaluating treatment outcome. J Am Acad Audiol 1998;9(2):153-60. (PMID:9564679).
10. Schuknecht HF, Gacek MR. Cochlear pathology in presbycusis. Ann Otol Rhinol Laryngol 1993;102(1 Pt2):1-16. (PMID:8420477).
11. Zagolski O. Management of tinnitus in patients with presbycusis. Int Tinnitus J 2006;12(2):175-8. (PMID:17260884).
12. Rosenhall U. The influence of ageing on noise-induced hearing loss. Noise Health 2003;5(20):47-53. (PMID:14558892).
13. Ratnayake SA, Jayarajan V, Bartlett J. Could an underlying hearing loss be a significant factor in the handicap caused by tinnitus? Noise Health 2009;11(44):156-60. (PMID:19602769).
14. Shulman A. Specific Etiologies of Tinnitus, The Aging Process, In: Shulman A (Ed). Tinnitus Diagnosis and Treatment. 2 Edition, Lea & Febiger, Philadelphia 1991, pp 382–7.
15. Schaette R, Konig O, Hornig D, Gross M, Kempter R. Acoustic stimulation treatments against tinnitus could be most effective when tinnitus pitch is within the stimulated frequency range. Hear Res 2010;269(1-2):95-101. (PMID:20619332).
16. Baguley D, McFerran D, Hall D. Tinnitus. Lancet 2013;382(9904):1600-7. (PMID:23827090).
17. Jastreboff PJ, Hazell JW. A neurophysiological approach to tinnitus: clinical implications. Br J Audiol 1993;27(1):7-17. (PMID:8339063).
18. Davis PB, Paki B, Hanley PJ. Neuromonics Tinnitus Treatment: Third clinical trial. Ear Hear 2007;28(2):242-59. (PMID:17496674).
19. Searchfield GD, Kaur M, Martin WH. Hearing aids as an adjunct to counseling: tinnitus patients who choose amplification do better than those that don't. Int J Audiol 2010;49(8):574-9. (PMID:20500032).
20. Moffat G, Adjout K, Gallego S, et al. Effects of hearing aid fitting on the perceptual characteristics of tinnitus. Hear Res 2009;254(1-2):82-91. (PMID:19409969).
21. Surr RK, Kolb JA, Cord MT, Garrus NP. Tinnitus Handicap Inventory (THI) as a hearing aid outcome measure. J Am Acad Audiol 1999;10(9):489-95. (PMID:10522622).
22. Hoare DJ, Edmondson-Jones M, Sereda M, Akeroyd MA, Hall D. Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Cochrane Database Syst Rev 2014;1(CD010151. (PMID:24482186).
23. Shekhawat GS, Searchfield GD, Stinear CM. Randomized Trial of Transcranial Direct Current Stimulation and Hearing Aids for Tinnitus Management. Neurorehabil Neural Repair 2013. (PMID:24213961).
24. Ferreira LM, Ramos Junior AN, Mendes EP. Characterization of tinnitus in the elderly and its possible related disorders. Braz J Otorhinolaryngol 2009;75(2):249-55. (PMID:19575111).

Turkish Journal of Geriatrics
2014; 17 (2) 157-163

Çiğdem AYHAN[1]
Öznur BÜYÜKTURAN[2]
Nuray KIRDI[1]
Yavuz YAKUT[1]
Çağatay GÜLER[3]

İletişim *(Correspondance)*

Çiğdem AYHAN
Hacettepe University, Faculty of Health Sciences, Physiotherapy and Rehabilitation ANKARA

Tlf: 0312 305 25 25
e-posta: cayhan@hacettepe.edu.tr

Geliş Tarihi: 12/06/2013
(Received)

Kabul Tarihi: 25/12/2013
(Accepted)

[1] Hacettepe University, Faculty of Health Sciences, Physiotherapy and Rehabilitation ANKARA
[2] Ahi Evran University, School of Physical Therapy and Rehabilitation KIRŞEHİR
[3] Hacettepe University, Faculty of Medicine, Department of Public Health ANKARA

RESEARCH

THE TURKISH VERSION OF THE ACTIVITIES SPECIFIC BALANCE CONFIDENCE (ABC) SCALE: ITS CULTURAL ADAPTATION, VALIDATION AND RELIABILITY IN OLDER ADULTS

ABSTRACT

Introduction: To describe the cultural adaptation of the Turkish Activities Specific Balance Confidence Scale and to examine the factor structure, reliability and validity of the scale in older adults.

Materials and Method: One hundred and six elderly people were recruited in the study. The assessments included the Turkish Activities Specific Balance Confidence Scale, Falls Efficacy Scale, Berg Balance Scale, Mini Mental State Test, Yesavage Geriatric Depression Scale, and Short Form-36 (physical function and mental health subgroups). Outcome measures were conducted twice within 2 weeks (test–retest) for reliability.

Results: The Cronbach's α coefficient was 0.9649 for the test and 0.9648 for the re-test. The Intraclass Correlation Coefficient for the test–retest reliability was 0.997 with 95% confidence interval 0.996–0.998. A strong negative correlation was found between the Turkish Activities Specific Balance Confidence Scale and the Falls Efficacy Scale ($r=-0.835$, $p<0.001$). There were strong positive correlations between the scale and the physical function subgroup of the Short Form-36 ($r=0.614$, $p<0.001$), and the Berg Balance Scale ($r=0.748$, $p<0.001$). No significant correlation was found between the scale and the mental health subgroup of the Short Form-36 ($r=-0.110$, $p=0.262$). Results of a factor analysis conducted on the scale showed evidence of a 2-domain structure.

Conclusion: The Turkish Activities Specific Balance Confidence Scale showed excellent reliability and good validity. It can be suggested that the scale promises to be useful and practical when used with different groups of elderly for the assessment and management of balance confidence.

Key Words: Aged; Accidental Falls, Postural Balance; Fear; Outcome Assessment (Health Care).

ARAŞTIRMA

AKTİVİTEYE ÖZGÜ DENGE GÜVEN ÖLÇEĞİNİN TÜRKÇE VERSİYONU: YAŞLI BİREYLERDE KÜLTÜREL ADAPTASYON, GÜVENİRLİK VE GEÇERLİK ÇALIŞMASI

ÖZ

Giriş: Bu çalışmanın amacı, Aktiviteye Özgü Denge Güven Ölçeğinin Türkçe kültürel adaptasyonunu yapmak ve yaşlı bireylerde faktöriyel yapısını geçerlik ve güvenirlik özelliklerini test etmekti.

Gereç ve Yöntem: Çalışmaya katılmayı kabul eden 106 yaşlı birey dahil edildi. Değerlendirme kapsamında Aktiviteye Özgü Denge Güven Ölçeği, Düşme Etkinlik Ölçeği, Berg Denge Ölçeği, Mini Mental Durum Testi, Geriatrik Depresyon Ölçeği, Kısa Form-36'nın Fiziksel fonksiyon ve Mental sağlık alt başlıkları yer aldı. Ölçekler test-tekrar test güvenirliği değerlendirmek için iki hafta arayla tekrarlandı.

Bulgular: İç tutarlıkta, Cronbach alfa değeri, test için 0.9649, ve tekrar test için 0.9648 olarak belirlendi. Aktiviteye Özgü Denge Güven Ölçeğinin tekrar test güvenirliği (Intraclass Correlation Coefficient) 0,997, % 95 güven aralığı 0,996–0,998 olarak bulundu. Ölçütsel geçerlik yönünden, Aktiviteye Özgü Denge Güven Ölçeği ve Düşme Etkinlik Ölçeği ($r=-0,835$, $p<0,001$) arasında negatif ilişki kaydedildi. Aktiviteye Özgü Denge Güven Ölçeği, Kısa Form-36 Fiziksel fonksiyon alt başlığı ($r=0,614$, $p<0,001$) ve Berg Denge Ölçeği ($r=0,748$, $p<0,001$) arasında pozitif yönde ilişki saptandı. Aktiviteye Özgü Denge Güven Ölçeği ve Kısa Form-36 mental sağlık arasında herhangi bir ilişki ($r=-0,110$, $p=0,262$) saptanmadı. Kullanılan faktör analizi iki faktörün belirlenmesi ile sonuçlandı.

Sonuç: Bu çalışma, Aktiviteye Özgü Denge Güven Ölçeğinin yaşlı bireylerde kabul edilebilir derecede güvenilir ve geçerli olduğunu gösterdi. Aktiviteye Özgü Denge Güven Ölçeği, yaşlı bireylerin denge güven durumunun değerlendirme ve tedavisinde kullanılabilecek yararlı ve kullanımı kolay bir ölçektir.

Anahtar Sözcükler: Yaşlı; Düşmeler; Denge; Korku; Ölçekler.

INTRODUCTION

The occurrence of "fear of falling" (FOF) among non-falling elderly is between 12% and 65%; while it is between 29% and 92% among elderly who have fallen. FOF, which is multifactorial in etiology, may lead to serious physical, psychological and social problems in the elderly (1). Activity restriction, decreased mobility, social isolation, anxiety, and depression are the most important consequences of the FOF (1,2).

In recent years there has been a growing focus on the measurement of FOF in the elderly with a view to developing prevention and rehabilitation management strategies (3). Tinetti (1990) has defined fall-related self-efficacy or balance confidence as people's personal beliefs about their own abilities to perform certain activities (4). The Fall Efficacy Scale (FES) is the first developed scale to be reported in the literature; it focuses on the performance of indoor activities by the elderly. This scale was reported to have a high level of test-retest reliability and internal consistency (5). However, the FES measures only simple indoor activities and does not provide information about more difficult and complex outdoor activities.

The Activity Specific Balance Confidence Scale (ABC) is an alternative scale for assessing FOF, developed by Powell and Myers. The ABC scale was designed to measure subjective balance confidence for both indoor and outdoor activities in ambulatory community-dwelling elderly (6). Up to now, this scale has been translated into many languages (7-14). Previous studies have reported that the ABC scale has good psychometric properties with high internal consistency and test-retest reliability.

The Turkish version of the ABC scale (ABC-T) was used by Karapolat et al. (2010) on patients with unilateral peripheral vestibular diseases, which demonstrated acceptable measurement properties (15). The aim of this study was to produce a cross-cultural adaptation of the scale and to test the psychometric quality of the scale in elderly participants.

MATERIALS AND METHOD

Participants

One hundred and six elderly people who agreed to participate in the study were recruited from hospital units. Inclusion criteria for the study were that participants were over age 65, volunteered for the study, were able to stand independently and unsupported for 90 seconds, and were cognitively able to communicate adequately. Participants whose mother language was not Turkish, who had malignancy, and who had hearing or vision loss were excluded from the study. All participants were asked to sign an informed consent form and were informed about the study prior to its start. The study was approved by the Research Ethics Board.

Demographic data of the participants, including age, gender, history of falls and detailed medical history were recorded at the baseline assessment. All assessments were made during face-to-face interviews including Mini Mental State Test (MMST), Short Form 36 (SF-36) Mental Health subgroup and Yesavage Geriatric Depression Scale (GDS). Balance-related assessments included ABC scale, FES, Berg Balance Scale (BBS) and SF-36 Physical Function subgroup. ABC, FES, BBS, GDS and SF-36 tests were made twice within 2 weeks. All assessments were completed on the same day.

Activity Specific Balance Confidence Scale (ABC)

The ABC scale was developed by Powell and Myers. This scale contains 16 tasks related to indoor and outdoor daily living activities, to measure balance confidence in elderly people who have various levels of functioning. Scores range from 0% (no confidence) to 100% (complete confidence) for each question item. Higher scores indicate greater confidence (6).

The cross-cultural adaptation process of the ABC scale was performed by following the guidelines provided by Beaton et al (16). Those guidelines are as follows: First, two independent translators performed the forward translations from English to Turkish. The translations were compared and discrepancies were resolved. Second, bilingual translators, whose mother language was English, back translated the same version. Although one of the translators was aware of the study, the other translator was not aware of it. Third, the two back-translations were synthesized by the authors to achieve a consensus. Finally, a second meeting was held with participation of all the interested professionals. This team reviewed the English and Turkish versions of the translations to control for and pinpoint possible meaning differences and inconsistencies. A final version was established and field tested on 30 elderly adults after a number of slight corrections and changes by consensus.

Mini Mental State Test (MMST)

The MMST evaluates the cognitive status of the elderly. It contained seven domains, each with an assigned point value totaling 30. MMST scores higher than or equal to 24 were considered as normal cognitive function, while scores lower

than 24 indicated cognitive impairment. Low MMST scores have also been associated with an increased fall risk in elderly adults (17).

Yesavage Geriatric Depression Scale (GDS)

The GDS consists of 30 questions to be answered as "yes" or "no", with a maximum score of 30 points. The Turkish version of the GDS was used in this study. GDS scores equal to or higher than 6 were considered to indicate clinically significant depression (18).

Berg Balance Scale (BBS)

The BBS is a 14-item scale that measures sitting, standing and postural changes while performing tasks. Each task is scored from 0 points to 4 points. Higher scores indicate better balance control. Scores of 0-20 indicate a high fall risk, 21-40 indicates a medium fall risk, and 41-56 indicates a low fall risk (19).

Tinetti Falls Efficacy Scale (FES)

The FES was designed to assess the level of self-perceived FOF during the performance of daily living activities by the elderly. The FES consists of 10 simple indoor activities rated on a 10-point scale. The scores are summed to give a total score ranging from 10 to 100 points, where lower scores indicate a low level of confidence. Tinetti reported a test-retest reliability for the FES in a community-based elderly population of r=0.71 (5).

Short Form-36 Quality of Life Questionnaire

The SF-36 was developed by the RAND Corporation and the Medical Outcomes Study (20). SF-36 has eight subgroups with a total of 36 questions. The Turkish version of the SF-36 has shown acceptable measurement properties (21). "Physical Function" and "Mental Health" subtests of the SF-36 were used in this study. Higher scores indicate higher levels of health.

Falls

A fall history was obtained from the responses to the question "How many times did you fall during the past year?" (22). Falls were recorded as numbers.

Statistical Analysis

All analyses were conducted using the Statistical Package for the Social Sciences 15.00 (SPSS Inc., Chicago, USA). The variables were expressed in terms of arithmetic means (X) and standard deviation (SD) values. The critical level of significance was set at $p<0.05$.

The psychometric properties of the ABC scale were evaluated in terms of reliability and validity. Test-retest reliability was determined by calculating the intraclass correlation coefficient (ICC), which shows the strength of agreement. ICC values are defined as fair (<0.40), moderate (0.40-0.59), substantial (0.60-0.79), and excellent (≥0.80). Internal consistency, which means that all items of the scale measure aspects of a single construct, was assessed using Cronbach's alpha, which is expected to be above 0.70. A Pearson correlation coefficient was used to assess the strength of the linear relationships. (23)

Concurrent convergent validity refers to the extent to which an instrument correlates with other measures of the same construct, which it is theoretically predicted to correlate with. Concurrent convergent validity of the ABC scale with other measures was estimated using Pearson's correlation coefficient. The correlation between the ABC scale and the FES (taken as a criterion variable), which is referred as criterion validity, was performed. Construct validity was evaluated by the principal component and factor analysis method.

RESULTS

One hundred and six elderly people between the ages of 65 and 88, with an average of 69.52±5.17 years, were included in the study as subjects, of which 49 (46%) were females and 57 (54%) were males. Demographic data of the participants are shown in Table 1. The scores on the FSS, MSS, GDS and FES are also shown in Table 1.

Content Equivalence of ABC-T Scale: Three of the 16 items on the ABC scale were found to be culturally irrelevant due to differences in the physical living environment and climate in Turkey. First, in item 4 we used the term "height level" instead of "eye level". This is a more common expression in Turkey. In item 8, "to a car parked in the driveway" was modified as "to the street", as most elderly people do not use a car for transportation in Turkey, and they usually live in a house without a driveway. In item 16 we replaced "icy sidewalks" with "slippery sidewalks" because of the climate of Turkey. The three modified questions are summarized in Table 2.

Reliability: The Cronbach's α coefficients for the ABC Scale were 0.9649 for the test and 0.9648 for the re-test, which indicated a higher internal consistency than was expected. Item-total correlations for all items ranged from 0.578 to



Table 1— Demographic Characteristics of the Participants.

	Participants (n=106)
Age (years) (X±SD)	69.52±5.17
65-74 (n (%))	88 (83.0)
75-84 (n (%))	17 (16.0)
85< (n (%))	1 (1.0)
Height (cm) (X±SD)	165.34±8.99
Body weight (kg) (X±SD)	77.03±12.81
Body Mass Index (kg/m2) (X±SD)	28.31±5.23
MMST (0-30) (X±SD)	29.76±0.43
Falls during twelve months (n (%))	
Non fallers	48 (45.3)
Fallers	
1 time	25(23.6)
2 times	16 15.1)
3 times	8 (7.5)
4 times	9 (8.5)
ABC (0-100)	86.97±22
BBS (0-56)	53.91±3.71
FSS (0-100)	47.38±12.96
MSS (0-100)	46.17±6.78
GDS (0-30)	3.14±2.56
FES (10-100)	23.75±21.49

MMST: Mini Mental State Test, BBS: Berg Balance Scale, FSS: Physical function subgroup of SF-36, MSS: Mental health subgroup of SF-36, GDS: Geriatric Depression Scale, FES: Falls Efficacy Scale.

0.894, which demonstrates moderately strong evidence (Table 3). The ICC for the test–retest reliability of the ABC Scale was 0.997, with a 95% confidence interval (CI) 0.996–0.998, which suggested reasonably high test-retest reliability for the ABC Scale (Table 3). The ICC values for individual items ranged from 0.962 to 0.999, with the highest ICC value for item 15 (Step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing) and the lowest value for item 2 (Walk up or down stairs) (Table 3).

Convergent Validity: The total score of the ABC scale was negatively correlated with a history of falls (r=-0.770, p<0.001). There were high positive correlations between ABC scores and the physical function subgroup score of the SF-36 (r=0.614, p<0.001), and the BBS (r=0.748, p<0.001). There was no significant correlation between ABC scores and the mental health subgroup score of SF-36 (r=-0.110, p=0.262).

Criterion Validity: There was a high negative correlation between ABC scores and FES scores (r=-0.835, p<0.001).

Table 2— Results of the Cultural Adaptation of the ABC Scale.

Original Items of The ABC Scale	Modified items of the ABC-T Scale
4. Reach for a small can off a shelf at eye level?	Reach for a small can off a shelf at height level?
8. Walk outside the house to a car parked in the driveway?	Walk outside the house to the street?
16. Walk outside on icy sidewalks?	Walk outside on slippery sidewalks?

Construct Validity: The ABC scale was factor analyzed using principal component analysis with Varimax (orthogonal) rotation. The Kaiser–Meyer Olkin value was 0.849, p=0.000, which suggested that the sample was factorable. Chi-square was 2514.168 (120 degrees of freedom, p<0.001) in Bartlett's test of sphericity, indicating that the correlation matrix was an identity matrix. The analysis yielded two factors, explaining a total matrix variance of 78.629% (Table 4). The factor analysis was performed without imposing any preconceived structure on the outcome. Two factors were extracted, as was estimated in the theoretical phase. Seven items, numbers 7,11,12,13,14,15,16, were loaded onto Factor 1. This factor was labeled "Attentional demands activities" and explained 68.651% of the variance (Table 4). Factor 2 was labeled "Simple demands activities" due to high loadings on tasks numbered 1,2,3,4,5,6,8,9,10. This factor explained 9.978% of the variance (Table 4).

Discussion

Balance confidence is an important issue among the elderly population in terms of functional mobility, participation and personal well-being. The present study investigated the psychometric properties and factorial analysis of the ABC-Tin elderly participants. The results of the study indicate that the Turkish ABC scale has strong measurement properties, which make it a reliable and valid instrument for research and practice.

Test-retest reliability indicates whether the items of the ABC scale measure a single construct or not. In the original study, test–retest reliability of the ABC Scale in community dwelling older people was high (ICC=0.92). Similarly, in other studies performed on elderly adults, the ICC values ranged from 0.73 to 0.98. Test-retest reliability was found to vary between 0.67 to 0.92 in the Turkish version of the scale. In this study, the ABC scale has high test-retest reliability

Table 3— Test-retest Reliability and Item Total Correlations of the Turkish Version of the ABC Scale.

	r	ICC	95% CI	
			Lower	Upper
1. Walk around the house?	0.887*	0.970	0.9562	0.9795
2. Walk up or down stairs?	0.875*	0.962	0.9449	0.9741
3. Bend over and pick up a slipper from the front of a closet floor?	0.821*	0.987	0.9817	0.9915
4. Reach for a small can off a shelf at height level?	0.578*	0.993	0.9911	0.9958
5. Stand on your tiptoes and reach for something above your head?	0.817*	9.985	0.9785	0.9900
6. Stand on a chair and reach for something?	0.817*	0.997	0.9957	0.9980
7. Sweep the floor?	0.811*	0.998	0.9978	0.9990
8. Walk outside the house to the street?	0.870*	0.998	0.9974	0.9988
9. Get into or out of a car?	0.853*	0.987	0.9815	0.9913
10. Walk across a parking lot to the mall?	0.894*	0.989	0.9843	0.9927
11. Walk up or down a ramp?	0.890*	0.994	0.9919	0.9962
12. Walk in a crowded mall where people rapidly walk past you?	0.843	0.997	0.9967	0.9985
13. Are bumped into by people as you walk through the mall?	0.891*	0.998	0.9983	0.9992
14. Step onto or off of an escalator while holding onto a railing?	0.790*	0.993	0.9911	0.9958
15. Step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing?	0.746*	0.999	0.9985	0.9993
16. Walk outside on slippery sidewalks?	0.806*	0.993	0.9897	0.9952
Total		0.997	0.9967	0.998

r , Pearson correlation coefficient, item-total correlation
*p<0.001
ICC, intraclass correlation coefficient
CI, Confidence interval

Table 4— Varimax Rotated 2-Factor Solution of the ABC Scale.

Item nb.	Factor loadings of Factor 1 Attentional Demands Activities	Factor loadings of Factor 2 Simple Demands Activities
15	0.936	0.083
13	0.852	0.381
16	0.839	0.263
11	0.820	0.417
14	0.773	0.330
12	0.742	0.444
7	0.697	0.424
4	-0.042	0.921
3	0.343	0.852
1	0.484	0.787
2	0.466	0.781
10	0.577	0.710
6	0.477	0.663
8	0.588	0.653
9	0.587	0.636
5	0.569	0.606

The total percentage of matrix variance is 78.629.

(ranged from 0.962 to 0.999), similar to that found in other studies performed with the community dwelling elderly.

The ABC scale has shown high internal consistency with community-dwelling older people in previous studies (6,8-12). The Cronbach's alpha of Turkish version of ABC scale performed in patients with unilateral peripheral vestibular dysfunction also showed high internal consistency with a value of 0.95 (15). In line with the previous studies the Turkish ABC scale showed high internal consistency in older adults in this study.

Results of the factor analysis in the Chinese Cantonese version of the ABC scale showed evidence of a coherent 1-domain structure (11); however, two factors were extracted in the Chinese Mandarin version (12). Botner et al. also calculated 2 factors that were labeled according to the levels of perceived risk (24). Similarly, in this study two factors were extracted. The first factor, which was labeled "attentional demands activities", mostly, included difficult outdoor activities. The second factor, which was labeled "simple demands activities", included simple activities. Tasks such as walking outside on icy sidewalks, walking up or down a ramp, stepping onto or off an escalator, etc. need more postural control with respect to the difficulty of the task, environmental influences and unstable sensory information. The attentional demands of balance control vary according to the complexity of the situation. Balance control in the elderly, following an external perturbation, requires more attention than it does for younger adults; hence, increased attentional requirements of certain activities could affect task execution (25).

In the study by Karapolat, significant correlation was observed between the Turkish ABC scale and, Dizziness Handicap Inventory but no correlation was found with the other tests including various balance and gait outcome measures. The lack of correlation was explained with the balance problems in patients with peripheral vestibular disease (15). However, the ABC scale demonstrated good convergent and criterion validity in community dwelling older people. The original scale and the French Canadian version of the scale, used among people with stroke, showed a moderate level of correlation with BBS comfortable and maximum gait speeds, Time Up and Go Test (TUG), 6 Minutes Walking Test (6MWT), the Barthel Index and the GDS (13). Concurrent validity between the ABC and the physical performance tests and self-reported health status were significant. Thus, it was suggested that the scale might be used for rehabilitation targeting to improve physical function. Similarly, in this study there was a positive correlation between ABC scores and the physical function subgroup of the SF-36 ($r=0.614$, $p<0.001$); BBS ($r=0.748$, $p<0.001$); and FES ($r=-0.835$, $p<0.001$). In addition, there was a significant difference in the German version of the ABC scores between the fallers and non-fallers, the fallers having lower scores than the non-fallers (10). In this study, a significant correlation was found between scores on the ABC scale and the patient's history of falls ($r=-0.770$, $p<0.001$).

Divergent validity was established by correlating the ABC and mental health subgroup scores of the SF-36 in a study of Ylva (14). No significant correlation between these scores ($r=-0.110$, $p=0.262$) was found.

The incidence of balance problems and falls in the elderly is associated with the severity of FOF. Therefore, the measurement of FOF should be complementary to geriatric assessments with respect to fall management. This study analyzed the psychometric qualities of the ABC-Tin terms of reliability, validity and factorial structure. The results showed that the scale had excellent reliability and good validity. In conclusion, the ABC-T appears to be a promising tool to use with different elderly groups for the assessment and management of balance confidence.

REFERENCES

1. Legters K. Fear of falling. Phys Ther 2002;82:264-72. (PMID:11869155).
2. Fletcher PC and Hirdes JP. Restriction in activity associated with fear of falling among community-based seniors using home care services. Age Ageing 2004;33:273-9. (PMID:15082433).
3. Jorstad EC, Hauer K, Becker C, Lamb SE. Measuring the psychological outcomes of falling: a systematic review. J Am Geriatr Soc 2005;53:501-10. (PMID:15743297).
4. Tinetti ME, Richman D, Powell L. Falls efficacy as a measure of fear of falling. J Gerontol 1990;45:239-43. (PMID:2229948).
5. Tinetti ME, Powell L. Fear of falling and low self-efficacy: A cause of dependence in elderly persons. J Gerontol 1993;48:35-8. (PMID:8409238).
6. Powell LE, Myers AM. The Activities-specific Balance Confidence (ABC) Scale. J Gerontol A Biol Sci Med Sci 1995;50:28-34. (PMID:7814786).
7. Parry SW, Steen N, Galloway SR, Kenny RA, Bond J. Falls and confidence related quality of life outcome measures in an older British cohort. Postgrad Med J 2001;77:103-8. (PMID:11161077).
8. van Heuvelen MJ, Hochstenbach J, de Greef MH, Brouwer WH, Mulder T, Scherder E. Is the Activities-specific Balance Confidence Scale suitable for Dutch older persons living in the community? Tijdschr Gerontol Geriatr 2005;36(4):146-54. (PMID:16194061).

9. Schott N. German adaptation of the Activities-specific Balance Confidence (ABC) scale for the assessment of falls-related self-efficacy. Z Gerontol Geriatr 2008;41(6):475-85. (PMID:18327692).
10. Mak KM, Lau AL, Law FS, Cheung CC, Wong SI. Validation of the Chinese translated Activity-Specific Balance Confidence Scale. Arch Phys Med Rehabil 2007;88:496-503. (PMID:17398252).
11. Guan Q, Han H, Li Y, Zhao L, Jin L, Zhan Q. Activity-specific Balance Confidence (ABC) Scale adapted for mainland population of China. Clin Rehabil 2011;26(7):648-55. (PMID:22169829).
12. Salbach NM, Mayo NE, Hanley JA, Richards CL, Wood-Dauphinee S. Psychometric evaluation of the original and Canadian French version of the activities-specific balance confidence scale among people with stroke. Arch Phys Med Rehabil 2006;87(12):1597-604. (PMID:17141639).
13. Ylva N, Anette F. Psychometric properties of the Activities-Specific Balance Confidence Scale in persons 0-14 days and 3 months post stroke. Disabil Rehabil 2012;34(14):1186-91. (PMID:22148983).
14. Arnadottir SA, Lundin-Olsson L, Gunnarsdottir ED, Fisher AG. Application of rasch analysis to examine psychometric aspects of the activities-specific balance confidence scale when used in a new cultural context. Arch Phys Med Rehabil 2010;91(1):156-63. (PMID:20103411).
15. Karapolat H, Eyigor S, Kirazli Y, Celebisoy N, Bilgen C, Kirazli T. Reliability, validity, and sensitivity to change of Turkish Activities-specific Balance Confidence Scale in patients with unilateral peripheral vestibular disease. Int J Rehabil Res 2010;33(1):12-8. (PMID:20183891).
16. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000;25(24):3186-3191. (PMID:11124735).
17. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild demantia in Turkish population. Turk Psikiyatri Derg 2002 Winter; 13(4):273-81. (PMID:12794644).
18. Ertan T, Eker E. Reliability, validity and factor structure of the Geriatric Depression Scale in Turkish elderly: Are their different factor structure for different cultures? Int Psychogeriat 2000;12:163-72. (PMID:10937537).
19. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument Can J Public Health 1992;83 Suppl 2:7-11. (PMID:1468055).
20. Ware JE, Sherbourne CD. The MOS 36-item short form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83. (PMID:1593914).
21. Kocyigit H, Aydemir O, Fisek G, Olmez N, Memis A. Validity and reliability of Turkish version of Short form 36. Journal of Drug and Therapy 1999,12:102-6 (in Turkish).
22. Anstey KJ, vond Sanden C, Luszcz MA. An 8 year prospective study of the relationship between cognitive performance and falling in very old adults. J Am Geriatr Soc 2006;54(8):1169-76. (PMID:16913981).
23. Deyo RA, Diehr P, Patrick DL. Reproducibility and responsiveness of health status measures statistics and strategies for evaluation. Control Clin Trials 1991;12(4):142-58. (PMID:1663851).
24. Botner EM, Miller WC, Eng JJ. Measurement properties of the Activities-specific Balance Confidence Scale among individuals with stroke. Disabil Reh 2005;27(4):156-63. (PMID:15824045).
25. Brown LA, Shumway-Cook A, Woollacott MH. Attentional demands and postural recovery: The effects of aging. J Gerontol A Biol Sci Med 1999;54(4):165-71. (PMID:10219006).

Turkish Journal of Geriatrics
2014; 17 (2) 164-171

Ezgi MUTLUAY[1]
Sabire YUTSEVER[2]

RESEARCH

CHRONIC PAIN AND ANXIETY IN GERIATRIC CANCER PATIENTS

ABSTRACT

Introduction: This paper aims to determine the chronic pain and anxiety of geriatric cancer patients.

Materials and Method: This was a descriptive study of 106 patients aged 65 or over who had been diagnosed with cancer. Study data were collected using a Personal Information Form, the McGill Pain Questionnaire to define pain characteristics, and the State-Trait Anxiety Inventory.

Results: Average patient age was 70.16, 79.2% being between 65 and 74; 54.7% were male; 55.7% were literate or had finished elementary school; 63.2% lived with their spouses. Pain medication was used by 90.6%, while all patients reported that their pain did affect their activities of daily living. The pain level was found to be significantly higher in patients who experienced vomiting due to chemotherapy or radiation therapy frequently or occasionally, and in patients who reported that feeding, mobility, eating, housekeeping/gardening and sleeping among their activities of daily living were severely affected ($p<0.05$). State-Trait Anxiety Inventory scores were higher in patients who experienced anorexia or diarrhea/constipation frequently, those who experienced continuous pain during the day, and those who reported their feeding, mobility, housekeeping/gardening activities of daily living to be severely affected ($p<0.05$). A positive correlation was found between the frequency of pain and the patients' trait anxiety levels ($p<0.01$).

Conclusion: A negative influence of pain on the activities of daily living and anxiety level of the elderly was established; the anxiety level increased in parallel with the pain.

Key Words: Geriatrics; Cancer; Chronic Pain; Anxiety.

ARAŞTIRMA

GERİATRİK KANSER HASTALARINDA KRONİK AĞRI VE KAYGI

ÖZ

Giriş: Bu çalışmanın amacı geriatrik kanser hastalarında kronik ağrı ve kaygı durumlarının belirlenmesidir.

Gereç ve Yöntem: Araştırma, tanımlayıcı nitelikte olup, araştırma kapsamına kanseri tanısı alan 65 yaş ve üzeri 106 hasta alınmıştır. Araştırmanın verileri, hastaların tanıtıcı bilgilerini içeren "Kişisel Bilgi Formu", hastaların ağrı özelliklerini belirlemek amacıyla "McGill Ağrı Soru Formu" ve hastaların kaygı düzeylerini belirlemek amacıyla "Durumluk ve Sürekli Kaygı Envanteri" kullanılarak toplanmıştır.

Bulgular: Çalışma kapsamına alınan hastaların yaş ortalamaları 70,16 olup, %79,2'si 65-74 yaş arasında idi. Hastaların %54,7'si erkek, %55,7'si okuryazar/ilköğretim mezunu ve %63,2'si eşi ile birlikte yaşamakta idi. Hastaların %90,6'sının ağrı tedavisi aldığı ve hastaların tümü deneyimledikleri ağrının günlük yaşam aktivitelerini etkilediğini belirtmişlerdir. Hastalık süresi beş yıldan fazla olan, kemoterapi/radyoterapi nedeni ile "sık sık" ya da "bazen" bulantı-kusma yaşayan, Günlük Yaşam Aktivitelerinden beslenme, hareket, yemek, ev / bahçe işleri ve uyku aktivitelerinin "çok" etkilendiğini belirten hastaların ağrı düzeylerinin daha yüksek olduğu saptanmıştır ($p<0,05$). Araştırmada "sık sık" iştahsızlık ve "sık sık" diyare-konstipasyon yaşayan, gün içinde "sürekli" ağrı deneyimleyen, ağrı nedeniyle Günlük Yaşam Aktivitelerinden beslenme, hareket, ev / bahçe işleri aktivitelerinin "çok" etkilendiğini ifade eden hastaların Durumluk ve Sürekli Kaygı Envanteri ölçek puan ortalamaları daha yüksek bulunmuştur ($p<0,05$). Hastaların ağrı sıklıkları ile durumluk sürekli kaygı düzeyleri arasında pozitif yönde anlamlı bir ilişki olduğu saptanmıştır ($p<0,01$).

Sonuç: Yaşanılan ağrının yaşlıların günlük yaşam aktivitelerini ve kaygı düzeylerini olumsuz yönde etkilediği, ağrı düzeyi arttıkça anksiyete düzeyinin arttığı belirlenmiştir.

Anahtar Sözcükler: Geriatrik; Kanser; Kronik Ağrı, Anksiyete.

İletişim *(Correspondance)*

Ezgi MUTLUAY
Hacettepe Üniversitesi, Hemşirelik Fakültesi ANKARA

Tlf: 0530 382 72 69
e-posta: ezgimutluayezgi@hotmail.com

Geliş Tarihi: 30/12/2013
(Received)

Kabul Tarihi: 05/03/2014
(Accepted)

[1] Hacettepe Üniversitesi, Hemşirelik Fakültesi ANKARA
[2] Mersin Üniversitesi, Sağlık Yüksekokulu MERSİN

Introduction

A diagnosis of cancer affects the individual from the biopsychosocial viewpoint, leading to a number of disturbing symptoms, the principal among them being pain and anxiety. Continuous, refractory or untreated cancer pain may negatively affect every aspect of the patient's life (1). Pain, the most widely experienced symptom among cancer patients, may negatively influence the individual's ADL and quality of life. Defining the incidence of pain is difficult due to its being a subjective complaint. Taking into account all types and stages of cancer, the incidence of cancer pain is reported to be between 40 and 80% (2, 3). Prevalence rates for pain were reported as 28% in recently diagnosed cancer patients, 50-70% in those actively given cancer therapy, and 64-80% among patients with advanced-stage cancer (4). Studies have shown pain to be particularly frequent among elderly cancer patients (5-7). Pain also adversely affects the ADL of elderly cancer patients (8). One study has indicated that pain negatively affected movement in 69.1%, sleep habits in 63.6%, nutrition in 27.3% of elderly patients (9).

The cognitive components of pain include the importance attributed by the individual to the disease symptoms, believing that it will be impossible to control the pain, and the anxiety in the course of the disease (10). The cancer diagnosis is the most important source of anxiety for patients, due to the life-threatening, chronic and lethal character of the disease, in addition to its being a major problem that elicits emotional, mental and behavioral reactions (11,12). In elderly patients with cancer, the appearance of regression and insufficiencies in biological, physiological and psychological processes, the loss of professional efficiency, and the increased dependency for one's ADL are additional anxiety factors that reduce the patients' quality of life by affecting their anxiety level and psychological condition (8,13). Anxiety incidence is reported to be more than 50%, chronic anxiety being present in about 30% of cancer patients (14).

Cancer may cause emotional distress and negative thoughts. Pain may also be considered a harbinger of situations such everything going wrong, that the disease is not responding to treatment or of approaching death. Thus, the anxiety seen in most cancer patients is a factor further intensifying cancer pain (15). Studies have shown the experience of pain to be particularly frequent among elderly cancer patients (5-7,16), who according to other reports frequently experience anxiety (5,17-19).

Among cancer patients, especially the elderly, pain negatively affects the individual's life, causing fear, anger and anxiety. It is hypothesized that the individual patient's fear and anxiety may be reduced by controlling pain. Control of pain therefore assumes a major significance in maintaining physiological, psychological and spiritual well-being and improving quality of life. Defining and evaluating pain and anxiety levels in the aged patient is important for the treatment procedures and the quality of life.

Materials and Method

Participants

This cross-sectional study was conducted between December 1, 2010 and May 31, 2011 at the Mersin University Health Research and Implementation Center 1st Internal Medicine Department and Outpatient Chemotherapy Unit, and at the Mersin State Hospital Outpatient Chemotherapy Unit, Medical Oncology Department and Radiation Oncology Department. During this period, 123 patients aged 65 or above presented at the mentioned clinics.

Inclusion criteria were as follows:

- Age 65 or older,
- Chronic pain for three months or longer,
- Physical and cognitive capacity sufficient to answer the forms used in the study,
- Absence of pain only during the data collection,
- Voluntary participation in the study.

A total of 106 patients responding to the eligibility criteria were recruited into the study.

Instruments

Study data were collected using a Personal Information Form for personal characteristics, the McGill Pain Questionnaire (MPQ) to define the pain characteristics, and the State-Trait Anxiety Inventory (STAI) to evaluate the patients' anxiety levels.

The Personal Information Form was developed, after an extensive literature search, to collect certain sociodemographic data and characteristics related to disease and treatment, which were considered to possibly affect the patients' pain and anxiety (4, 17-20). This form contained ten questions regarding sociodemographic characteristics (such as sex, age, marital status, educational level, financial condition, household members, etc.) and ten other questions regarding disease and treatment characteristics (such as disease duration, treatment methods, concomitant disease, etc.)

The MPQ was developed in 1971 by Melzack and Torgerson (21) and the study of its validity and reliability for our country was conducted by Kuğuoğlu et al. (22). The MPQ consists of four parts. In the first part, the patient is invited to mark the location of the pain on a drawing. The second part contains 20 sets of words to assess the pain from the sensory, affective and evaluative aspects. The third part contains word groups to assess the pain duration and frequency and the factors that intensify or reduce it. The fourth part contains five word groups covering pain intensities from mild to excruciating and, separately, six questions to characterize the level of pain "one can live with" or "target pain level", i.e., a pain level that the patient can tolerate or live with without being incapacitated (22).

The State-Trait Anxiety Inventory (STAI-I and STAI-II) was developed in 1970 by Spielberger et al. to evaluate state anxiety and trait anxiety levels separately from each other. Its validity and reliability for Turkey was assessed by Öner and Le Compte (23). Each of the two scales of this self-report assessment consists of 20 questions, to evaluate state anxiety and trait anxiety. The total score increases along with the anxiety level of the person answering the questionnaire (23).

Data Collection

Necessary Ethical Committee approvals and institutional authorizations were obtained before starting data collection. The patients were informed about the objective of the study and their consent obtained. Considering the frequent impairment of eyesight and generally low level of literacy among elderly patients, the questions were asked orally by the investigator. The individual time to answer questionnaires ranged from 5 to 10 minutes for the Personal Information Form, 10-15 minutes for the MPQ and 15-25 minutes for the STAI. The disease diagnosis, concomitant chronic disease, treatment cycle or radiation session numbers were obtained from the patients' medical records.

Statistical Evaluation

We confirmed the normality of scores of McGill Pain Questionnaire (MPQ) and The State-Trait Anxiety Inventory with Shapiro and Wilks normality test. Student's t-test and one-way analysis of variance (ANOVA) were used to compare the different scores according to demographic characteristics. Correlations between scores were tested by Pearson's correlation analysis. Pairwise comparison by the Least Significant Difference (LSD) test was applied for significant differences. Means and standard deviations were used as descriptive statistics. The limit for statistical significance was accepted as a p-value <0.05.

Results

Of the patients in the study, 79.2% were aged 65-74; 54.7% were male, 55.7% were literate or had finished elementary school; 83.0% were not gainfully occupied. While 77.4% were part of a nuclear family, 56.6% had an income lower than their expenses (Table 1). No statistically significant differences according to the various socio-demographic characteristics could be identified for the MPQ and STAI scores.

Time since diagnosis was shorter than a year in 48.1% of patients. MPQ sub-dimension scores and total score means in patients with a disease duration longer than five years were higher than in patients diagnosed less than a year ago ($p<0.05$). Another, concomitant, chronic disease was present in 62.3% of the cases. Patients reported "feeling sick" in a proportion of 71.7%. The MPQ sensory, affective and mixed sub-dimension scores and total scores were found to be higher in those patients who felt "very sick" compared to those who reported feeling "sick" ($p<0.05$).

Table 1— Sociodemographic Characteristics of the Patients.

Sociodemographic Characteristics	n	%
Age		
65-74	84	22.0
75 and over	79.2	20.8
Gender		
Female	48	45.3
Male	58	54.7
Education status		
Iliterate	37	34.9
Literate /primaryeducation	59	55.7
High school/graduate/undergraduate	10	9.4
Work status		
Working	18	17.0
Unemployed	88	83.0
Family type		
Extended family	24	22.6
Nuclear family	82	77.4
Income status		
Low income	60	56.6
Income equal to expenses	46	43.4

Patients reported very frequently experiencing the following: nausea/vomiting in 53.9%, loss of appetite in 76.4% and diarrhea/constipation in 46.1%. Statistically significant differences were found in the MPQ total score as well as sensory, affective and mixed sub-dimension scores according to the frequency of experienced nausea/vomiting episodes ($p<0.05$). The STAI showed a significant difference according to the frequency of anorexia ($p<0.05$). The MPQ score of patients who experienced "frequent" diarrhea/constipation was higher than that of patients who had it "rarely" ($p<0.05$) (Table 2).

The mean duration of the painful condition was 9.18±10.49 months (range 3-60); 12.3% of patients described its frequency as "continuous" and 55.7% as "several times daily". The MPQ total score and sub-dimension and the STAI score of patients who experienced "continuous" pain throughout the day were found to be higher than those of patients who described its frequency as "several times weekly" ($p<0.05$). "Any time during the day" was the description of the timing of pain for 66% of patients. The MPQ total score and mixed and evaluative sub-dimension score means were higher for patients who described the timing of pain as "at noon and in the afternoon", or "mornings and evenings" compared to those who experienced pain "anytime in the day" ($p<0.05$). The STAI score average of patients experiencing pain predominantly "mornings and evenings" was also higher than for the three other groups ($p<0.05$). Pain was felt as being "deep" by 42.5%, "superficial" by 9.4% and "both deep and superficial" by 48.1% of the patients. The difference among these groups was statistically significant ($p<0.05$) (Table 3).

The overall pain level of patients was moderate and their anxiety level high (Table 4). Both total and sub-dimension MPQ scores were positively correlated with their STAI scores ($p<0.001$) (Table 5).

Discussion

The overall pain level of patients in our study was moderate and their anxiety level high (Table 4). A parallel correlation was established between the patients' pain and anxiety mean scores. Studies have shown the experience of pain to be particularly frequent among elderly cancer patients, as it was in our study (5-7,16,17). Our literature search failed, however, to discover a study exploring the correlation between pain and anxiety in geriatric cancer patients.

The perception of pain may be affected by the age-related impairment of nerve conduction velocity and opioid receptor density, invasive interventions for the diagnosis and treatment of cancer, tumor infiltration, insufficient frequency of pain evaluation, anxiety about opioid addiction, neglect of pain treatment as a priority, social isolation related to the diagnosis and negative experiences related to pain (24,25). Age-related factors that may increase the elderly patient's anxiety level include the increased incidence of chronic disease, the loss of friends and relatives, the loss of a social role, difficulties in coping with ADL, fear of death, fear of known or unknown aspects of cancer, anxiety about the future, the thought that therapy is not working, the length of treatment, the adverse effects of both disease and treatment, social isolation and insufficient social support (13,17,26). It may also be said that, in addition to the above, the experience of pain adversely influences the anxiety level of elderly patients; anxiety level increases with increasing pain. It has also been suggested that a high anxiety level contributes to increased sensitivity to pain.

Time since diagnosis was shorter than a year in 48.1% of the patients in the study. Those who had been diagnosed with cancer longer than five years ago were found to have elevated scores on the sensory, affective and mixed sub-dimensions of the MPQ. This might be related to an increased vulnerability over time to pain caused by both cancer and its treatment.

More than half of the aged patients in the study receiving chemotherapy and/or radiation experienced "frequent" nausea/vomiting. A study similar to ours found that patients over 60 experienced more intense/frequent post-chemotherapy nausea (25,26). We found that, among patients treated with chemotherapy and/or radiation, those who described the frequency of nausea/vomiting, loss of appetite and diarrhea/constipation as "frequently" displayed a high level of both pain and anxiety. Cancer-related symptoms, adverse effects of chemo-radiotherapy and the lack of control of these adverse effects may be increasing the patients' anxiety level and pain perception. A study report indicated that the extended duration of chemotherapy and the uncontrolled adverse effects of cancer cause an increase in anxiety level (26).

"Several times a day" and "Any time during the day" was the description of the timing of pain for more than half the patients. The pain and anxiety levels of patients experiencing pain predominantly "mornings and evenings" were also higher than in other groups. A published study has indicated that elderly patients experienced pain predominantly in the afternoon or during the entire day (9). While acute pain in cancer patients is often related to diagnostic and therapeutic procedures, chronic pain is the result of tumor infiltration of or

Table 2— Distribution, by Symptoms Experienced by the Patients, of Average McGill Pain Questionnaire and State Trait Anxiety Scores.

Symptomsand Incidence	n	%	McGill Pain Questionnaire Score Averages					The State-Trait Anxiety Inventory Score Averages	
			Sensory (mean±sd)	Affective (mean±sd)	Evaluative (mean±sd	Mixed (mean±sd)	MPQTotal (mean±sd)	State Anxiety Inventory Score (mean±sd)	Trait Anxiety Inventory Score (mean±sd)
Nausea/vomiting (n= 89)									
Frequently	48	53.9	18.71±6.39	5.83±2.10	3.79±1.15	8.06±3.19	36.40±11.57	50.38±6.46	43.90±6.00
Sometimes	26	29.2	20.50±5.34	6.31±1.76	3.88±0.99	8.85±2.81	39.54±9.56	49.69±5.25	43.19±5.28
Rarely	15	16.9	15.07±6.15	4.60±2.03	3.40±1.06	6.73±2.66	29.80±10.86	49.93±6.20	42.73±4.38
p			0.025	0.033	0.370	0.100	0.026	0.894	0.739
Appetite (n= 89)									
Frequently	68	76.4	19.16±6.07	5.93±1.99	3.76±1.11	8.16±3.04	37.01±10.91	51.12±6.14	44.18±5.84
Sometimes	16	18.0	16.88±6.95	5.38±2.42	3.81±0.98	7.88±3.24	33.94±12.83	47.25±4.70	41.38±3.84
Rarely	5	5.6	16.80±6.38	4.80±1.30	3.40±1.34	7.40±3.05	32.40±11.10	45.40±2.88	41.00±3.00
p			0.340	0.353	0.753	0.834	0.460	0.012	0.109
Diarrhea/constipation (n= 86)									
Frequently	41	46.1	20.15±5.69	6.24±2.08	3.88±1.10	8.54±3.02	38.80±10.72	51.63±5.80	45.22±5.26
Sometimes	34	38.2	17.91±6.49	5.50±1.94	3.76±1.07	8.06±3.05	35.24±11.16	49.74±6.17	43.03±5.80
Rarely	11	12.4	16.36±6.33	5.00±1.95	3.55±1.04	7.00±3.03	31.91±11.54	44.33±6.66	40.27±2.80
p			0.112	0.191	0.273	0.243	0.114	0.038	0.005

Table 3— Distribution of Pain Characteristics by McGill Pain Questionnaire and State Trait Anxiety Scores.

			McGill Pain Questionnaire Score Averages					The State-Trait Anxiety Inventory Score Averages	
Symptomsand Incidence	n	%	Sensory (mean±sd)	Affective (mean±sd)	Evaluative (mean±sd	Mixed (mean±sd)	MPQTotal (mean±sd)	State Anxiety Inventory Score (mean±sd)	Trait Anxiety Inventory Score (mean±sd)
The frequency of experiencing pain									
Continuous	13	12.3	21.31±6.90	6.92±1.93	4.31±0.85	9.23±2.71	41.85±11.23	52.15±7.01	45.85±6.88
Several times daily	59	55.7	19.76±5.38	6.03±1.88	3.93±0.98	8.68±2.87	38.41±9.68	50.78±5.70	44.42±5.16
Several times weekly	34	32.1	14.65±5.97	4.44±1.85	3.00±1.10	6.15±2.70	28.24±10.47	47.06±5.21	39.56±3.38
P			p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	0.004	p<0.001
Time of occurrence of pain									
Evening	9	8.5	18.22±6.18	6.00±2.74	4.00±1.22	8.00±3.04	36.22±12.29	49.00±6.61	44.75±6.06
At noon and in the afternoon	16	15.1	20.81±4.94	6.25±1.34	4.31±0.60	9.94±2.74	41.31±8.14	50.31±5.00	44.13±4.98
Anytime in the day	70	66.0	17.47±6.07	5.24±2.02	3.49±1.11	7.37±2.92	33.59±10.91	48.90±5.65	41.90±4.83
Morning and evening	11	10.4	20.09±8.53	6.91±1.92	3.73±1.27	8.55±3.21	39.27±14.15	55.00±6.77	47.27±7.13
p			0.196	0.034	0.041	0.018	0.055	0.015	0.009
Pain feature									
Deep	45	42.5	16.93±6.43	5.27±2.09	3.56±1.08	7.31±2.63	33.07±11.18	48.67±5.74	42.04±5.13
Superficial	10	9.4	12.80±6.20	4.10±1.52	2.70±1.16	5.60±2.01	25.20±9.99	47.80±5.51	40.90±3.90
Both deep and superficial	51	48.1	20.61±5.10	6.25±1.89	3.98±1.01	8.94±3.18	39.80±9.70	51.10±6.08	44.33±5.74
P			p<0.001	0.002	0.002	0.001	p<0.001	0.076	0.050

impingement on bone, soft tissues, nerves, and blood and lymph vessels. As a result, continuous and intermittent pain is often seen in cancer patients. The increase of the duration of pain during the day and the unpredictability of its time of onset may cause anxiety by negatively affecting the patients' ALD, quality of life and coping capacity. Almost half of the patients in our study experienced pain as being "both deep and superficial". Uncontrollable pain is the most frequent cause of anxiety in cancer patients. The feeling of pain as being both deep and superficial may negatively impact the patient's pain sensation, perception of pain intensity and anxiety level. Pain medication was being used by 90.6% of our patients. It was established that the pain and anxiety levels of patients who were receiving pain medication were higher than in those who were not. More than half our patients reported experiencing cancer pain "several times a day". The persistence of pain during the day may be influencing the anxiety level. Also, positive correlation was founded between the patient's' pain and anxiety mean scores in our study. So that anxiety level may be increasing pain level. Studies report indicated that the high anxiety level cause an increase in pain level (11,13).

Table 4— Patient's MPQ and the State-Trait Anxiety Inventory Score Averages (n= 106).

	mean±sd	*Min-Max
MPQ-Sensory	18.31±6.27	5.00-33.00
MPQ-Affective	5.63±2.05	1.00-10.00
MPQ-Evaluative	3.68±1.11	1.00 - 5.00
MPQ-Mixed	7.93± 3.04	3.00-15.00
MPQ-Total	35.57±11.29	11.00-60.00
State Anxiety Inventory	49.75±5.98	38.00-66.00
Trait Anxiety Inventory	43.04±5.45	33.00-59.00

*Min: Minimum

*Max: Maximum

Table 4— Patient's McGill Pain Questionnaire Inventory Total and Subdimension Score and State Trait Anxiety Inventory Score Correlations

	Sensory (r)	Affective (r)	Evaluative (r)	Mixed (r)	McGill Total (r)	StateAnxiety Inventory (r)	TraitAnxiety Inventory (r)
Sensory	1	0.777**	0.683**	0.706**	0.953**	0.296**	0.392**
Affective		1	0.618**	0.749**	0.874**	0.381**	0.427**
Evaluative			1	0.777**	0.799**	0.238*	0.281**
Mixed				1	0.872**	0.305**	0.348**
McGill					1	0.338**	0.415**
State Anxiety Inventory						1	0.830**
Trait Anxiety Inventory							1

**p<0.01 significant; *p<0.05

REFERENCES

1. Allard P, Maunsell E, Labbe J, Dorval M. Educational interventions to improve cancer pain control; A systematic review. Journal of Palliative Medicine 2001;4(2):191-203. (PMID:11441627).
2. Cherny NI, Portenoy RK. Cancer pain management. Cancer 1993;72(1):3415-93. (PMID:7902204).
3. Swenson CJ. Pain management, In: Otto S. (Eds). Oncology Nursing. 4th edition, St. Louis: Mosby, 2001, pp 865-916.
4. Melzack R, Wall DP, Erdine S. Manual for pain manegement. Güneş Bookstore, Ankara; 2006, pp 10-30.
5. Bernabei R, Gambassi G, Lapane K, et al. Management of pain in elderly patients with cancer. Journal of the American Medical Association 1998;279(23):1884-7. (PMID:9634258).
6. Rao A, Cohen HJ. Symptom management in the elderly cancer patient: Fatigue, pain, and depression. Journal of the National Cancer Institute Monographs 2004;32:150-7. (PMID:15263059).
7. Torvik K, Hølen J, Kaasa S, et al. Pain in elderly hospitalized cancer patients with bone metastases in Norway. International Journal of Palliative Nursing 2008;14:238-45. (PMID:18563017).
8. Alacacıoğlu A, Yavuzşen T, Diriöz M, et al. Changes in anxiety levels patients with cancer receiving chemotherapy. International Journal of Hematology and Oncology 2007;2(17):87-93.
9. Yıldız A, Erol S, Ergün A. Pain and depression risk among elderly people living in a nursing home. Turkish Journal of Geriatrics 2009;12(3):156-64. (in Turkish).
10. Turk DC, Okifuji A. Psychological factors in chronic pain: Evolution and revolution. Journal of Consulting and Clinical Psychology 2002;70(3):690-678. (PMID:12090376).

11. Wasan AD, Artamonov M, Nedeljkovic SS. Delirium, depression, and anxiety in the treatment of cancer pain. Techniques in Regional Anesthesia and Pain Management 2005;9(3):139-44. [Internet] Available from: http://www.techreganesth.org/article/S1084-208X%2805%2900047-9/pdf. Accessed:01.10.2013.
12. Oz F. Uncertainty in Illness Experience. Turkish Journal of Psychiatry 2001;12(1):61-8.
13. Chen ML, Chang HK, Yeh CH. Anxiety and depression in Taiwanese cancer patients with and without pain. Journal of Advenced Nursing 2000;32(4):944-51. (PMID:11095234).
14. Marrs JA. Stress, fears and phobias; The impact of anxiety. Clinical Journal of Oncology Nursing 2006;10(3):322-319. (PMID:16789576).
15. Otis-Green S, Sherman R, Perez M, et al. An integrated psychosocial-spiritual model for cancer pain management. Cancer Practice 2002;10(1):65-58. (PMID:12027971).
16. Eyigor S, Eyigor C, Uslu R. Assessment of pain, fatigue, sleep and quality of life (QOL) in elderly hospitalized cancer patients. Archives of Gerontology and Geriatrics 2010;51(3):57-61. (PMID:20044154).
17. Cheng KK, Lee DT. Effects of pain, fatigue, insomnia, and mood disturbance on functional status and quality of life of elderly patients with cancer. Critical Reviews in Oncology/Hematology 2011; 78(2):127–37. (PMID:20403706).
18. Theobald DE. Cancer pain, fatigue, distress and insomnia in cancer patients. Clinical Cornerstone 2004;6(1):21-15.(PMID:15675653).
19. Villagomeza LR. Spiritual distress in adult cancer patients: Toward conceptual clarity. Holistic Nursing Practice 2005;19(6):285-94. (PMID:16269948).
20. Coşkun U, Özkurt ZN, Günel N. Manegement of cancer pain. International Journal of Hematology and Oncology 2002;12(1): 45-55.
21. Melzack R, Torgerson WS. On the language of pain. Anesthesiology 1971;34(1):50-9. (PMID:4924784).
22. Kuğuoğlu S, Eti Aslan F, Olgun N. Melzack McGill Pain Questionnaire (MPQ)'s adaptation to Turkish. Pain 2003;15(1):47-52.
23. Oner N, Le Complete A. Manual for State Trait Anxiety Inventory. 2nd edition, Boğaziçi University Publications, İstanbul 1985, pp 20-40.
24. Önal A. Pain, In: Erdine S. (Eds). Cancer pain. Nobel Bookstore, İstanbul, 2007, pp 551-62. (in Turkish).
25. Tuna S. Comorbidity and clinical assessment in geriatric patients with cancer. Turkish Journal of Oncolgy 2007;22(4):192-6.
26. Dedeli Ö, Karadeniz G. An integrated psychosocial-spiritual model for cancer pain management. Pain 2009;21(2):45-53.

Turkish Journal of Geriatrics
2014; 17 (2) 172-179

Yakup Tolga ÇAKIR[1]
Mehmet SONBAHAR[2]
Hüseyin CAN[3]
Mehmet Ali KURNAZ[3]
Rıfkı ÖNDER[3]

RESEARCH

DRUG USAGE HABITS AND MULTIPLE DRUG USAGE OF ELDERLY INDIVIDUALS IN NURSING HOMES

ABSTRACT

Introduction: This investigation has been performed to determine the knowledge level and the attitudes of elderly individuals regarding the usage of prescription drugs, to examine the multiple drug usage by elderly, and to assess the factors affecting this situation.

Materials and Method: This study was performed in November-December 2012 with 171 individuals, aged 65 years and over, residing in Bursa Metropolitan Nursing Home, having no restraints on study participation, and volunteering to participate in the study. The questionnaire, developed as a result of the subject-related literature search, and composed of 37 open- and closed-ended questions, was applied with face-to-face interview technique. In the statistical analysis; mean±standard deviation (minimum-maximum values), percentage (number) were used in descriptive data; and Chi-Square Test was used in inter-group comparisons. p<0.05 value was regarded as significant.

Results: 51.5% of 171 individuals included in the study (n=88), aged 65 years and over, were men; the mean age of men was 73.04±0.7 years (65-94), and the mean age of women was 72.91±0.7 years (65-88). The usage of non-prescription drugs was 36.3%. The most used group of prescription drugs was anti-hypertensive drugs, and the most used group of non-prescription drugs was non-steroid anti-inflammatory drugs. 55.6% of the individuals were informed on the drugs they used and received this information from the doctor (60.7%) at the most. 56.3% of the individuals indicated that side effects occurred in relation to the drugs they used. The most frequently observed side effects were abdominal pain and nausea.

Conclusion: It has been detected that as the amount of drugs used by the individuals increases the prevalence of side effects also increase, that informing patients on treatment decreases the usage of non-prescription/OTC drugs and the side effects, and ensures that people use and store their drugs accurately.

Key Words: Aged; Adverse Effects; Polypharmacy.

ARAŞTIRMA

HUZUREVİNDEKİ YAŞLI BİREYLERİN İLAÇ KULLANIM ALIŞKANLIKLARI VE ÇOKLU İLAÇ KULLANIMI

ÖZ

Giriş: Bu araştırma yaşlı bireylerin reçete edilen ilaçlarını kullanmada sahip oldukları bilgi düzeyinin ve tutumlarının belirlenmesi, yaşlılarda çoklu ilaç kullanımının incelenmesi ve bu duruma etki eden faktörlerin değerlendirilmesi amacıyla yapılmıştır.

Gereç ve Yöntem: Bu çalışma Kasım-Aralık 2012 tarihleri arasında, Bursa Büyükşehir Huzurevi'nde yaşayan, çalışmaya katılmaya engeli olmayan ve çalışmaya katılmaya gönüllü 65 yaş ve üzeri 171 bireyle yapıldı. Konu ile ilgili literatür taraması sonucunda geliştirilen, açık ve kapalı uçlu 37 sorudan oluşan anket yüz yüze görüşme tekniği ile uygulandı. İstatistiksel analizde; tanımlayıcı verilerde ortalama±standart sapma (minimum-maksimum değerler), yüzde (sayı); gruplar arası karşılaştırmalarda Ki Kare Testi kullanıldı. p<0.05 değeri anlamlı olarak kabul edildi.

Bulgular: Çalışmaya dahil edilen 65 yaş ve üzeri 171 bireyin %51,5'i (n=88) erkek olup, erkeklerin yaş ortalaması 73,04±0,7 yıl (65-94), kadınların yaş ortalaması 72,91±0,7 yıl (65-88) idi. Reçetesiz ilaç kullanımı %36,3'tü. Reçeteli en fazla kullanılan ilaç grubu antihipertansifler, reçetesiz olarak en fazla steroid olmayan antiinflamatuar ilaçlar kullanılmaktaydı. Bireylerin %55,6'sı kullandığı ilaçlarla ilgili bilgi almışlardı ve bu bilgiyi de en fazla doktordan (%60,7) almıştı. Bireylerin %56,3'ü kullandığı ilaçlarla ilgili yan etki oluştuğunu belirtti. En sık gözlenen yan etkiler karın ağrısı ve mide bulantısı idi.

Sonuç: Bireylerin kullandığı ilaç miktarı arttıkça yan etki görülme sıklığının arttığı, hastaları tedavi konusunda bilgilendirmenin reçetesiz ilaç kullanımını ve yan etkileri azalttığı, kişilerin kullandığı ilaçları doğru şekilde kullanmasını ve muhafaza etmesini sağladığı saptanmıştır.

Anahtar Sözcükler: Yaşlı; Yan Etkiler; Çoklu İlaç Kullanımı.

İletişim *(Correspondance)*

Hüseyin CAN
İzmir Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Aile Hekimliği İZMİR

Tlf: 0232 244 44 44
e-posta: drhuseyincan@hotmail.com

Geliş Tarihi: 26/01/2014
(Received)

Kabul Tarihi: 24/02/2014
(Accepted)

[1] Uzundere Devlet Hastanesi, Aile Hekimliği ERZURUM
[2] İzmir Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, İç Hastalıkları İZMİR
[3] İzmir Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Aile Hekimliği İZMİR

Introduction

Inappropriate polypharmacy and prescription practice entails increased burdens of impaired quality of life and drug related morbidity and mortality. Polypharmacy in the elderly also complicates therapy, increases cost, and is a challenge for healthcare agencies (1). Elderly consume 45% of all drugs in United Kingdom (UK), and 33% of all drugs in United States of America (USA). It is foreseen that elderly people, residing in nursing homes, use more drugs compared to the ones living in the community, and that they experience side effects more frequently (2). Medication therapy in elderly patients is difficult to manage and always has the potential of being hazardous. With the age-related changes that affect the pharmacokinetics and pharmacodynamics of a medication, prescribing medications is further complicated. Similarly, assessment of a medication's efficacy is difficult. The situation becomes more complicated when the patient is taking multiple medications (3).

Multiple drug usage is a health issue frequently observed in old age and is defined by the presence of at least one unnecessary drug in the treatment, or by the usage of drugs more than required, or by the concomitant usage of five or more drugs. It has been reported that there is a positive relationship between the chronic disease and the drug usage, and that elderly people, residing in nursing homes, use more drugs (1,4). There may be problems and mistakes in drug usages due to the conditions such as the increasing possibility of multiple diseases in elderly patients, the concomitant usage of different treatments, the physiological changes occurring with aging, and the reductions in sensory functions (1). The border between rational and irrational drug use in geriatric medicine is narrow. Drugs may be taken at very high or very low doses by elderly. They may be used at the wrong times or they may be completely forgotten. Moreover, since they are the group with the highest combined drug usage, they also have the most undesired effects.

Study has been conducted to determine the drug usage habits, the knowledge level and the attitudes of elderly individuals regarding the usage of their prescription drugs, to examine the multiple drug usage by elderly, and to assess the factors affecting this situation.

Materials and Method

In this study conducted on November 2012-December 2012 in Bursa Metropolitan Municipality Nursing Home; individuals, aged 65 years and over, and residing in the nursing home, have formed the universe of the study. The study is a cross-sectional study.

The questionnaire form has been composed after literature search, including 7 questions for socio-demographic characteristics of the participants, 5 questions for their conditions in the nursing home, 2 questions for chronic disease status, 6 questions for the drugs they use, and 17 questions for determining their knowledge and their attitudes related to the drugs they use. The questionnaire form, composed of a total of 37 questions, has been applied by face-to-face interview method. The open- and closed ended questions, included in the questionnaire form composed, have been asked to 83 women and 88 men, who reside in the nursing home, who are aged 65 years and over, who have no restraints on study participation, and who have accepted to participate in the study, after their oral consents have been obtained. Individuals in the nursing home have been informed on the subject, and their study participation has been voluntary. Individuals, who have physical, psychological, and cognitive diseases at a level to constrain face-to-face interviewing and questionnaire completion, and who do not accept to participate in the study, have not been included in this study. Before the study, official permit has been received from Bursa Metropolitan Municipality Social Services Head Office to conduct a study in the nursing home. Moreover, the approval, dated 19.10.2012 and numbered 52, has been obtained from İzmir Katip Çelebi University Non-Interventional Clinical Trials Ethics Committee.

In descriptive data; mean±standard deviation (minimum-maximum values), percentage (number) were used, and Chi-Square Test was used in inter-group comparisons. $P<0.05$ value was regarded as significant.

Results

More than half of the participants were men (51.5% of 171 individuals); the mean age of men was 73.04±0.7 years (min:65-max:94), and the mean age of women was 72.91±0.7 years (min:65-max:88). It was detected that 80.1% of the study participants had children, and the average number of children was 2.0±0.2. Other socio-demographic characteristics of the individuals participating in the study are presented in Table 1.

The majority of elderly individuals (74.3%; n=127) in the nursing home indicated that they had at least one chronic disease. The ratio of the ones with four and more chronic diseases

Table 1— Distribution of Socio-demographic Characteristics of Elderly Individuals.

Characteristics		n	%
Age (years)	65- 69	67	39.2
	70- 74	40	23.4
	75- 79	32	18.7
	80- 84	19	11.1
	85 and over	13	7.6
Gender	Female	83	48.5
	Male	88	51.5
Educational status	Illiterate	18	10.5
	Literate	19	11.1
	Primary school	58	33.9
	Secondary school	26	15.2
	High school	35	20.5
	College – university	15	8.8
Marital status	Married	48	28.0
	Single	15	8.8
	Widow	62	36.3
	Divorced	46	26.9
Health insurance	Yes	143	83.6
	None	28	16.4
Children	Yes	137	80.1
	None	34	19.9
Regular monthly income	Yes	145	84.8
	None	26	15.2
Duration of residence in the nursing home (years)	1- 4	116	67.8
	5- 8	35	20.5
	9 and over	20	11.7
Total		171	100.0

was 19.3% (n=33). The distribution of chronic diseases of the individuals by gender is shown in Table 2. 48.0% of the individuals, participating in the study, have indicated that they have been diagnosed hypertension. Thyroid gland diseases and osteoporosis were observed more apparently in women compared to men (p=0.044; p=0.002).

While 88.3% of the ones (n=151), participating in the study, have used at least one drug. While only 52.6% of the individuals (n=90) have used prescription drugs regularly, 26.3% have used both prescription and non-prescription drugs. The ratio of the ones using only non-prescription drugs was 9.4%. While 10.8% of women (n=9) and 8% of men (n=7) have used one drug daily; 44.6% of women (n=37) and 40.8% of men (n=36) have used five and more drugs daily. It was detected that the ratio of the usage of seven and more drugs daily was 24.1% (n=20) in women, and 10.2% (n=9) in men. When all elderly individuals, residing in the nursing home, were assessed; it was detected that the ratio of the ones using five and more drugs 42.8% (n=73).

When the prescription drugs used by the individuals are reviewed, anti-hypertensive drugs were used the most in both genders in compliance with their chronic diseases (48.5%). The prescription drugs used by women and men are shown in Table 3.

It was indicated that 69 of 73 individuals (94.5%), using five and more drugs daily, had drug-related side effects. 81.2% of the ones, having side effects due the drugs used, were using five and more drugs (p< 0.01). Observation of side effects increased proportionally with the number of drugs used daily. While the ratio of observing side effects was 8.7% in the ones using two drugs daily, this ratio was 31.8% in the ones using there drugs, it was 90.5% in the ones using five drugs, and the ratio of side effect occurrence was 100% in the ones using seven and more drugs.

Table 2— Distribution of Chronic Diseases by Gender.

Chronic disease	Male n (%)	Female n (%)	Total
Hypertension	38 (45.8)	44 (50.0)	82 (48.0)
Diabetes mellitus	24 (28.9)	23 (26.1)	47 (27.5)
Cardiovascular system*	25 (30.1)	19 (21.6)	44 (25.7)
Respiratory system	9 (10.8)	15 (17.0)	24 (14.0)
Psychiatric	11 (13.3)	10 (11.4)	21 (12.3)
Gastrointestinal system	12 (14.4)	12 (13.6)	24 (14.0)
Thyroid diseases	6 (7.2)	1 (1.1)	7 (4.1)
Osteoporosis	11 (13.3)	1 (1.1)	12 (7.0)
Rheumatoid	8 (9.6)	9 (10.2)	17 (9.9)
Cerebrovascular system	6 (7.2)	10 (11.4)	16 (9.4)
BPH+	0 (0.0)	11 (12.5)	11 (12.5)
Arthritis	12 (14.5)	9 (10.2)	21 (12.3)
Cancer	1 (1.2)	0 (0.0)	1 (0.6)
Sensory system	2 (2.4)	7 (8.0)	9 (5.3)
Anemia	8 (9.6)	3 (3.4)	11 (6.4)
Dermatological disease	2 (2.4)	3 (3.4)	5 (2.9)
Urinary incontinence	4 (4.8)	1 (1.1)	5 (2.9)

*Cardiovascular system diseases excluding hypertension, +BPH: Benign Prostate Hypertrophy, percentage of male patients (n=88).

Table 3— Prescription Drugs Used by Gender.

Prescription Drugs Used	Gender				Total	
	Female		Male			
	n	%	n	%	n	%
Anti-hypertensive drugs	38	45.8	44	50.0	83	48.5
Anti-diabetics	24	28.9	23	26.1	47	27.5
Cardiovascular system drugs	25	30.1	19	21.6	43	25.1
Gastric drugs	15	18.1	8	9.1	23	13.5
Psychiatric drugs	13	15.7	10	11.4	23	13.5
Respiratory system drugs	8	9.6	15	17.0	23	13.5
Prostate drugs	–	–	11	12.5	11	12.5
Anti-inflammatory drugs	10	12.0	10	11.4	20	11.7
Anti-rheumatoid drugs	9	10.8	7	8.0	16	9.4
Cerebrovascular system drugs	6	7.2	10	11.4	16	9.4
Iron preparations	9	10.8	4	4.5	13	7.6
Ophthalmic preparations	4	4.8	7	8.0	11	6.4
Osteoporosis drugs	9	10.8	1	1.1	10	5.8
Thyroid drugs	6	7.2	1	1.1	7	4.1
Dermatological drugs	3	3.6	3	3.4	6	3.5
Hemorrhoid drugs	2	2.4	4	4.5	6	3.5
Urinary system drugs	4	4.8	1	1.1	5	2.9
Anti-neoplastic drugs	1	1.2	–	–	1	0.6

Less than half of elderly individuals (35.7%) in the nursing home were using non-prescription drugs, and these ratios were detected as 38.6% in women, and as 33.0% in men. It was detected that the non-prescription drugs used the most were analgesics (72.6%). Then following analgesics respectively, vitamins (24.2%), gastric drugs (17.7%), skin creams (12.9%), common cold drugs (9.7%), anti-histaminic drugs (4.8%), antitussive drugs (3.2%), and antibiotics (3.2%) were being used.

When it was questioned why the individuals were using non-prescription drugs; the individuals indicated the most that they have used non-prescription drugs since they have thought of its working out for their diseases (59.0%). The ratio of the ones using non-prescription drugs, recommended by friends, was 27.9%. 8.1% of the ones purchasing non-prescription drugs indicated that they did not need prescriptions since they have used the drug continuously, and 5.0% of them indicated that they did not need prescriptions since social security did not reimburse for the drug.

The ratio of the ones, being examined and prescribed by the doctor due to his/her disease, but not purchasing the prescription drugs, was 23.4% (n=40). 35.0% of these (n=14) indicated they did not purchase the drugs since they thought that they did not recover, 25.0% (n=10) indicated that they did not purchase the drugs since they thought that the drugs used had side effects, 20.0% (n=8) indicated that they did not purchase the drugs since their complaints resolved, 12.5% (n=5) indicated that they did not purchase the drugs since the taste of the drug was unpleasant, and 7.5% (n=3) indicated that they did not purchase the drugs since the tablets given were big.

While 58.3% of the elderly individuals, using drugs in the nursing home, indicate that they know the name of the drug they use, 75.0% of these individuals indicated that they have received information from a doctor, a nurse, or a pharmacist on the drugs required to be used. For the ones, receiving information related to the drugs used, the ratio for knowing the name, the dose, the side effects, and the drug-food interactions of the drug was higher compared to the ones, not receiving information related to the drugs used. Status of knowledge on drugs used for the individuals in the nursing home is shown in Table 4.

The majority of 30 people (96.7%; n=29), storing the drugs they use at storage conditions indicated in drug package, and 91.5% of 47 people (n=43), reading the package insert of the drug they use, indicated that they received information on the drugs used. These ratios were highly significant compared to the ones, not receiving information on the drugs used ($p<0.01$). It was detected that the ones, receiving information on the drug to be used, have stored their drugs at more accurate conditions compared to the ones not receiving information ($p<0.01$).

While 31.1% of the elderly individuals (n=47), using drugs in the nursing home, have read the package insert of the drug used, 68.9% (n=104) have indicated that they have not read the package insert. When the reasons for not reading the

Table 4— Status of Knowledge Related to the Drugs Used.

Status of Knowledge Related to the Drugs Used		Status of Being Informed Related to the Drugs Used				P
		Informed		Not Informed		
		n	%	n	%	
Knows about names	Yes	66	75.0	22	25.0	**<0.01**
	No	18	28.6	45	71.4	
Knows about doses	Yes	47	88.7	6	11,3	**<0.01**
	No	37	37.8	61	62.2	
Knows about how many are required to be taken daily	Yes	76	57.6	56	42.4	**0.204**
	No	8	42.1	11	57.9	
Knows about side effects	Yes	38	95.0	2	5.0	**<0.05**
	No	46	41.4	65	58.6	
Knows about interactions	Yes	29	96.7	1	3.3	**<0.05**
	No	55	45.5	66	54.5	
Knows about the usage purpose	Yes	75	78.1	21	21.9	**<0.01**
	No	9	16.4	46	83.6	

package insert were reviewed; it was detected the most as not being able to understand the statements written (n=42, 40.4%). Other reasons were respectively, not feeling the need to read the package insert (n=36, 34.6%), being illiterate (n=14, 13.5%), and having vision problems (n=12, 11.5%).

The majority of the elderly individuals in the nursing home (55.6%; n=84) indicated that they have received information on the drugs used; 60.7% (n=51) have indicated that they have received this information from the doctor, 27.4% (n=23) from the nurse, and 11.9% (n=10) from the pharmacist. When the reasons for not applying the information were reviewed; they indicated the most that they did not apply the information since they forgot the information provided (n=6, 37.5%), and since they did not understand the information (n=5, 31.2%). When the relationship between the educational levels of the individuals and their status of being informed was examined; it was detected that 91.7% of the ones (n=44), having high school education and higher levels of education, and 38.8% of the ones (n=40), having secondary school and lower levels of education, received information on drugs used. As the educational level increased, the ratio of receiving information on drugs also increased ($p<0.01$).

While 76.2% (n=64) of the ones, receiving information on the drugs used, did not use non-prescription drugs, only 23.8% (n=20) used non-prescription drugs. 61.2% (n=41) of the ones, not receiving information on drugs used, indicated that they used non-prescription drugs. It was detected that the non-prescription drug usage was higher in the ones, not receiving information on drugs used, compared to the ones receiving information ($p<0.05$). It was detected that informing the patient decreased the usage of non-prescription drugs, which is one of the significant problems in drug usage.

The majority of 151 elderly individuals (56.3%; n=85), who used drugs, indicated that side effects occurred due to the drugs used. Respectively, the most frequently observed side effects were indicated to be abdominal pain (n=45, 29.8%), nausea (n=20, 13.2%), dizziness (n=19, 12.6%), dry mouth (n=15, 9.9%), itching/rash (n=9, 6.0%), and diarrhea (n=5, 3.3%).

While 75.5% (n=114) of the individuals, participating in the study and using drugs, indicated that they received their drugs on time, 24.5% (n=37) indicated that they did not receive their drugs on time. Individuals indicated the most frequently that they did not take their drugs on time since they forgot it (n=15, 40.5%). Other reasons, detected respectively, were negligence (n=10, 27.0%), receiving the drug when he/she feels that it is required (n=9, 24.4%), not liking to receive drugs (n=1, 2.7%), not being able to have the drug prescribed (n=1, 2.7%), and not finding the drug appropriate for himself/herself (n=1, 2.7%).

Elderly individuals, using drugs, indicated the most that they stored their drugs in a closed cupboard (n=75, 49.7%). It was detected that the ratio of the ones, storing in an open place, was 24.4% (n=37), the ratio of the ones, storing in drug package and at specified conditions was 19.9% (n=30), and the ones, storing in the refrigerator, was 6.0% (n=9).

Discussion

More than half of the individuals, participating in our study, had more than one chronic disease. In many studies conducted in elderly, hypertension leads the list of chronic diseases most frequently observed in both genders (5). The data, revealed as a result of our study, demonstrate similarities with the chronic disease characteristics of the elderly population. Co-existence of more than one disease in elderly individuals is also rather common; 19.3% of the individuals in our study had four and more chronic diseases. While thyroid diseases, osteoporosis, and urinary incontinence were observed in women significantly more than men, no significant difference was detected in the prevalence of other chronic diseases between women and men, participating in our study.

The most used drugs were respectively also anti-hypertensive drugs, anti-diabetic drugs, and cardiovascular system drugs, in compliance with the diseases most frequently observed in our study. In a study conducted in broad scope as to cover many nursing homes in our country, it has been detected similar to our study that drugs for hypertension, diabetes, and cardiac diseases are used more (5). One study concluded that aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and cardiovascular drugs caused 91% of the adverse drug reactions necessitating hospital admissions. Because of common geriatric ailments, such as osteoarthritis and degenerative joint disease, NSAIDs are necessary, and they effectively relieve pain in the elderly. Unfortunately, NSAIDs can also potentiate, increase, or decrease the effect of many prescription drugs that this population takes. The most common and deadliest interactions are with anticoagulants, oral hypoglycemics, diuretics, and antihypertensives (6). The ratio of non-prescription drug usage was found high in our study (36.3%). While the drugs, used the most as non-prescription were NSAIDs, vitamins were used at second most frequency. Analgesics are the non-prescription drug group, used the most frequently in the world (3,5,7). In our study, a

result has been also reached in parallel to these results. While 58.1% of the ones, using non-prescription drugs, thinking that they work out well for their diseases, the studies conducted also demonstrate that individuals use non-prescription drugs, thinking of them as working out for themselves the most (3,5,7).

In a study conducted in nursing homes in our country, it has been detected that 60% of women and 53% of men used at least one drug (8). In another study conducted, the most commonly used medications were for the cardiovascular and central nervous systems. The number of medications per person increased from 3.1±2.8 to 3.8±3.1 (p=.0001), and polypharmacy (concominant use of over five medications) increased from 19 to 25% (p=.006). These changes were most prominent among persons aged 85 years or over, especially among women (9). Almost 89.0% of women and 88.3% of men in our study group have been using at least one drug similar to the studies conducted. In our study, it has been detected that women consumed more drugs than men; while the amount of drug consumed by women daily was 4.12 units, the amount of drug consumed by men daily was 3.76 units. The amounts of drugs used daily have been found higher in our study compared to other studies; this situation may be due to the high amount of non-prescription drugs used. While the non-prescription drug usage was 23.8% in the ones, receiving information on the drug used, 67.2% of the ones using non-prescription drugs have not received information on the drug used. The non-prescription drug usage of the ones, who have received information on the drug used, is significantly less than the ones, who have not received information; this situation demonstrates the importance of informing the patients while treating them, and of preventive medicine.

In ours study, the prevalence of side effects in individuals using drugs has been found high (56.3%). This situation can be explained by the high number of drugs used by the individuals daily and the high number of chronic diseases; as the number of drugs used daily increases, the side effect prevalence also increases proportionally (10). While side effects are observed in 20.5% of the individuals, using four and less drugs daily, side effects are observed in 94.5 of the ones, using five and more drugs daily. The amount of drugs used daily may be reduced by the effect of the patient and the examining physician. Especially patient's showing all drugs used to the examining physician may prevent the unnecessary prescription of the same drugs with similar effects. Patients' receiving non-prescription drugs may be reduced by the trainings provided to the patient, information about "rational use of medicine" may be provided to physicians by on-the-job trainings, it may be emphasized that giving drugs is not good treatment, and informing the patient during the treatment process, treatment monitoring, and patient's compliance with the treatment are also important. Physician's questioning the drugs used by the patient is significant in efficient treatment. The studies conducted report that one of the significant problems, affecting the drug usage in elderly, is the low level of education (10,11). Also in our study, as the educational level increases in individuals, the level of receiving information on drugs used also increases; nearly all individuals, having high school education or higher levels of education, receive from physicians information on drugs used.

When it is asked from whom the elderly receive the information on drug usage, 44.4% state that they receive no information, 60.7% of the ones, receiving information, state that they receive information from the physician. 80.9% of the individuals, participating in our study, have indicated that they have applied this information they have received on the drugs used. The ones, who do not apply the information provided to themselves, have indicated that they do not apply the information provided to themselves due to reasons such as forgetting the information and not understanding the information most frequently; this situation demonstrates the importance of informing the patient in written, visually, and orally in accordance with the educational and social level of the patient and the repetitive explanation of this information in each patient examination.

The majority of individuals (68.9%), participating in our study, have indicated that they do not read the package insert of the drug used, and that they do not read it since they do not understand the written statements the most. As it can also be seen in our study, informing patients on their treatments decreases the defects in drug usage; therefore undesired effects may be reduced.

In conclusion; we think that controlling the chronic diseases in elderly, training healthcare employees on rational use of medicine, informing the elderly on the drugs they use, and controlling the drugs in regular intervals, and again informing the elderly on the side effects and the storage conditions of drugs will prevent poly-pharmacy. Although we think that this study may contribute to the review of the dimensions of the drug usage in elderly individuals, to the reduction of drug-related problems, and to the development of some strategies in this field, we also consider that studies on the subject should be conducted in broader scope.

REFERENCES

1. Onar E, Kapucu S. Polypharmacy in the elderly. The Journal of Academic Geriatrics 2011;3(1):22-8. (in Turkish).
2. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriat Pharmacother 2006;4(1):36-41. (PMID:16730619).
3. Larsen PD, Martin JL. Polypharmacy and elderly patients. AORN J 1999;69(3):619-22, 625, 627-8. (PMID:11957456).
4. Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Ses S, Kaboli PJ. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006;54(10):1516-23. (PMID:17038068).
5. Arslan Ş, Atalay A, Gökçe–Kutsal Y. Drug use in older people. J Am Geriatr Soc 2002;50(6):1163-4. (PMID:12110084).
6. Durrance SA. Older adults and NSAIDs: Avoiding adverse reactions. Geriatr Nurs 2003;24(6):348-52. (PMID:14694323).
7. Frazier SC. Health outcomes and polypharmacy in elderly individuals: an integrated literature review. J Gerontol Nurs 2005;31(9):4-11. (PMID:16190007).
8. Işık AT, Doruk H, Mas MR. The principles of pharmacotherapy in elderly. Klinik Gelişim 2004;17(2):25-31.
9. Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivela SL, Isoaho R. Use of medications and polypharmacy are increasing among the elderly. J Clin Epidemiol 2002;55(8):809-17. (PMID:12384196).
10. Şahin G, Baydar T. Use of drugs among older persons. In: Troisi J, Gokçe–Kutsal Y (Eds). Aging in Turkey: International Institute on Ageing and Hacettepe University Research Center of Geriatrics Sciences- GEBAM,Vertas Pres, Malta 2006, pp 55-84.
11. Keskinoğlu P, Bilgiç N, Pıçakçıefe M, Uçku R. The prevalence of the chronic disease and disability in elderly population at Camdibi-1 Health Center's region in Izmir. Turkish Journal of Geriatrics 2003;6(1):27-30. (in Turkish).

Turkish Journal of Geriatrics
2014; 17 (2) 180-187

Bahire ULUS[1]
Arzu İRBAN[2]
Nadi BAKIRCI[3]
Ela YILMAZ[1]
Yasemin USLU[1]
Nurullah YÜCEL[4]
Fatma ETİ ASLAN[1]

RESEARCH

DETERMINATION OF PAIN CHARACTERISTICS, PAIN BELIEF AND RISK OF DEPRESSION AMONG ELDERLY RESIDENTS LIVING AT NURSING HOME

ABSTRACT

Introduction: The aim of this study was to determine pain frequency, pain characteristics, pain beliefs and depression status of elderly people living in nursing homes.

Materials and Method: This descriptive study was carried out in nursing homes affiliated with Istanbul Metropolitan Municipality. Elderly people who were residents in these nursing homes were included in the study. Data were collected with the Descriptive Data Form, Pain Evaluation Form, Geriatric Depression Scale and Pain Beliefs Questionnaire.

Results: One hundred forty-six people were included in the study. 76% of the elderly people complained about pain, especially leg pain. This was severe chronic pain of a high intensity (Numerical Rating Scale 5-7). This chronic pain adversely affected their daily activities. The risk of depression even higher in older patients with neurological disease. Half of the elderly residents (51%) stated that it was easier to cope with the pain when they were happy, and also that pain was an indicator of having something wrong with their body.

Conclusion: In the light of this study, we can say that pain is a frequently seen symptom in elderly residents living in nursing homes. The psychological status of the residents has a great impact on the management of their pain. Therefore people's psychological status and their beliefs related to pain should also be assessed.

Key Words: Aged; Pain, Depression.

ARAŞTIRMA

HUZUREVİNDE YAŞAYAN YAŞLILARDA AĞRI ÖZELLİKLERİ, AĞRI İNANÇLARI VE DEPRESYON RİSKİNİN BELİRLENMESİ

ÖZ

Giriş: Bu araştırmanın amacı huzurevinde yaşayan yaşlılarda ağrı sıklığı, ağrı inançları ve depresyon riskini değerlendirmektir.

Gereç ve Yöntem: Tanımlayıcı olarak planlanan bu araştırma İstanbul Büyükşehir Belediyesi'ne bağlı huzurevlerinde yapıldı. Veriler, Tanıtıcı Veri Formu, Ağrı Değerlendirme Formu, Geriatrik Depresyon Ölçeği ve Ağrı İnançları ölçeği ile toplandı.

Bulgular: Çalışmaya 146 birey dahil edildi. Huzurevinde yaşayan yaşlıların %76'sında en çok bacak bölgesinde yerleşim gösteren ve 5-7 şiddetinde (Numerical Rating Scale) olan, günlük aktivitelerini olumsuz yönde etkileyen kronik ağrıları olduğu saptandı. Depresyon riski nörolojik hastalığı olan yaşlılarda daha yüksek olarak saptandı (p=0,020). Yaşlıların yarısı (%51,0) "mutlu iken ağrı ile baş etmenin daha kolay" olduğuna ve "ağrı çekmenin vücutta bir şeylerin ters gittiğinin işareti" olduğuna inanmaktadır.

Sonuç: Bu çalışmanın ışığı altında huzurevinde yaşayan yaşlılarda ağrının sık görülen bir semptom olduğu söylenebilir. Bireyin psikolojik durumunun ağrı yönetimi üzerinde büyük bir etkisi olduğu görülmüştür. Bu nedenle bireylerin psikolojik durumları ve ağrı inançları da değerlendirilmelidir.

Anahtar Sözcükler: Yaşlı; Ağrı; Depresyon.

İletişim *(Correspondance)*

Bahire ULUS
Acibadem Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü

Tlf: 0216 500 41 62
e-posta: bahire62@gmail.com

Geliş Tarihi: 13/01/2014
(Received)

Kabul Tarihi: 24/03/2014
(Accepted)

[1] Acıbadem Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü İSTANBUL
[2] Medipol Üniversitesi, Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı İSTANBUL
[3] Acıbadem Üniversitesi, Tıp Fakültesi, Halk Sağlığı Anabilim Dalı İSTANBUL
[4] İstanbul Büyükşehir Belediyesi, Sosyal Hizmetler Daire Başkanlığı, Darülaceze Müdürlüğü İSTANBUL

Introduction

Pain and depression are declared to be the most common diagnoses for elderly people who stay in nursing homes. Researches about nursing home residences in the World and in Turkey have shown that the frequency of pain in old people is 25-50% (1-3).

Pain and depression in old people negatively affect their everyday life. It is declared that the frequency of depression in old people who stay in nursing home residences in Turkey is even higher, between 36% and 76% (2,4). Depression can be the reason for chronic pain, just as depression might be observed in old people who suffer from chronic pain. Since pain and depressive symptoms in old people are generally observed at the same time, in addition to the feature of pain, their pain experience, depression and pain beliefs should be taken into consideration while evaluating pain (2,4).

In this study, besides pain frequency we also aimed to determine pain characteristics, beliefs about pain and the risk of depression at elderly people living in nursing homes affiliated to Istanbul Metropolitan Municipality.

Materials and Method

This descriptive study was carried out between March and July 2012 at Istanbul Metropolitan Municipality Nursing Homes. Ethics Committee approval from the researchers' university (ATADEK, 2012-298) and approval from executives of nursing homes affiliated with Istanbul Metropolitan Municipality where the study would be carried out were obtained. In the process of data collection, it was explained to all individuals that participation was voluntary. Written informed consent was obtained from individuals participating in the study. The 146 people who agreed to participate in the research were included in study group. Data collection tools included the Descriptive Data Form, Pain Evaluation Form, Geriatric Depression Scale and Pain Beliefs Questionnaire.

In the Descriptive Data Form, which was developed by the researchers there are questions about demographic information (age, gender, marital status, chronic disease, medication) and pain experience. In the Pain Evaluation Form there are questions about the region, quality, severity, conditions which increase and decrease pain, and methods consulted in order to relieve pain (taking pain-killers, alternative medicine practices, and exercise).

The 30-question Geriatric Depression Scale (GDS) was developed by Yesavage et al.(3); Turkish validity and reliability was established by Ertan . Giving a reply of "no" to positive questions and "yes" to negative questions yields 1 score on the evaluation scale, and having a score of 6 and above is accepted as significant for depression symptoms (4).

The Pain Beliefs Questionnaire was developed by Edwards et al. (1992)(5) and its validation and reliability were established in Turkey by Berk (6). The Pain Beliefs Questionnaire has 12 questions which evaluate two different belief types, psychological and organic, for the source and results of pain.

Data was collected by the researchers through face to face interviews; each interview lasted 20-30 minutes. Data were analysed using SPSS (Statistical Package for Social Sciences for Windows) 13. Apart from descriptive statistics (frequency, percentage, average, standard deviation), the Kolmogrov – Smirnov distribution test, Pearson chi-square test, Fisher Exact test (independent samples), t-test, one- way ANOVA test, Pearson correlation analysis and linear regression analysis were used to analyse the normality of the distributions and test for main effects and correlations.

Results

Thirty point eight percent of the individuals who participated in the study were female and 69.2% were male. According to the American Psychological Association classification system, 12.3% were adults (under 65 years of age), 45.2% were young old (65-74), 35.6% were middle old (75-84), and 6.8% were oldest old (85 and above). In terms of educational status, 34.2% were literate, 42.5% were elementary school graduates, 8.2% were secondary school graduates, 8.9% were high-school graduates, and 6.2% were university graduates. Body Mass Index (BMI) of more than half of the elders was 25 and above. Eighty point eight percent of participants stated they had experienced pain in the last month and 47.9% had leg pain, 16.4% had backache, and 13.7% had pain in the front part of their body.

According to the Numerical Rating Scale, 27.1% of individuals had pain of 5-7 severity and 22% had pain of 8-10 severity. With respect to pain type and duration, it was determined that 76% of participants had chronic pain, 4.8% had acute pain, 30.1% had continuous pain, and 45.9% had discontinuous pain. (Table 1)

Table 1 shows the demographic characteristics and pain severity of individuals in the study group. When the age of individuals was used as the dependent variable, there was no statistically significant relationship between age and severity of pain (p=0.305). In the young old group 46.9% complained

Table 1— Pain Severity by Demographic Characteristics.

		Mild Pain		Severe Pain		Unbearable Pain		
		n	%	n	%	n	%	
Age	< 65	6	10.0	6	18.8	5	19.2	X^2=7.174
	65-74	25	41.7	15	46.9	9	34.6	p=0.305
	75-84	24	40.0	11	34.4	8	30.8	
	>85	5	8.3	–	–	4	15.4	
Gender	Female	23	38.3	9	28.1	8	30.8	X^2=1.116
	Male	37	61.7	23	71.9	18	69.2	p=0.572
Education Status	Literate	18	30.0	15	46.9	9	34.6	X2=10.676
	Elementary school	32	53.3	12	37.5	8	30.8	p=0.221
	Secondary school	2	3.3	3	9.4	3	11.5	
	High school	5	8.3	2	6.3	3	11.5	
	License	3	5.0	–	–	3	11.5	
BMI	18-25	26	43.3	13	41.9	11	42.3	X^2=2.624
	25-30	22	36.7	10	32.3	6	23.1	p=0.623
	30 +	12	20.0	8	25.8	9	34.6	

Numeric Rating Scale: 1-4 mild pain, 5-7 severe pain, 8-10 unbearable pain.

of severe pain and 34.6% of unbearable pain. When pain severity is analyzed according to gender, 28.1% of those who had severe pain were female and 71.9% were male; 30.8% of those who had very severe unbearable pain were female, 69.2% were male. There was no statistically significant relation between gender and pain severity (p= 0.572).

When pain severity was analyzed according to educational status, 46.9% of those who had severe pain were literate, 37.5% were elementary school graduates, 9.4% were secondary school graduates, and 6.2% were high-school graduates. Thirty-four point six percent of those who had very severe pain were literate, 30.8% were elementary school graduates, 11.5% were secondary school graduates, and 11.5% were high-school graduates. There was no statistically significant relationship between educational level and pain severity (p=0.221).

With respect to factors that increase pain, we found that walking (28.4%), standing (17.8%), and climbing stairs (13.6%) increase pain, while resting (50.3%), lying down (15.2%), sleeping (13.1%) and doing exercise (11.7%) decrease pain. When the effects of pain on daily life were analyzed, we determined that it caused limitation of movement among 61.9% of participants, insomnia among 44.1% and loss of strength in arms and legs among 43.2%.(Table 2)

When pain beliefs of the study participants were analysed, we observed that the beliefs that "It is easier to cope with pain when we are happy" and "Pain is a sign of disease" were expressed at the same frequency (51%), the belief that "feeling depressed worsens pain" was expressed by 48%, "feeling pain is a sign that something is going wrong within the body" was expressed by 47%, and the belief that "amount of pain depends on tissue damage" was expressed by 45%.

Nearly half of the elderly participants (42%) answered "always" to the statements "Being worried worsens pain", "It is easier to cope pain when we are happy", "Thinking of pain worsens it", and "Feeling depressed worsens pain," which are included within the psychological belief group. T-test results showed that psychological belief score means differed significantly, according to participants' pain status (t=1.559; p=0.045). The psychological belief scores of participants who did not have pain were higher than those for participants who did have pain (sd=1.583). When correlation between pain severity and pain belief was searched, It was revealed that only psychological belief has a negative impact on the pain severity (r=-0.241; p=0.003) (Table 3, 4).

It was determined that 86.3% of the elderly participants residing in nursing homes had one or more chronic diseases, and 51.4% had signs of depression. Statistical analysis revealed that 58.7 % of participants with chronic pain and 57.1% of participants with acute pain also had symptoms of depression (X^2=12.496, p= 0.002). With respect to medication status, 27.4% of participants did not use any drugs for

Table 2— Results of the Pain Beliefs Questionnaire.

Organic Beliefs	Ajwaxs %	Almost Always %	Often %	Sometimes %	Rarely %	Neyer %	Mean
1. Pain is the result of dam age to the tissues of the body	42	12	8	15	13	10	2.74
2. Physical exexc.ise makes, pain, worse	25	14	7	16	10	29	3.57
3. It is impossible to do much for oneself to relieve pain	25	8	12	21	12	22	3.53
5. Experjencing pain is a sign that something is wrong with the body	47	16	11	10	5	10	2.42
7.Being in pain prevents you from enjoying hobbies and social activities	38	12	10	16	5	19	2.95
8. The amount of pain is related to the, amount of damage.	45	15	16	14	5	4	2.34
10. It is impossible to control pain on your own	33	9	11	20	12	16	3.16
11. Pain is a sign of illness	51	18	9	11	5	6	2.21
Psychological Beliefs							
4. Being anxious makes pain worse	41	12	6	14	10	16	2.89
6. When relaxed pain is easier to cope with	51	16	6	8	10	9	2.36
9. Thinking about pain makes it worse	42	16	6	10	12	14	2.75
12. Feeling depressed makes pajn seem	48	14	9	12	8	10	2.47

Table 3— Pain Characteristics and Depression in Elderly.

		Depression				
		No		Yes		
		n	%	n	%	
Pain type	Chronic pain	45	41.3	64	58.7	X^2=12.496
	Acute pain	3	42.9	4	57.1	p=0.002
Pain pattern	Continuous	17	39.5	26	60.5	X^2=13.775
	Intermittent	28	42.4	38	57.6	p=0.008
	Instant	2	66.7	1	33.3	

Table 4— Correlation Between Pain Severity and Subgroup of Pain Belief.

		Pain Severity	Organic Belief Score	Psychological Belief Score
Pain severity	r	1.000	-0.075	-0.241
	P	0.000	0.365	0.003
	N	146	146	146
Organic belief score	r	-0.075	1.000	0.400
	P	0.365	0.000	0.000
	N	146	146	146
Psychological belief score	r	-0.241	0.400	1.000
	P	0.003	0.000	0.000
	N	146	146	146

pain, 41.8% used only one drug, and 30.8% used two or more types of drug. When drug use was analyzed according to group, it was determined that the most used drugs were in the anti-depressant group (28.8%), 4.1% were nonsteroid anti-inflammatory drugs (NSAI), 3.4% were antiepileptic drugs, and 3.4% were analgesic drugs. When methods used by participants to reduce pain were analyzed, it was determined that 69.6% used pain-killers and 10.4% preferred physical treatment methods.

Pain and depression influence physical functions of the elderly negatively. In this study it was observed that neurological disease and chronic pain are factors that influence depression. In a study by Gümüş, acute or chronic pain influences depression (2). In the present study, it was determined that risk of depression is higher among the elderly who have chronic pain (p=0.002). Esp. it was frequently seen in neurological disease when compared with other chronic diseases (Table 5).

Table 5— Correlation of Depression and Chronic Diseases.

		Absent		Present		
		n	%	n	%	
Cardiovascular system	No	20	48.8	21	51.2	X^2=0.001
	Yes	50	48.5	53	51.5	p=0.563
Osteoarthritis	No	53	49.1	55	50.9	X^2=0.037
	Yes	17	47.2	19	52.8	p=0.500
Diabetis mellitus	No	56	48.7	59	51.3	X^2=0.002
	Yes	14	48.3	15	51.7	p=0.567
Urinary system	No	52	48.6	55	51.4	X^2=0.000
	Yes	18	48.6	19	51.4	p=0.573
Central & Peripheral nervous system	No	57	54.3	48	45.7	X^2=4.998
	Yes	13	33.3	26	66.7	p=0.020
Psychiatric	No	44	53.0	39	47.0	X^2=l.519
	Yes	26	42.6	35	57.4	p=0.144
Oncology	No	68	47.9	74	52.1	X^2=2.144
	Yes	2	100.0	–	–	p=0.235
Vitamine deficiency	No	49	49.5	50	50.5	X^2=0.099
	Yes	21	46.7	24	53.3	p=0.447
Respiratory system	No	51	48.1	55	51.9	X^2=0.040
	Yes	19	50.0	19	50.0	p=0.495
Anemia	No	55	48.2	59	51.8	X^2=0.029
	Yes	15	50.0	15	50.0	p=0.513
Gastritis	No	53	53.0	47	47.0	X^2=2.524
	Yes	17	38.6	27	61.4	p=0.079
Others	No	53	48.6	56	51.4	X^2=0.000
	Yes	17	48.6	18	51.4	p=0.575
Number of diseases which patient have at the time of questionaires	0	3	30.0	7	70.0	
	1	11	91.7	1	8.3	
	2	13	43.3	17	56.7	
	3	12	60.0	8	40.0	X^2=14.341
	4	14	48.3	15	51.7	p=0.073
	5	8	42.1	11	57.9	
	6	5	33.3	10	66.7	
	7	2	33.3	4	66.7	
	8	2	66.7	1	33.3	

Discussion

The frequency of pain reported by the elderly varies between 45% and 80% according to age, gender and the region where they live. In a study carried out with the elderly in 7 cities in Turkey, it was reported that pain prevalence is 89% and chronic pain prevalence is 65% (2). Seventy–eighty five percent of the elderly living in nursing homes have chronic pain that disrupts activities of daily life and influences their quality of life (1,7). In a study carried out at a nursing home in Holland by van Herk et al., pain prevalence was recorded as 66% (8); in a study carried out in America in 2005 by Cadogan it was 51% (9); and in a study carried out in Canada in 2003-2005 the prevalence of musculoskeletal pain was 64% (10).

When the pain severity of elderly people was analyzed, it was determined that nearly half of those who participated in the study had pain of 5-10 severity according to the nominal pain scale. Studies have reported medium levels of pain severity among the elderly (8,9). In the present study, chronic pain prevalence was determined to be 76%.

Perception of pain is influenced by many factors such as educational status, gender, and previous pain experiences. In this study, we determined that age, gender, educational status and BMI do not have a significant effect on pain severity. In a literature review by Takai et al., it was reported that age did influence pain severity (11).

We determined that 47.9% of participants had pain in their legs. In different studies it has generally been reported that pain is generally arthralgia (74.2%), which is followed by pain in the knees (19.5%) and hips (16.5%) (12).

In the literature it has been reported that 59% of pain in elderly people (age 65 and over) is caused by osteoarthritis (8). Elderly people who are suffering from pain may have sleep disorders, hopelessness, loss of self-confidence and/or depression and even lose the ability to carry out activities of daily life (13).

In relieving pain with drugs, opioid (narcotic analgesics – NA), non-steroid anti-inflammatory (NSAI) drugs, local anesthetics, and adjuvant group drugs are generally used. In clinical studies, it has been found that the efficiency of treatments decreases as a person gets older. In spite of this, the first attempt at relieving pain among the elderly is generally drug treatment (14).

Since all pharmacokinetic phases of drugs with respect to metabolism, absorption, excretion and distribution volumes are influenced by old age, drug interactions are observed more frequently. Since drug doses applied to the elderly may show relatively higher blood levels and a longer half-life, low doses are suggested at the beginning (15).

Methods apart from drugs are commonly used among the elderly for relieving pain. When non-drug methods for relieving pain were analyzed, it was observed that 30% of people pray, 26.2% do exercises, 23.3% have a massage, and 18.4% prefers thermal springs or healing water (16).

The present study determined that most of the elderly living in nursing homes (86.3%) have one or more chronic disease. In similar studies, this frequency varies between 47.9% and 68.4%. Chronic disease among the elderly was higher in our study (11).

Chronic diseases which increase together with old age result in multiple drug use. In this study it was observed that 41.8% of the elderly used at least one drug and the drug group which is most commonly used is anti-depressants. In the studies of 23 nursing homes in Turkey, it was found that the most commonly used drugs were cardiovascular system drugs and analgesics (20.8%) (12). The findings from the present study differ from those in the literature.

Pain influences physical functions of elderly people negatively. In this study it was determined that it causes insomnia, limitation of movement, and loss of strength in arms and legs. In the literature it has been reported that pain decreases sleep and activity levels and causes loss of strength in arms and legs. The literature findings and the results of this study are similar (1,2,7).

When factors that increase pain were analyzed, we found that walking, standing, and climbing stairs increase pain, and that the elderly generally (69.6%) preferred using pain-killers in order to cope with it. Gümüş et al. reported that the factor which had the greatest effect on inducing pain was an increase in activity (2). Our result is similar to the literature findings.

Pain may cause social isolation, anxiety and depression among the elderly, or conversely, the reason for chronic pain may be depression. For example, the prevalence of depression among elderly people living in nursing homes in Turkey was found to range from 36.0% to 76.0% (2). Pain and depression influence quality of life and physical functions of the elderly negatively; therefore, depression should definitely be investigated when evaluating pain findings among individuals (14).

Another factor which influences pain perception among the elderly is previous experiences and pain beliefs of the individual. It has been reported that pain, which is thought to emerge as a biological reaction depending on tissue damage, in fact is related to genetic, emotional, cultural, belief and

individual factors, and therefore, although pain is related to physiological reasons, the pain experience and severity should be analyzed according to individual differences (13).

In a study by Koçoğlu and Özdemir in which pain beliefs were analyzed, it was reported that socio-demographic and economic status influence various properties of pain. For example this study found that being old, female, and having low educational and economic levels are factors which increase the experience of pain. Moreover, it was also emphasized that it is important in pain evaluation to know the interpretations of elderly people and the meaning they attribute to pain (17).

In the literature, it has been reported that organic beliefs about pain are related to physical function level, and as organic pain belief decreases there is an increase in functional level (17). In this study, the belief that "Pain results from tissue damage" was adopted by 42% of the elderly and the belief that "Pain is a sign of disease" was adopted by 51%. According to this result, it can be accepted that individuals living in nursing homes perceive pain as a disease.

In geriatric patient group, during evaluation of pain severity, pain belief also should be evaluated due to the interaction between them (17). The presence of negative correlation between pain severity and pain behaviour should be kept in mind during evaluation of geriatric patient.

The risk of depression has an important place among mental problems experienced in old age. In some of the studies that have been carried out in our country since 1991, depression prevalence among the elderly living in nursing homes varied between 6% and 50% (18). Demir et al. reported that depression prevalence among the elderly in nursing home was 68.9% (19). In this study risk of depression was observed among more than half of the elderly (51.4%).

The risk of depression and pain influence physical functions of the elderly negatively. In this study, it was observed that neurological disease and chronic pain are factors that influence risk of depression. In a study by Gümüş, acute or chronic pain influences depression (2). In the present study, it was determined that the risk of depression is higher among the elderly who have chronic pain.

In the light of this study we can say that pain is frequently seen as a common symptom in elderly residents living in nursing homes. It was revealed that pain severity has strong correlation between pain beliefs. In order to improve their quality of life, during pain management we have take patient's pain belief into consideration.

References

1. Zanocchi M, Maero B, Nicola E, et al. Chronic pain in a sample of nursing home residents: Prevalence, characteristics, influence on quality of life. Arch Gerontol Geriatr 2008;47(1):121-8. (PMID:18006088).
2. Gümüş BA, Keskin G, Orgun F. Pain and living activities in elderly at a nursing home: An investigation in terms of depressıon, anxiety and somatization. Turkish Journal of Geriatrics 2012;15(3):299-305. (in Turkish).
3. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: A preliminary report. J Psychiatr Res 1983;17(1):37-49. (PMID:7183759).
4. Ertan T, Eker E, Şar V. Reliability and validity of the Geriatric depression scale in Turkish elderly population. Archives of Neuropsychiatry 1997;34(2):62-71.
5. Edvards LC, Pearce CA, Turner-Stokers L, Jones A. The pain beliefs questionnaire: An Investigastion of beliefs in the causes and consequences of pain. Pain 1992;51(3):267-72. (PMID:1491853).
6. Sertel Berk H Ö, Bahadır G. The experience of chronic pain and pain beliefs. The Journal of The Turkish Society of Algology 2007;19 (4):5-16. (PMID:18159574).
7. Cavalieri TA. Management of pain in older adults. J Am Osteopath Assoc 2005;105 (3 Suppl 1):12-7. (PMID:18154193).
8. Van Herk R, Boerlage AA, Van Dijk M, Baar FP, Tibboel D, de Wit R. Pain management in Dutch nursing homes leaves much to be desired. Pain Manag Nurs 2009;10(1):32-9. (PMID:19264281).
9. Cadogan MP, Edelen MO, Lorenz KA, et al. The relationship of reported pain severity to perceived effect on function of nursing home residents. J Gerontol A Biol Sci Med Sci 2008;63(9):969-73. (PMID:18840802).
10. D'Astolfo CJ. Humphreys BK. A record review of reported musculoskeletal pain in an Ontario long term care facility. BMC Geriatrics 2006;6(5):1-7. (PMID:16556306).
11. Takai Y, Yamamoto-Mitani N, Okamoto Y, Koyama K, Honda A. Literature review of pain prevalence among older residents of nursing homes. Pain Manag Nurs 2010;11(4):209-23. (PMID:21095596).
12. Gündüzoğlu ÇN, Karadakovan A. Pain management in elderly people. Journal of Geriatric and Geriatric Neuropsychiatry 2011;2(2-3):41-8.
13. Mimi MY Tse, Suki SK Ho. Pain management for older persons living in nursing homes: A pilot study. Pain Manag Nurs 2013;14(2):10-21. (PMID:23688367).
14. Onar E, Kapucu S. Polypharmacy in the elderly. Journal of Academic Geriatrics 2011;3(1):22-8.
15. Lapene KL, Quilliam BJ, Chow W, Kim MS. Pharmacologic management of non-cancer pain among nursing home residents. J Pain Symptom Manage 2013;45(1):33-42. (PMID:22841409).

16. Monsivais D, McNeill J. Multicultural influences on pain medication attitudes and beliefs in patients with nonmalignant chronic pain syndromes. Pain Manag Nurs 2007;8(2):64-71. (PMID:17544125).
17. Koçoğlu D, Özdemir L. The relation between pain and pain beliefs and sociodemographic-economic characteristics in an adult population. Agri 2011;23(2):64-70. (PMID:21644106). (in Turkish).
18. Tiong WW, Yap P, Huat Koh GC, Phoon Fong N, Luo N. Prevalence and risk factors of depression in the elderly nursing home residents in Singapore. Aging and Mental Health 2013;17(6):724-31. (PMID: 23461826).
19. Demir G, Ünsal A, Gürol AG, Çoban A. Study of prevalence of depression among elders living at nursing home and house. Gümüşhane University Journal of Health Sciences 2013;2(1):1-12. (in Turkish).

Turkish Journal of Geriatrics
2014; 17 (2) 188-195

Önder İLGİLİ[1]
Berna ARDA[1]
Kerim MUNİR[2]

Review Article

ETHICS IN GERIATRIC MEDICINE RESEARCH

Abstract

This article aims to evaluate the research process in geriatrics from the ethical point of view. The elderly population is increasing rapidly, but there is no parallel in the amount of research concerning this demographic. On the other hand, in the light of research ethics, this group mainly represents vulnerable people and requires more sensitivity. Taking into account all these features, fundamental principles in research ethics are first considered: the soundness of the scientific project, qualifications of the investigators, ethics committee approval, informed consent, confidentiality and privacy, beneficence/nonmaleficence, and justice are evaluated. Special ethical issues in geriatric research such as ageism and research inclusion, paucity of research involving elderly people, vulnerability of elderly subjects, and cognitive impairments are discussed separately.

Key Words: Ethics; Research; Geriatrics.

Derleme

GERİATRİ ARAŞTIRMALARINDA ETİK

Öz

Bu makale geriatri alanındaki araştırmaları etik açıdan değerlendirmeyi amaçlamaktadır. Bir yandan tüm dünyada yaşlı nüfus giderek artarken, yaşlılarla ilgili araştırmaların buna paralel olarak artmadığı görülmektedir. Öte yandan geriatrik populasyon araştırma etiği açısından çoğunlukla zedelenebilir bir grubu temsil etmekte bu nedenle de hassasiyet gerektirmektedir. Bu özellikler dikkate alınarak, öncelikle araştırma deseninin sağlamlığı, araştırmacıların nitelikleri, etik kurul onayı, aydınlatılmış onam, gizlilik ve mahremiyet, yararlılık ve zarar vermeme, adalet gibi araştırma etiğinin temel ilkeleri üzerinde durulmuştur. Geriatri araştırmalarındaki etik açıdan özel kabul edilen; yaş ve araştırmaya dahil edilmeye etkisi, zedelenebilir yaşlı denekler, bilişsel bozuklukların bulunduğu yaşlı deneklerde aydınlatılmış onam sorunları ayrıca irdelenmiştir.

Anahtar Sözcükler: Etik; Araştırma; Geriatri.

İletişim *(Correspondance)*

BERNA ARDA
Ankara University School of Medicine, History of Medicine and Ethics Department Dalı ANKARA

Tlf: 0312 595 81 61
e-posta: arda@medicine.ankara.edu.tr

Geliş Tarihi: 09/09/2013
(Received)

Kabul Tarihi: 24/01/2014
(Accepted)

[1] Ankara University School of Medicine, History of Medicine and Ethics Department Dalı, ANKARA, Türkiye
[2] Boston Children's Hospital, Developmental Medicine, BOSTON, ABD

INTRODUCTION

The world population aged 65 and older is estimated to be 420 million (1). The increase in the proportion of aged citizens across the globe presents important ethical challenges and obligations in confronting health care needs. The demand for medical services for the elderly is expected to rise exponentially, especially in emerging free-market economies, both in terms of the need for intensive multidisciplinary care and also in terms of the increasing cost of complex and long-term services as a proportion of overall health care. Geriatric medicine will represent an important dimension in the lives of all members of society. This review examines the ethical dimension of research in geriatric medicine in the emerging free market countries. In High Income Countries as a whole, an estimated 73 percent of people aged 65 and over lived in urban areas in 1990, and this figure is projected to reach 80% by 2015. In Low Income Countries over one-third (34%) of people aged 65 and older are estimated to live in urban areas. This proportion is expected to exceed 50% by the year 2015. At the national level for most Low Income Countries, there is a lack of systematic research regarding the social, economic, and health status indicators of the elderly population segment (1).

At the outset it needs to be emphasized that geriatrics needs to be examined in a positive framework. Human longevity is a cause of celebration as a result of advances in medical research. There are unique aspects of research in geriatric medicine. A critical issue is that too often research involving the young and even the middle-aged as adult subjects of medical investigations does not necessarily benefit the elderly. In order to address the emerging issues, many programs need to train professionals specialized in research in geriatrics. A number of journals specializing in geriatrics are now flourishing and international funding for reseach on aging is expanding. Parallel to this progress, many important ethical concerns that are emerging involve older subjects as research participants, as well as their families, with respect to the duties and responsibilities of investigators, caregivers, funding agencies, institutions, providers, industry, communities and multisite and multi-disciplinary collaborative relationships (2-4). Conventional research ethics literature and legislation provides guidance for the ethical conduct of research, but clinical realities related to the medical care of older subjects inevitably have a major impact on the actual conduct of research. Some of these aspects can be summarized as follows: compromised health, susceptibility to dangers owing to multiple age-related comorbid conditions, polypharmacy, and difficulties related to reduced mobility, communication, and cognitive functioning (3,4). Nonetheless it is essential that inclusion of the elderly is promoted in terms of distributive justice. This entails the need for a "new" approach to the establishment of inclusion and exclusion criteria, careful assessment of the benefit-burden ratio, and consideration of issues related to gender disparities, process of informed consent, assessment of competency, and protection of privacy (3). The main theme of this review is the discussion of the research process with the elderly people as a vulnerable group, associated limitations and difficulties, and the effects of ageism in light of the relevant literature. Both fundamental and special geriatric aspects of research ethics are included for guidance.

Fundamental Principles in Research Ethics

Scientifically Sound Research Project: Research designates a set of procedures designed to test a hypothesis and permit conclusions to be drawn; thereby its outcome contributes to generalizable knowledge. A characteristic feature of a research project involves a formal protocol, setting forth an objective and a set of procedures designed to reach the project's aims. In some cases research and therapeutic practice may be carried out together, especially when research is designed to evaluate the safety and efficacy of a therapy. Invariably, considerations related to the well-being of the human subject take precedence over the interests of science and society (5). Therefore medical research involving human subjects must conform to generally accepted scientific principles, and be based on a thorough knowledge of the scientific literature as well as other relevant sources of information, and on the provision of adequate laboratory facilities. The human subject research considerations should be at the core for achievement of scientific objectives of any study; participation of human subjects can only be justified if these conditions are ensured (5,6).

Potential research subjects ought to be made aware of any risks or unfavorable circumstances, especially from proposals advocating trivial but commercially motivated research. These include post-licensing drug comparisons that have more to do with marketing than with useful clinical comparisons (7). Recruiting human subjects for such clinical trials represents an unnecessary and potentially exploitative use of their trust and altruism (2).

Qualifications of the Investigators: The highest degree of skill and care is required through all stages of research, and procedures should be conducted only by scientifically qualifi-



ed professionals and under the supervision of medical personnel according to good clinical practice (5,8).

Research Ethics Committee Approval: Research activities should undergo a thorough review process with the objective of protection of human subjects (6). Research protocols should be submitted for consideration and comment as well as guidance, and approved by an independent ethical review committee. Protocols should include information regarding sources of funding, sponsorships, institutional affiliations and compensation-incentives. As it is stated in the Helsinki Declaration, research ethics committees should have the responsibility to monitor ongoing trials. The researchers should be obligated to provide monitoring information to the committee, with clearly defined guidelines with respect to reporting occurrence of any adverse events (5,6).

Informed Consent: The Nuremberg Code dictates that the consent of human subjects be voluntary. A central premise of this is the legal capacity of a subject to give informed consent without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion. In order to exercise this right, a subject needs to possess sufficient knowledge and comprehension of the elements of the research: its risks and benefits, nature, duration, and purpose, as well as possible conflicts of interest and institutional affiliations of the researchers. Whenever therapies are involved, the subjects need to be offered alternative procedures (5,8). It is necessary to adapt the presentation of information to the subject's intellectual and mental capacities (6). To avoid misunderstanding, subjects should be provided with the opportunity to ask questions and to contact the researchers if additional questions arise or if they change their decision at any time. After ensuring that the subject has understood the information, the researcher should then document the subject's freely-given consent. If the consent cannot be obtained in written form, non-written consent must be elicited and again formally documented and witnessed. During the whole process, the professionals should be particularly cautious if the subject is in a dependent relationship or may consent under duress (5).

For elderly subjects who are legally incompetent, physically or mentally unable to give consent, the investigators must obtain informed consent from their legally authorized representatives in accordance with applicable law. The subjects should not be included in research unless the research is necessary to promote the health of the population represented, and cannot otherwise be performed on legally competent persons. When the subject is deemed to be legally incompetent but nonetheless is able to give assent to the decision for research participation, the investigator must obtain their assent in addition to the consent of the legally authorized representative. The refusal of a patient to participate in a study must never interfere with the patient–physician therapeutic relationship (5). Eventually the subjects should be informed of the right to withdraw consent to participate at any time without reprisal (6).

Confidentiality and Privacy: Investigators should establish adequate protections to respect and safeguard the privacy, confidentiality and integrity of the research subjects during the study procedures and to ensure that any information that can potentially identify a person is kept in secure and restricted files and away from unmonitored and unauthorized access (2,5).

Beneficence/Nonmaleficence: All research proposals should be preceded by careful assessment of any predictable risks and burdens, in comparison with foreseeable benefits to the participants (5). This perspective for protection of human subjects has absolute priority over social and scientific aspects. Furthermore, the benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic and therapeutic methods. This does not exclude the use of placebos, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists (5). At this time the local standard of treatment with respect to the best available current treatment option continues to be under debate. Nevertheless, the argument recognized by the FDA for resource poor countries does not apply to the US, or to all other highly developed countries. At this time the US regulations stand alone on this issue.

Justice: The distribution of burdens and benefits of research should be considered carefully by the researchers and the relevant ethics committees. Medical research is only justified if there is a reasonable likelihood that the populations within which the research is carried out stand to benefit from the results of the research (5). The selection of research subjects needs to be scrutinized in order to determine whether some classes of vulnerable subjects are being systematically selected simply because of convenience, cost, easy of availability, compromised status, or their manipulability, rather than for reasons directly related to the problem being studied (6). These subjects include not only women, children, and racial and ethnic minorities, but the elderly, persons with disabilities, those confined to institutions, and patients on public assistan-

ce. A further issue under debate is the premise that at the conclusion of the study, every subject entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study (5). Again, this principle has been linked by the FDA to the concept of locally available best standard of treatment, only applicable in resource poor countries, but not necessarily applicable in the context of resource poor settings within developed countries. Some have argued that such an adjustment of the principle of distributive justice would set a double standard, and that at least for the purposes of research involving human subjects such an exemption ought not to be applied.

Collection and Dissemination of Data: Investigators should ensure that they have no conflict of commitment with undue incentives to complete the research rapidly, without adequate regard for the validity and value of research results (2). Valid results, regardless of both positive and negative outcomes, represent valuable knowledge to the medical community, patients, and caregivers. All parts have a legitimate interest in receiving relevant information as soon as possible. In recognition of this, both researchers and journal editors should be committed to disseminating knowledge generated by studies in a timely manner consistent with the best scientific and ethical standards (2,5).

Investigators should adhere to accepted standards for publication and keep clear of scientific misconduct, fraud, sloppy research, fabrication, falsification and plagiarism (2,9). Roots of research misconduct related to individuals include lack of education and scientific discipline, excessive desire for institutional and academic promotions, desire for money, reputation (Hollywood syndrome), disproportionate institutional pressure, "publish or perish" perception and psychiatric disorders (10). Although there are several guidelines governing the responsible conduct of research, the ethical responsibilities primarily lie with the principal investigators (with institutional oversight) who design and carry out the research and publicize their findings (7).

Special Issues Concerning Ethics in Geriatric Research

Ageism and Research Inclusion

Until the 1980s, people over age 65 were excluded from clinical trials. Bugeja et al. examined all original research papers in four leading medical journals and found that of the 490 papers involving older subjects, 170 studies (35%) excluded those aged 75 years and above without any meaningful scientific justification (10). By 2005, the situation was noted by the authors to have improved, with 15% of the studies still excluding older subjects without due justification (11). Comorbidity, reduced life expectancy, polypharmacy and specific drug use, cognitive and physical impairment examined as main exclusion criteria in two recent studies and results supported the poor justification claims (12,13).

A parallel finding in 2000 involving a study of research ethics committee decisions revealed that review processes had not identified the non-inclusion of older people as an ethical issue (14).

A study conducted by Crome et al. in nine European countries over 540 subjects and six categories of professionals (geriatricians, general practitioners, nurses, clinical researchers, ethicists and pharmacists) revealed that 84% of the respondents believed that older people were underrepresented in clinical trials and that such underrepresentation caused difficulties for clinicians (79%), thus disadvantaging older people as a result (73%) (11).

Paucity of Research Involving Older Persons

Older people receive a disproportionately lesser share of the burdens and benefits of clinical research compared to young and middle aged adult subjects (4). There are multiple factors that limit research involving older subjects. These involve practical difficulties in conducting geriatric research, difficulties in the implementation of specific research procedures, social and cultural barriers to access, impaired capacity to provide informed consent, inconvenience, cost, and the likelihood of higher incidence of adverse events. Finally, since many elderly persons may have more limited means to access new treatments, they may be deemed a less attractive market with respect to clinical trials (4).

Although an obvious rationale for excluding cognitively impaired elderly subjects in research is the application of the first ethical principle in the Belmont report (respect for persons), excluding them violates the third ethical principle in the report (justice), especially if the research questions at hand cannot otherwise be addressed to help sustain research benefits that may accrue specifically to the elderly. In other words individuals, irrespective of their age or other vulnerable circumstances, ought not to be systematically excluded if they are unlikely to benefit when the research is conducted without their participation (15).

While there are problems associated with the inclusion of the elderly in clinical trials, their exclusion altogether poses greater problems. Excuses in protocols related to such exclu-



sions based on ageism (often ages 70 and above) include: need for patients to be reliable/fully competent; able to follow instructions; and higher rates of poor compliance and dropping out (16). The work of Crome and colleagues (involving data from the Czech Republic, Lithuania, Italy, Israel, Netherlands, Poland, Romania, Spain and UK) agrees that exclusion from clinical trials on age grounds is unjustified (87%) and that under-representation of the elderly in trials causes difficulties for physicians (79%) and patients (73%) alike (11).

The poor representation of older patients in clinical trials leaves clinicians in a dilemma. If they prescribe treatments untested in older people, they do so in the absence of solid evidence of efficacy and toxicity for that age group. Alternatively, if they do not prescribe such treatments they may be denying them worthwhile benefits (11).

Vulnerable Elderly Subjects

Members of vulnerable subgroups of elderly include those with multiplex and chronic medical and mental conditions, cognitive impairments/dementia, those in nursing home or long-term care institutional settings, and those terminally ill and dying (16). An argument is that research involving the elderly subjects in each and every one of these sub-categories can and ought to be justified if indeed such research can benefit them. Elderly persons living in nursing homes have been thought of as particularly vulnerable, but with appropriate protections can participate in scientific research (16). Older people may experience conditions such as dementia or live in long-term care facilities that impair their ability to express their rights and interests (2). Nevertheless, by virtue of their burden they also deserve attention by the researchers, and protections need to be in place to ensure their inclusion. In this respect it may be important to appreciate that vulnerability can indeed arise through the under-researching of a group's particular condition or from not exposing them to the research process (16).

Particular attention ought to be paid to providing protections to ensure their participation. These include their deference to authority, obeisance, submissive dependence on others which may lead to a higher likelihood of manipulation or coercion, and/or lack of respect by others for the concept of their own lives and interests (16). There is a high level of gratitude from patients towards hospice staff. Because of this, patients may feel that they should not refuse to take part in research and consent may not necessarily be "freely given" (16).

Elderly Subjects with Cognitive Impairments

Some authors use cognitive impairment interchangeably with dementia. This is not necessarily correct, as elderly subjects experience varying degrees of cognitive impairments ranging from borderline to very severe (15); nevertheless, dementia in the elderly remains an overarching concern. Even subjects with Mini-Mental State exam scores as low as the 10-20 range may be able to give valid consent for projects. More complex information and more complicated decisions require greater degrees of cognitive function. Vulnerable elderly subjects of most concern in geriatric research remain those with dementia, and especially those who reside in long term care facilities. They are at particular risk of not gaining access to the fruits of the research endeavor, such as new and expensive medications or the latest diagnostic testing and surgical procedures (4).

Issues Related to the Process of Informed Consent: Informed consent means that the subject understands the relevant information and that the decision is made voluntarily. The cognitive and sensorineural deficits of some older persons may mean that they require more time to comprehend information. In practical terms, this extra time requires the commitment of empathic and well-trained staff and may need to include people who are responsible for the patient's health care. These research staff are as important to a well-designed protocol as the provision of adequate equipment and technical expertise (2). There are degrees of cognitive impairment and elderly patients with mild dementia generally have the capacity to consent (16). Incorporating the consent form questions into an information sheet so that questions follow relevant paragraphs that can be walked through in the consent process is helpful. Information sheets need to have a lower reading level and larger typeface (16). In addition, family will need to be involved in the consent process and the consenting subjects should have the right to express their point of view even if it is different from that of their relatives (16). Impaired decision making capacity and an inability to give informed consent may be a temporary condition or it may be permanent. Geriatric researchers often know patients or potential subjects before their loss of decision making capacity. There may be opportunities for advanced consent and proxy consent. Helping the subject to understand as fully as possible, and ascertaining how well the subject understands, is critical in geriatric research. A lot of authors have emphasized the importance of visual and hearing aids, such as pictures, vignettes, storybooks and audio- or videotapes. However, some of them showed that

these aids proved a distraction rather than an aid for elderly subjects. Educational training was also suggested as a method of enhancing decision-making capacity. Experienced consent seems a promising tool to optimize informed consent in frail elderly subjects (17).

Advance Directives: In general, the legal status of research advance directives is not clear. As an example, most of the state laws in the US creating advance directives focus on clinical decisions, especially those pertaining to the use of life-sustaining treatments. Promoting the use of advance directives for research might create the impression that they are required to do research on dementia. Only a small group of adults complete advance directives in daily clinical medicine; it is possible to assume that even fewer would be relevant to research, and one can envision a scenario in which research advance directives actually end up inhibiting rather than promoting dementia research (4).

Proxy Consent: A family member is most suitable for proxy consent because he or she knows the potential subject best and is most likely to make a decision that would be keeping with the subject's values. The proxy has the best interest of the subject at heart and will make the best decision. As a closely involved family member, the proxy is the person most likely to be affected by the decision. A negative aspect of proxy consent includes potential conflicts of interest. Data from clinical decision making studies demonstrate significant discord (4). Declaring someone unable to make decisions or to give consent should not be based on diagnostic labels. There is lack of legal clarity in using proxies. There is a need to ensure the proxy's independence from the research team and to overrule any possibility of conflict of interest. A key problem is how to ensure dispassionate proxy consent (16).

A role for assent: The ability of a research subject to express his or her willingness to agree to go along with a research protocol, even if the subject cannot provide informed consent, involves the process of assent that is often used in research involving adolescents. When given information about specific research protocols, even with very impaired people with dementia, it is possible to see that assent supports the ability to reveal the subjects' values and preferences (4).

Challenges Involving Subjects with Serious Cognitive Impairments

There are many ethical and legal challenges central to research subjects with cognitive impairments. These include: (1) determining capacity; (2) surrogate decision making; (3) assessment of risk; (4) potential benefits; and (5) measures to increase study understanding (15). Grisso and Appelbaum (1998) note four factors relevant to assessing capacity. These include the ability to: (i) communicate a choice; (ii) understand relevant information; (iii) appreciate alternatives/consequences; and (iv) think rationally about issues involved (16).

These factors need to be considered in a purely cognitive sense, but at the same time there may be a lack of emotional appreciation. In particular, in subjects with dementia or pseudodementia there may be comorbidity with depression that is unrecognized and untreated.

Challenges in Rrecruitment and Specialized Research Settings

Recruitment: Challenges in the recruitment phase of a research project are highly important in that this phase is directly linked to representative sampling frame, study validity and generalizability, as well as ethical principles with respect to the promotion of diverse and just participation, and consideration of feasibility and retention of participants (3).

Homebound Elderly Subjects: One challenge involving research with homebound elderly adults is that they may not closely monitored by health professionals. Furthermore, they often remain socially isolated. Conducting studies with homebound older adults involves additional vulnerabilities, especially in terms of the separation of researcher and therapeutic roles. The venue of the research also provides greater access to participants' otherwise private home lives and thereby presents further ethical challenges. Care must be taken to describe the course of action that will be taken if specific risks are observed during the course of investigation. Researchers will need to be in close contact with the primary physician or home health nurse. Researchers will need to further inform potential participants that if any sign of abuse or neglect is observed, they will notify adult protective services. Furthermore, if a threatening situation is observed, this will be notified to the research ethics committee as an adverse event (18).

Palliative Care: Palliative care is "the active, total care of patients whose disease is not responsive to curative treatment. Control of pain, other symptoms and psychological, social and spiritual problems are paramount. The goal of palliative care is the achievement of the best quality of life for patients and families" (16). Direct therapeutic benefits of research for palliative care patients can be seen, like better pain and symptom control, fine tuning of sedation, and better understanding of nutrition and hydration. Attention, understanding, worth, hope, being altruistic and being valued are indirect benefits.

There are costs to be borne by palliative care patients involved in research. It seems important to engage the whole multi-professional team in defining hospice research priorities. Hospice staff should be involved in early discussions and designing of research and in the progress of studies through ethical approval (16).

Recommendations for Training in Responsible Conduct of Research and Service on Research Ethics Committees

Training in Responsible Conduct of Research: Investigator training in Responsible Conduct of Research (RCR) is currently implemented in the USA as a requirement in all federally sponsored research training. The model is also increasingly disseminated in Europe as well as by many major funding agencies promoting research in Low and Middle Income countries. This needs to be coupled with good research management and work of the research ethics committees in the institutional context (9).

Service on Research Ethics Committees: Geriatrics healthcare professionals should serve on these committees to provide input about the experiences of care and research in the elderly (2). Investigators should cultivate relationships with patient organizations to include expertise derived from the direct experience of aging and disease. Patient groups can assist the research team in the evaluation of risks and benefits and the value assessment at consensus conferences and workshops. This kind of participation will help researchers to decide whether to pursue particularly risky or innovative research (2).

CONCLUSIONS

As generally accepted, the ethical principles of beneficence and nonmaleficence were first mentioned in biomedical research, the respect for autonomy subsequently following in due course. The process of "informed consent" has become the respected beacon for the application of these ethical principles in research practice. There are now various levels of safeguards for ethical research practice: international codes and guidelines, national legislations and the ensuing work of research ethics committees. Maintaining the rights of participants and preventing probable injury or harm to human subjects continue to be the overarching aim in the conduct of biomedical research involving human subjects worldwide.

In geriatric medicine, and also in pediatrics, child psychiatry and psychiatry, there are common concerns for the application of these ethical principles, especially with respect to the difficulties relevant to the process of obtaining informed consent. Special difficulties mentioned concerning research on geriatric populations include less willingness or fewer opportunties available to them to participate in research. There are myriad reasons for the exclusion of elderly human subjects from biomedical research, the least of which ought to involve their higher likelihood to suffer from multiple ailments (including their greater probability of suffering from hearing and visual losses, and limitations in cognitive abilities including onset of dementia), or the probability of their being subjected to a multitude of procedures and/or polypharmacy. In fact, one would imagine that these factors ought to be grounds for their inclusion in research, as it would entail benefits to them if they are indeed to be implictly included rather than excluded. Nor would one exclude the elderly because they reside in environments in which their individual rights may be constrained by virtue of isolation, or living in long term care settings. Ironically, a major barrier to the elicitation of informed consent is also implicit as a barrier to applying the principle of distributive justice. Protecting the rights of elderly participants and preventing them from the risk of exposure to harm or injury during research, although an overarching aim, ought therefore not to be a criterion for exclusion. Inclusion implies respect for a better life with all the potential benefits and fruits of research.

In this paper we argue that greater attention ought to be paid to the principle of distributive justice, with emphasis on the expenditure of the needed time and effort to ensure that researchers, institutions and funding agencies appreciate the inclusion of elderly subjects. The era of excessive protections as a rationale for exclusion of the elderly from research can no longer be a convenient excuse for not resolving challenging informed consent problems. Protections per se are not an adequate solution to ensuring beneficence, or detering malficence, since benefits cannot accrue without inclusion. This is an essential fact. The approaches to resolve these concerns that we argue herein are likely to strenghten the enterprise of geriatric research in the future, especially in the context of evolving demographics worldwide.

REFERENCES

1. Aksoydan E. Are developing countries ready for ageing populations? An examination on the socio-demographic,economic and health status of elderly in Turkey. Turkish Journal of Geriatrics 2009;12(2):102–9.
2. AGS Ethics Committee; AGS Research Committee. The responsible conduct of research. J Am Geriatr Soc 2001;49(8):1120–2. (PMID:11555077).

3. Seppet E, Pääsuke M, Conte M, Capri M, Franceschi C. Ethical aspects of aging research. Biogerontology 2011;12(6):491–502. (PMID:21604188).
4. Sachs GA, Cohen JH. Ethical challenges to research in geriatric medicine. In:Cassel KC (Eds).Geriatric Medicine. Fourth Edition. Springer, New York, USA 2003, pp 1253–61.
5. WMA. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bull World Health Organ 2001;79(4):373-4. (PMID:11357217).
6. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. 1979. [Internet] Available from: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html. Accessed: 28.03.2013.
7. Farsides C. The ethics of clinical research. In: Eckstein S (Eds). Manual for research ethics committees. 6th edition. Cambridge University Press, London, UK 2003, pp 5–14.
8. The Nuremberg Code. 1949. [Internet] Available from: http://www.hhs.gov/ohrp/archive/nurcode.html Accessed:25.01.2013
9. Başağaç Gül T. Research ethics in health sciences. (Sağlık Bilimlerinde Araştırma Etiği).In: B Arda, E Kahya, T Basagac Gul (Eds). Science Ethics and History of Science (Bilim Etiği ve Bilim Tarihi).2nd edition, Ankara Üniversitesi Basımevi, Ankara, Turkey 2009, pp 217–34. (in Turkish).
10. Bugeja G, Kumar A, Banerjee AK. Exclusion of elderly people from clinical research: A descriptive study of published reports. BMJ 1997;315(7115):1059. (PMID:9366735).
11. Crome P, Lally F, Cherubini A, et al. Exclusion of older people from clinical trials: Professional views from nine European countries participating in the PREDICT study. Drugs Aging 2011;28(8):667–77. (PMID:21812501).
12. Cherubini A, Oristrell J, Pla X, et al. The Persistent exclusion of older patients from ongoing clinical trials regarding heart failure. Arch Internal Med 2011;171(6):550-6. (PMID:2144844).
13. Cruz-Jentoft A, Carpena-Ruiz M, Montero-Errasquin B, Sanchez-Castellano C, Sanchez-Garcia E. Exclusion of older adults from ongoing clinical trials about type 2 diabetes mellitus. J Am Geriatr Soc 2013;61:734-8. (PMID: 23590338)
14. Bayer A, Tadd W. Unjustified exclusion of elderly people from studies submitted to research ethics committee for approval: descriptive study. BMJ 2000;321(7267):992–3. (PMID:11039965).
15. Monroe BT, Herr AK, Mion CL, Cowan LR. Ethical and legal issues in pain research in cognitively impaired older adults. Int J Nurs Stud 2012;50(9):1283-7. (PMID:23245707).
16. Eckstein S. Research involving vulnerable participants: some ethical issues. In:Eckstein S (Ed).Manual for research ethics committees. 6th edition. Cambridge University Press, London, UK 2003, pp 105–9.
17. Rikkert MG, Van Den Bercken JH, Ten Have HA, Hoefnagels WH. Experienced consent in geriatrics research: A new method to optimize the capacity to consent in frail elderly subjects. J Med Ethics 1997;23(5):271–6. (PMID:9358345).
18. Locher JL, Bronstein J, Robinson CO, Williams C, Ritchie CS. Ethical issues involving research conducted with homebound older adults. Gerontologist 2006;46(2):160–4. (PMID:16581879).

Turkish Journal of Geriatrics
2014; 17 (2) 196-199

Barçın ÖZCEM[1]
Feyza YAYCI[2]
Serpil DEREN[2]

Case Report

PROPOFOL-RELATED INFUSION SYNDROME IN A GERIATRIC PATIENT FOLLOWING THE USE OF PROPOFOL IN LOW DOSES AND SHORT DURATION, DURING AND AFTER CARDIAC SURGERY

Abstract

Propofol, is a potent short-acting intravenous sedative-hypnotic agent used for induction and maintainance of general anesthesia and to provide continuous sedation in the intensive care unit. Propofol-related infusion syndrome (PRIS) is a rare yet often fatal syndrome associated with the continuous infusion of propofol. It is characterized by severe metabolic acidosis, cardiac failure, bradycardia, myoglobinuria and renal failure. Hereby we present a case of PRIS which developed in a geriatric patient (74y), following coronary artery by-pass grafting and aortic valve replacement surgery in the early postoperative period. Propofol was used in low doses both intraoperatively and in the intensive care unit (ICU) postoperatively. The patient developed severe lactic acidosis, oliguria and bradycardia requiring cardiac pacing in the 6th hour postoperatively. Lactic acidosis and clinical condition improved promptly within a few hours, following the discontinuation of propofol infusion.

Key Words: Propofol; Acidosis, lactic; Cardiac Surgical Procedures; Aged.

Olgu Sunumu

GERİATRİK HASTADA AÇIK KALP AMELİYATI SIRASINDA VE SONRASINDA, PROPOFOLÜN DÜŞÜK İNFÜZYON DOZUNDA VERİLMESİNE RAĞMEN GELİŞEN PROPOFOL İNFÜZYON SENDROMU

Öz

Propofol, genel anestezi indüksiyonunda ve idamesinde, ayrıca yoğun bakımda sedasyon amacıyla kullanılan, kısa etkili potent bir hipnotik-sedatif ajandır. Propofol infüzyon sendromu, propofolün devamlı infüzyonuna bağlı gelişebilen, ender, ancak sıklıkla ölümle sonuçlanabilen bir durumdur. Ağır metabolik asidoz, kalp yetersizliği, bradikardi, miyoglobinüri ve böbrek yetersizliği ile karakterizedir. Bu makalede, koroner arter bypass greftleme ve aort kapağı replasmanı uygulanan geriatrik (74y) bir hastada postoperative erken dönemde gelişen propofol infüzyon sendromu bildirilmektedir. Hem anestezi sırasında, hem de postoperatif yoğun bakım sedasyonu sırasında düşük doz propofol uygulanan hastada, postoperative altıncı saatte ağır laktik asidoz, oligüri ve pacemaker gerektiren bradikardi gelişti. Propofol kesildikten sonra laktik asidoz ve hastanın genel durumunda bir kaç saat içinde hızlı bir düzelme kaydedildi.

Anahtar Sözcükler: Propofol; Laktik Asidoz; Kardiyak Cerrahi; Yaşlı.

İletişim ***(Correspondance)***

Barçın ÖZCEM
Yakın Doğu Üniversitesi Tıp Fakültesi Kalp ve Damar Cerrahisi Anabilim Dalı Lefkoşa, Kuzey Kıbrıs TC

Tlf: 0392 675 10 00
e-posta: drbarcinozcem@gmail.com

Geliş Tarihi: 27/08/2013
(Received)

Kabul Tarihi: 26/11/2013
(Accepted)

[1] Yakın Doğu Üniversitesi Tıp Fakültesi, Kalp ve Damar Cerrahisi Anabilim Dalı, Lefkoşa, Kuzey Kıbrıs TC
[2] Yakın Doğu Üniversitesi Tıp Fakültesi , Anastezi ve Reanimasyon Anabilim Dalı, Lefkoşa, Kuzey Kıbrıs TC

Introduction

Propofol, is a commonly used intravenous sedative-hypnotic agent utilized for anesthetic induction and maintenance, and sedation of the mechanically ventilated patients. Propofol-related infusion syndrome (PRIS) is a serious side effect of propofol infusion, characterized by severe metabolic acidosis, cardiac failure, bradycardia, hyperprexia, rhabdomyolysis, myoglobinuria and renal failure (1). PRIS is clasically known to occur in pediatric patients, and with propofol doses of higher than 4 mg/kg/hr and duration of infusion more than 48 hours (2). We present a case of PRIS in a geriatric patient (74y) who underwent coronary artery by-pass grafting (CABG) and aortic valve replacement (AVR) surgery. Propofol was used in doses smaller than usual, both in the induction and the maintenance of anesthesia, and in the early postoperative period in intensive care unit (ICU). Severe metabolic acidosis, oliguria and bradycardia requiring cardiac pacing developed in the 6th hour postoperatively. The clinical condition was attributed to PRIS, and cessation of propofol infusion led to recovery of the findings dramatically. Presenting that case, we wanted to emphasize that propofol infusion even in small doses could result in PRIS in geriatric patients.

Case Report

A 73 year-old male with severe aortic regurgitation and coronary artery disease was scheduled for CABG and AVR surgery. The patient was under antihypertensive and antilipidemic therapy and his baseline arterial blood pressure was 130/70mmHg, heart rate 66/min and left ventricular ejection fraction was 60 %. The induction of anesthesia was performed with midazolam 4mg, fentanyl 200mcg, propofol 50mg and rocuronium 50mg. The maintenance of anesthesia was implemented with sevoflurane inhalation, fentanyl infusion and incremental doses of propofol not exceeding a total dose of 250 mg. The course of anesthesia was uneventful except for a rise in lactic acid level up to 24 mg/dl with a compensated metabolic acidosis with negative base excess levels of 3-5 during the cardiopulmonary by-pass period. Following the removal of the x-clamp, infusion of norepinephrine and epinephrine in doses of 0.02 mcg/kg/min was initiated. In the ICU an infusion of propofol 2mg/kg/h was given during the mechanical ventilation. In the 1st hour of ICU stay, the patient became hypertensive and the propofol infusion was increased to a dose of 2.5 mg/kg/h while the vasopressor support was terminated. By the 6th hour of the ICU stay, the patient developed severe bradycardia (35/min) requiring cardiac pacing eventually. The blood gases revealed metabolic acidosis with gradually increasing lactate levels accompanied by hyperkalemia and oliguria (Table 1). The rate of intravenous fluid infusion was increased with the guidance of central venous pressure and vasopressor therapy with epinephrine (0.02mcg/kg/min) and norepinephrine (0.02mcg/kg/min) was initiated to restore tissue perfusion. Laboratory tests revealed a significant elevation in liver enzymes and triglyceride, creatine kinase, ure-

Table 1— Postoperative Blood Pressure, Heart Rate, Blood Gases, Lactate and Urinary Output.

	Postop 0th	Postop 3rd	Postop 6th	Postop 7th	Postop 8th	Postop 9th	Postop 10th	Postop 11th	Postop 12th	Postop 15th
Blood pressure (mmHg)	115/85	130/65	95/65	127/75	105/70	90/60	123/83	135/85	142/85	125/70
Heart rate	85/dk	82/dk	35/dk a	80/dk a	80/dk a	80/dk a	80/dk a	80/dk a	93/dk	78/dk
pH	7.45	7.42	7.25	7.2	7.18	7.22	7.34	7.36	7.4	7.45
HCO_3(mmol/L)	28	26.2	18.5	15	16	16.5	23	23.5	25	28
Lactate (mg/dL)	30	35	40	107	134	144	80	15	10	12
Base excess (mmol/L)	4	1.8	-8.2	-12	-11.2	-12	-3.5	-3	1	2.5
Sodium (Na) (mmol/L)	134	138	135	142	145	148	146	145	145	142
Potassium (K) (mmol/L)	3.94	4.23	4.5	5.15	5.8	6.2	5.2	4.8	4.9	4.5
Urine output (mL/hr)	160	130	25	30	25	35	80	100	120	140

a cardiac pacing was calibrated at 80/dk
Postop: Postoperative.

Table 2— Preoperative and Postoperative 15 hrs Laboratory Test Results.

	Preoperative	Postoperative 15th hours	Normal Range
Urea mg/dl	45	80	18–55
Creatinine mg/dl	1.2	1.69	0.70–1.20
Creatine kinase U/L	80	2132	20–200
Myoglobin ng/ml	—	1120	19–51
Creatine kinase-MB U/L	12	124	0–25
Troponin ng/ml	0.01	0.07	0.000-0.014
SGOT U/L	15	120	0–40
SGPT U/L	16	24	0–40
Triglyceride mg/dl	140	280	0–150

a and creatinine levels (Table 2). In the 8th postoperative hour the patient developed diffuse skin rash following antibiotherapy, which was attributed to an allergic reaction and treated with 125 mg methylprednisolone causing a deterioration in lactic metabolic acidosis. Exclusion of potential etiologic factors led us to the diagnosis of PRIS in the 10th postoperative hour. We discontinued propofol infusion resulting in a prompt and considerable improvement in the lactic acidosis, bradycardia and oliguria. The patient was discharged from the ICU on the postoperative 5th day with full recovery.

Discussion

PRIS was first defined by Bray in 1998 as a sudden onset of marked bradycardia resistant to treatment, with progression to asystole plus one of the following: hyperlipidemia, fatty infiltration of the liver, severe metabolic acidosis, or muscle involvement with evidence of rhabdomyolysis or myoglobinuria. There is both clinical and experimental evidence to suggest that propofol can trigger dysfunction of the mitochondrial respiratory chain, leading to depletion of ATP production and cellular hypoxia in tissues such as the heart and muscle (3). Fat overload associated with propofol infusion may contribute to increased plasma fatty acids which may lead to arrhythmias (4). This syndrome was initially recognized only in children, but has become increasingly recognized in adults (5). Postulated risk factors for PRIS include use of a high propofol dose (> 83 mcg/kg/min), a duration of therapy of > 48 hours, and concomitant vasopressor therapy. However, it needs to be stressed that PRIS can occur soon after the initiation of propofol therapy and even also at rather low doses (6). In our case, infusion dose of propofol was 2-2.5mg/kg/h (corresponding to a total dose of 40mcg/kg/min), and duration of the infusion was approximately 9 hours. Our case revealed that PRIS could also be seen with the use of propofol even in low doses and short duration in geriatric patients undergoing cardiac surgery. Presence of triggering factors such as catecholamine infusion or corticosteroids were also reported to contribute to the development of PRIS (2). There is evidence suggesting an association between propofol infusion and catecholamine response as a cause of PRIS (7). Besides, steroids are commonly cited as a cause of muscle damage which presents as rhabdomyolysis in the setting of critical illness (8).In our case, the use of catecholamines for the management of metabolic acidosis and corticosteroids for the skin rash, led to further deterioration in lactic acidosis. Our case also presented an increase in CK, CK-MB, troponine, myoglobine, urea and creatinine values postoperatively, which was hard to tell whether it was due to PRIS or cardyopulmonary by-pass (9, 3). On the other hand, the lipid profile is known to show no elevation due to cardiopulmonary bypass itself, but elevated triglyceride levels as in our case, are considered as an early marker in the development of PRIS (10,11). In a study by Fong et al., the mortality rate in PRIS was found to be 30 % and the predictors of mortality were defined. Death was more likely if patients were < or = 18 yrs, male, received a vasopressor, or had the following clinical manifestations: cardiac , metabolic acidosis , renal failure, hypotension, rhabdomyolysis, or dyslipidemia (12).Most of those factors existed in our case except for the age, and PRIS did not end up with mortality in our elderly patient after cessation of propofol.

In conclusion, we want to emphasize that, development of PRIS is not limited to prolonged use or high doses of propofol infusion especially in geriatric patients. Concomittant use of catecholamines, hypertriglyceridemia, elevated lactate le-

vels in the absence of tissue hypoxemia and bradycardia may indicate the development of PRIS. Recognizing the early signs and symptoms of PRIS, may have an important impact on the clinical outcomes of patients experiencing this syndrome.

References

1. Ahlen K, Buckley CJ, Goodale DB, Pulsford AH. The 'propofol infusion syndrome': The facts, their interpretation and implications for patient care. Eur J Anaesthesiol 2006 Dec;23(12):990-8. (PMID:16938158).
2. Laquay N, Prieur S, Greff B, Meyer P, Orliaguet G. Propofol infusion syndrome. Ann Fr Anesth Reanim 2010 May;29(5):377-86. (PMID:20399595).
3. Fudickar A, Bein B. Propofol infusion syndrome: update of clinical manifestation and pathophysiology. Minerva Anestesiol 2009 May;75(5):339-44. (PMID:19412155).
4. Cremer OL. The propofol infusion syndrome: more puzzling evidence on a complex and poorly characterized disorder. Crit Care 2009; 13(6):1012. (PMID:20017894). [Internet] Available from: http://ccforum.com/content/13/6/1012. Accessed: 04.08.2013.
5. Liolios A, Guérit JM, Scholtes JL, Raftopoulos C, Hantson P. Propofol infusion syndrome associated with short-term large-dose infusion during surgical anesthesia in an adult. Anesth Analg 2005 Jun;100(6):1804-6. (PMID:15920217).
6. Roberts RJ, Barletta JF, Fong JJ, et al. Incidence of propofol-related infusion syndrome in critically ill adults: A prospective, multicenter study. Crit Care 2009;13(5):R169. (PMID:19874582). [Internet] Available from:http://ccforum.com/content/13/5/R169 . Accessed: 04.08.2013.
7. Otterspoor LC, Kalkman CJ, Cremer OL. Update on the propofol infusion syndrome in ICU management of patients with head injury. Curr Opin Anaesthesiol 2008;21:544-51. (PMID:18784477).
8. Vasile B, Rasulo F Candiani A, Latronico N. The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome. Intensive Care Med 2003;29(9):1417-25. (PMID:12904852).
9. Fernández AL, García-Bengochea JB, Alvarez J, González Juanatey JR. Biochemical markers of myocardial injury in the pericardial fluid of patients undergoing heart surgery. Interact Cardiovasc Thorac Surg 2008 May;7(3):373-7. (PMID:18258649). [Internet] Available from: http://icvts.oxfordjournals.org/content/7/3/373.long. Accessed:05.08.2013.
10. Ooi M, Cooper A, Lloyd G, Jackson G. A study of lipid profile before and after coronary artery bypass grafting. Br J Clin Pract 1996 Dec; 50(8):433-5. (PMID:9039713).
11. Sirvinskas E, Andrejaitiene J, Raliene L, et al. Cardiopulmonary bypass management and acute renal failure: risk factors and prognosis. Perfusion 2008 Nov; 23(6):323-7. (PMID:19454560).
12. Fong JJ, Sylvia L, Ruthazer R, Schumaker G, Kcomt M, Devlin JW. Predictors of mortality in patients with suspected propofol infusion syndrome. Crit Care Med 2008;36:2281-7. (PMID:18664783).

Turkish Journal of Geriatrics
2014; 17 (2) 200-204

Dilek ARPACI[1]
Ülkü YILMAZ[2]
Selçuk YAYLACI[2]
Mehmet ÇÖLBAY[1]
Ali TAMER[2]

Case Report

FIRST SEIZURE PRESENTATION IN AN ELDERLY WOMAN WITH PRIMARY VITAMIN D DEFICIENCY: A CASE REPORT

Abstract

Vitamin D insufficiency is common in older people and is associated with several disorders related to aging such as osteoporosis, which leads to a significantly increased risk of bone fractures. This deficiency is more common in Mediterranean countries than in Northern European countries. Hypocalcemic seizures resulting from vitamin D deficiency are rare in adults, and fractures caused by seizures without evidence of direct trauma have not yet been reported. We present an unusual case of secondary right radius fracture caused by hypocalcemic seizures in a 63-year-old Turkish woman with primary vitamin D deficiency. After vitamin D supplementation, increased serum 25-hydroxy vitamin D and calcium levels and decreased parathormone levels were found. The seizures had not recurred. It is important to check for calcium levels in older patients who present with non-febrile seizures. When hypocalcemia was found serum 25-hydroxy vitamin D levels should be measured to find the underlying cause.

Key Words: Hypocalcemia; Seizure; Vitamin D Deficiency; Aged; Bone Fracture.

Olgu Sunumu

İLK BAŞVURUSU NÖBET OLAN PRİMER D VİTAMİNİ EKSİKLİĞİ OLAN YAŞLI BİR KADIN: BİR OLGU SUNUMU

Öz

Vitamin D eksikliği yaşlı insanlara sık rastlanmaktadır ve kemik kırık riskinin belirgin artışına yol açan osteoporoz gibi ciddi rahatsızlıklarla ilişkilidir. Bu eksiklik Akdeniz ülkelerinde Kuzey Avrupa ülkelerinden daha yaygındır. Vitamin D eksikliğine bağlı hipokalsemik nöbet erişkinlerde nadirdir ve direkt travma olmadan nöbete bağlı kırık henüz rapor edilmemiştir. Primer vitamin D eksikliğine bağlı hipokalsemik nöbetin neden olduğu sağ Radius kırığı olan 63 yaşında Türk kadın olgu sunmaktayız. Vitamin D replasmanı sonrası, serum 25-hidroksi vitamin D düzeyi ve kalsiyum seviyesinde artış ve parathormon seviyesinde ise azalma görülmüştür. Nöbet tekrarlamamıştır. Nonfebril nöbet ile gelen yaşlı hastalarda kalsiyum seviyesinin kontrolü önemlidir. Hipokalsemi tespit edildiğinde altta yatan nedeni bulmak için serum 25-hidroksi vitamin D düzeyi de bakılmalıdır.

Anahtar Sözcükler: Hipokalsemi; Nöbet; Vitamin D Eksikliği; Yaşlı; Kemik Kırığı.

İletişim *(Correspondance)*

Dilek ARPACI
Sakarya Eğitim Araştırma Hastanesi, Endokrinoloji Kliniği
SAKARYA

Tlf: 0264 255 08 65
e-posta: drarpaci@gmail.com

Geliş Tarihi: 01/11/2013
(Received)

Kabul Tarihi: 30/01/2014
(Accepted)

[1] Sakarya Eğitim Araştırma Hastanesi, Endokrinoloji Kliniği SAKARYA
[2] Sakarya Eğitim Araştırma Hastanesi, İç Hastalıkları Kliniği SAKARYA

Introduction

Vitamin D is an essential steroid involved in bone metabolism, cell growth, differentiation, and regulation of the minerals in the body. The main sources of this vital vitamin are adequate diet and photosynthesis in the skin. Vitamin D deficiency is common among elderly people and numerous studies have confirmed its high prevalence in both selected and unselected samples (1–4). Vitamin D deficiency is increasing worldwide, and it has been drawing much attention because of its association with various diseases, including osteomalacia. However, there is little information on the prevalence of osteomalacia in elderly people. As osteomalacia is essentially a histological diagnosis, assessment of its true prevalence is difficult, and reported prevalence has varied depending on the diagnostic criteria adopted (5). The main risk factors for vitamin D deficiency in an otherwise healthy person are inadequate exposure to sunlight because of housebound status, insufficient dietary intake, winter season, high latitudes, dark skin and older age, use of antiepileptic drugs, and malabsorption due to inflammatory bowel disease, gastric surgery, and biliary disease (6).

Hypocalcemic seizures resulting from vitamin D deficiency are very rare in adults, and fractures caused by seizures without evidence of direct trauma have not yet been reported.

Case Report

A 63-year-old Turkish woman was brought to the emergency department after having a first seizure while sitting on an armchair at home. It was witnessed by the patient's daughter and described as a 5-minute generalized self-resolving seizure with rhythmic shaking movements of all extremities and backward rolling of the eyes. It occurred at 1 a.m. after a night without sleep. The patient did not fall from the chair or experience any trauma during the seizure. On arrival at the emergency department, the patient was somnolent but able to answer questions. She complained of pain in her forearm. She reported having felt somewhat weak for the previous few days. Her medical history included subtotal thyroidectomy, no report of seizures, and there were no individuals with seizures in her immediate family.

In the emergency department, her vital signs were: temperature 36.8 °C; heart rate, 106 beats per minute; respiratory rate, 20 breaths per minute; blood pressure, 132/70 mmHg; oxygen saturation, 98% on room air; and pain score, 6/10. Chvostek's and Trousseau's signs were positive. Other physical examination was normal except for the musculoskeletal and neurologic components. Her right forearm revealed contracted muscles and pain on palpation of the wrist. X-ray of the right forearm was taken and fracture was seen on radiography (Figure 1). A splint was placed on the right forearm by an orthopedist. On neurologic examination done by a neurologist, the patient was somnolent but arousable and oriented to person, time and place. Deep-tendon reflexes were brisk all over. Brain computerized tomography (CT) and brain magnetic resonance imaging (MRI) 24 hours later were found to be normal. No additional tests were recommended by the neurologist.



Figure 1— Right radius fracture was shown on X-ray (black arrow).

Blood chemistry was significant for a calcium level of 5.8 mg/dL (8.5-10.5 mg/dL) and phosporus level of 2.8 mg/dL (2.5-4.5 mg/dL). Serum albumin level was 3.8 g/dL(3.5-5.2 g/dL). Albumin corrected calcium level was 5.96 mg/dL. Blood urine nitrogen (BUN), creatinine, sodium, potassium and magnesium levels were normal.

An electrocardiogram showed a normal sinus rhythm with a QTc of 405 milliseconds. The patient received intravenous calcium gluconate and was transferred to the endocrinology service. Serum parathyroid hormone (PTH) level was 224 pg/ml (15-65 pg/ml) and serum 25(OH) vitamin D level was 2.5 ng/mL (30-75 ng/mL). Serum alkaline phosphatase (ALP) level was 189 U/L (normal range 60-105 U/L). Serum bone al-

kaline phosphatase level was high (56.6 U/L), above the normal range of 13.0–33.9 U/L. Urinary calcium excretion was low (60 mg/day). Additional workup for malabsorption was negative (negative serology markers for celiac disease and stool negative for fat). We learned from the patient's history that she has been living alone and she had inadequate exposure to sunlight, being housebound for a long time, and had an unbalanced intake of fat-rich foods such as meats, oily fish, and milk. She didn't use any antiepileptic drugs, and she did not have malabsorption due to inflammatory bowel disease, gastric surgery, or biliary disease.

The patient was diagnosed with primary vitamin D deficiency. Vitamin D3 drops 50000 IU/week were given to the patient and she was told to take them for at least 8 weeks; calcium carbonate/vitamin D3 effervescent tablets were also administered. A bone mineral density (BMD) scan was taken and the T-Score from her lumbar vertebra (L2-4) was -2.7 standard deviations (SD), within the range of osteoporosis. Bisphosphonate treatment was postponed because of severe osteomalacia. Serum thyroid stimulating hormone (TSH) level was 6.67 IU/mL (0.4-4.5 IU/mL) , free thyroxine (fT3) and triiodothyronine (fT4) levels were normal, and thought to indicate subclinical hypothyroidism. We administered levothyroxine (LT4) 25 mcg/day to our patient. Her fasting plasma glucose was 200 mg/dl, HBA1C 5.9% and microalbuminuria 76 mg/day. We gave an oral antidiabetic (repaglinide) 0.5 mg/day, angiotensin converting enzyme (ACE) inhibitor (ramipril) 2.5 mg/day, and acetylsalicylic acid (ASA) 100 mg/day. Serum vitamin B12 level was low at 134 mg/dl (220-900 mg/dl) and parenteral vitamin supplementation was given. She was discharged on hospital day 16 with vitamin D3 drops 50000 IU/week, calcium carbonate/vitamin D3 effervescent tablets, ramipril+amlodipin, ASA, LT4 and repaglinide. A diet with increased calcium of at least 2 to 4 servings of dairy per day and daily vitamin D (400 IU) supplementation was recommended. One month after starting vitamin D supplementation, serum 25-hydroxyvitamin D increased to a level of 28 ng/mL and PTH decreased to a level of 119 pg/mL. Serum calcium was measured at 8.5 mg/dL and phosporus at 4.2 mg/dL, within normal ranges. During hospitalization no seizures were observed.

Discussion

Vitamin D deficiency is common in older individuals. Depending on the country and the definition used, the prevalence of vitamin D deficiency in the older Western population ranges from 0 to 90% (7). Low serum 25-hydroxyvitamin D (25(OH)D) in the elderly is caused by less efficient vitamin D production in the skin, low sunshine exposure and low dietary intake (7, 8). Older individuals often suffer from chronic diseases (9), requiring the frequent use of medication. Previous research, performed in the United States, demonstrated that 23% of women and 19% of men took five or more prescription medicines. In addition, rates of use increased with advancing age (10).

The clinical presentation of osteomalacia in the older population differs from the presentation in younger patients, however more them are asymptomatic. When symptomatic, they tend to present with signs of hypocalcemia such as neuromuscular irritability and, rarely, seizures. Radiographs of the long bones in these patients may not necessarily show radiologic changes of osteomalacia. It is thought that hypocalcemic symptoms secondary to vitamin D deficiency occur largely in patients with rapid growth rates, such as children younger than 1 year and adolescents. In a retrospective review of 65 hospitalized children with vitamin D deficiency in the United Kingdom, Ladhani et al. (11) reported that hypocalcemic symptoms occurred exclusively in children younger than 3 years or older than 10 years. Narchi et al. (12) reported 21 cases of symptomatic rickets in adolescents from Saudi Arabia. Most of their patients presented with carpopedal spasm, limb pain, or weakness. The incidence of seizures in adolescents with vitamin D deficiency is unknown. In the Ladhani et al. series, 16 patients presented with seizures, but it is unclear how many were in the older age group, whereas none of the adolescent patients in the Narchi et al. group had seizures.

Patients with a history of epilepsy seem to be at a higher risk for injuries, including head and dental trauma, lacerations, burns, sprains, and fractures. Surveys and population studies indicate that close to 20% of patients who experience a seizure sustain some kind of injury, and overall, 30% to 35% of patients with seizures have experienced secondary injury as a result of a seizure during their lifetime (13-15).

However, a recent meta-analysis reported that patients with epilepsy are twice as likely to sustain a fracture as patients without epilepsy, which may be a result of 1) increased risk of trauma, 2) decreased bone density caused by the use of antiepileptic drugs, and/or 3) comorbidities (16). Most of the fractures sustained during seizures are caused by direct trauma and typically involve the skull, nasal bones, and clavicles, but in rare instances, fractures can be caused by the muscular tension of the seizure itself. In these cases, the proximal hu-

merus and the shoulder are more commonly affected (17). Radius fractures caused by the muscular tension of a seizure itself seem to be unusual and have not been previously described. To the best of our knowledge, this is the first case of nontraumatic radius fracture in a patient over age 60 resulting from hypocalcemic seizures caused by primary vitamin D deficiency.

Laboratory testing after a first unexplained nonfebrile seizure should be considered, particularly in patients with suggestive clinical findings such as vomiting, diarrhea, or dehydration, failure to return to baseline alertness, or increased muscle tone or fractures such as our patient experienced. The workup should include electrolyte levels, including calcium, magnesium, and phosphorous. Toxicology screening should be considered if there is a question of drug exposure or substance abuse (18). The differential diagnosis of hypocalcemia in adolescence includes vitamin D deficiency, hypoparathyroidism, hypomagnesemia, malabsorption, and renal and hepatic failure, among others (19). Once hypocalcemia is found, additional laboratory investigations such as a basic metabolic panel, liver function tests, and PTH and vitamin D 25-hydroxy and 1,25-dihydroxy levels should be performed. A workup for malabsorption should be undertaken if it is suggested by history or initial laboratory results. The diagnosis of primary vitamin D deficiency is made when low vitamin

D levels along with a compatible history are accompanied by high levels of PTH, in the absence of other metabolic or gastrointestinal abnormalities. Dual-beam radiograph-based photon absorptiometry is the most sensitive routine method of detecting and quantifying

bone loss and may be considered for patients with vitamin D deficiency (20).

Hypocalcemic seizures should be treated with intravenous calcium. In general, calcium gluconate is preferred to calcium chloride because it is less irritating and is less likely to cause tissue necrosis if extravasation occurs. Intravenous therapy with calcium should be continued as long as the patient is symptomatic. Magnesium should be replaced if low levels are identified, and vitamin D replacement in the form of vitamin D3 may be initiated intramuscularly initially, and continued orally as long as the patient does not have malabsorption. Phosphate replacement is usually not necessary for vitamin D deficiency, because low levels are a result of the elevated PTH level, which resolves once adequate calcium and vitamin D are supplied. It is important to monitor serum calcium, phosphate, alkaline phosphatase, PTH, and vitamin D levels and the urinary calcium/creatinine ratio during treatment to assess the response and avoid complications of hypocalcemia or hypercalcemia. Every effort should be made to prevent this disease by encouraging adequate diet, sun exposure, and vitamin D supplementation for patients at risk (21).

In conclusion this case illustrates that emergency medicine physicians should carefully evaluate patients with seizures for secondary injuries, both at presentation and after the patient recovers from the postictal stage. Hypocalcemic seizures resulting from vitamin D deficiency are rare, although the incidence of vitamin D deficiency is increasing. Additional research into primary prevention of primary vitamin D deficiency in this population is warranted.

Competing Interest

The authors declare that they have no competing interests.

Contribution of the Authors

Ülkü Yılmaz analyzed and interpreted the endocrinological patient data. Dilek Arpacı was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

References

1. Inderjeeth C, Nicklason F, Al-Lahham Y, et al. Vitamin D deficiency and secondary hyperparathyroidism: clinical and biochemical associations in older noninstitutionalised southern Tasmanians. Aust N Z J Med 2000;30:209–14. (PMID:10833112).
2. Weatherall M. A meta-analysis of 25 hydroxyvitamin D in older people with fracture of the proximal femur. N Z Med J 2000;113:137–40. (PMID:10872433).
3. Passeri G, Pini G, Troiano L, et al. Low vitamin D status, high bone turnover, and bone fractures in centenarians. J Clin Endocrinol Metab 2003;88:5109–15. (PMID:14602735).
4. Gloth F, Gundberg C, Hollis B, Haddad J, Tobin J. Vitamin D deficiency in homebound elderly persons. JAMA 1995;274:1683–6. (PMID:8596218).
5. Francis R, Selby P. Osteomalacia. Baillieres Clin Endocrinol Metab 1997;2:145–63. (PMID:9222490).
6. Thomas M, Lloyd-Jones D, Thadhani R, et al. Hypovitaminosis D in medical inpatients. N Engl J Med 1998;338:777–83. (PMID:9504937).
7. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: Consequences for bone loss and fractures and therapeutic implications. Endocrine Reviews 2001;22:477–501. (PMID:11493580).
8. van Schoor NM, Visser M, Pluijm SMF, Kuchuk N, Smit JH & Lips P. Vitamin D deficiency as a risk factor for osteoporotic fractures. Bone 2008;42:260–6. (PMID:18289505).
9. Christensen K, Doblhammer G, Rau R & Vaupel JW. Ageing populations: The challenges ahead. Lancet 2009;374:1196–208. (PMID:19801098).

10. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE & Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. Journal of the American Medical Association 2002;287:337–44. (PMID:11790213).
11. Ladhani S, Srinivasan L, Buchanan C, Allgrove J. Presentation of vitamin D deficiency. Arch Dis Child 2004;89:781–4. (PMID:15269083).
12. Narchi H, El Jamil M, Kulaylat N. Symptomatic rickets in adolescence. Arch Dis Child 2001;84:501–3. (PMID:11369569).
13. van den Broek M, Beghi E. Accidents in patients with epilepsy: types, circumstances, and complications: a European cohort study. Epilepsia 2004;45:667–72. (PMID:15144432).
14. Buck D, Baker GA, Jacoby A, Smith DF, Chadwick DW. Patients' experiences of injury as a result of epilepsy. Epilepsia 1997;38:439–44. (PMID:9118849).
15. Neufeld MY, Vishne T, Chistik V, Korczyn AD. Life-long history of injuries related to seizures. Epilepsy Res 1999;34:123–7. (PMID:10210026).
16. Vestergaard P. Epilepsy, osteoporosis and fracture risk: A meta-analysis. Acta Neurol Scand 2005;112:277–86. (PMID:16218908).
17. Finelli PF, Cardi JK. Seizure as a cause of fracture. Neurology1989;39:858–60. (PMID:2725885).
18. Hirtz D, Ashwal S, Berg A, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Neurology. 2000;55:616–23. (PMID:10980722).
19. Guise TA, Mundy GR. Clinical review 69: Evaluation of hypocalcemia in children and adults. J Clin Endocrinol Metab 1995;80:1473–8. (PMID:7744987).
20. Singh J, Moghal N, Pearce SH, Cheetham T. The investigation of hypocalcaemia and rickets. Arch Dis Child 2003;88:403–7. (PMID:12716711).
21. Lehtonen-Veromaa MK, Mottonen TT, Nuotio IO, Irjala KM, Leino AE, Viikari JS. Vitamin D and attainment of peak bone mass among peripubertal Finnish girls: A 3-y prospective study. Am J Clin Nutr 2002;76:1446–53. (PMID:12450915).

Turkish Journal of Geriatrics
2014; 17 (2) 205-209

Süleyman BALDANE[1]
Süleyman H. İPEKÇİ[1]
Serap BULUT[2]
Emine GÜL BALDANE[3]
Gonca KARA GEDİK[4]
Levent KEBAPCILAR[1]

Case Report

A CASE OF PAGET'S DISEASE OF THE BONE PRESENTED WITH HEARING LOSS AS THE FIRST SYMPTOM

Abstract

A 67-year-old woman presented to the audiology clinic with a complaint of bilateral hearing loss over the past two years. Routine biochemical screening showed an alkaline phosphatase level of 381 U/L, and she was referred to our endocrinology unit. Her vitamin D and parathyroid hormone levels, as well as thyroid, liver and kidney function test results, were within normal ranges. Cranial x-ray radiography showed an increase in the diploe distance and a sclerotic pattern in the calvarium; while whole body bone scintigraphy demonstrated a diffuse increase in radioactive substance involvement of the calvarium. Serum osteocalcin and spot urinary deoxypyridinoline levels were increased. The patient was diagnosed with Paget's disease with hearing loss as the first symptom, and she was started taking zoledronic acid treatment. Three months later, her alkaline phosphatase level had returned to the normal range, and audiologic examination showed a mild improvement in hearing.

Key Words: Osteitis Deformans; Hearing Loss.

Olgu Sunumu

İLK YAKINMASI İŞİTME KAYBI OLAN HASTADA KEMİĞİN PAGET HASTALIĞI TANISI

Öz

Altmış yedi yaşında kadın hasta, her iki kulakta işitme kaybı nedeniyle odyoloji polikliniğine başvurdu. İki yıldır şikayeti olan hastanın rutin serum biyokimya incelemesinde alkalen fosfataz değerinin 381 U/L olması üzerine endokrinoloji ünitemize yönlendirildi. Hastanın vitamin D, parathormon, tiroid fonksiyon testleri, karaciğer fonksiyon testleri, böbrek fonksiyon testleri normal sınırlar içindeydi. Hastanın kranial grafisinde; diploe mesafesinde artış, kalvaryumda sklerotik görünüm ve tüm vücut kemik sintigrafisinde; kalvaryumda diffüz tarzda artmış radyoaktif madde tutulumu izlendi. Serum osteokalsin ve spot idrarda deoksipridinolin düzeyleri yüksek saptandı. İşitme kaybının ilk semptom olarak görüldüğü hastaya mevcut bulgular ile kemiğin paget hastalığı tanısı ile zolendronik asit tedavisi verildi. Tedaviden üç ay sonraki kontrolünde, alkalen fosfataz değerinde normal düzeye gerileme ve odyolojik incelemede hafif düzeyde bir düzelme izlendi.

Anahtar Sözcükler: Kemiğin Paget Hastalığı; İşitme Kaybı.

İletişim ***(Correspondance)***

Süleyman Baldane
Selçuk Üniversitesi Tıp Fakültesi Endokrinoloji ve Metabolizma Bilim Dalı KONYA

Tlf: 033244685
e-posta: baldane42@hotmail.com

Geliş Tarihi: 23/11/2013
(Received)

Kabul Tarihi: 13/01/2014
(Accepted)

[1] 1Selçuk Üniversitesi Tıp Fakültesi Endokrinoloji ve Metabolizma Bilim Dalı KONYA
[2] Selçuk Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Hastalıkları Anabilim Dalı KONYA
[3] Konya Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, KONYA
[4] Selçuk Üniversitesi Tıp Fakültesi , Nükleer Tıp Anabilim Dalı KONYA

Introduction

Paget's disease is a chronic progressive metabolic bone disease characterized by increased focal bone turnover, along with an interchange of normal bone structure with disorganized bone tissue (1). The etiology of Paget's disease is not well understood, although environmental factors, paramyxovirus infection, and several genetic factors are thought to be involved (1-3). The axial skeleton is primarily affected but involvement of other regions has been reported, including the pelvis (70%), femur (55%), lumbar vertebrae (53%), skull (42%) and tibia (32%) (1).

The most prominent symptom of Paget's disease involving the skull is hearing loss, which is encountered in approximately half of the patients (1). Hearing loss may be conductive, sensorineural or mixed-type, although its mechanisms have not been determined. In addition to being widespread, hearing loss is an early symptom of Paget's disease, making it useful for early diagnosis (4).

Case

A 67-year-old woman presented to the audiology clinic with bilateral hearing loss. Routine biochemical screening revealed an alkaline phosphatase (ALP) concentration of 381 U/L (normal limits: 40-150 U/L), and she was referred to our endocrinology unit. Systemic investigation revealed no other complaints than hearing loss. A detailed medical history revealed that the patient had experienced hearing loss for approximately two years. On previous hospital visits, she was told that the hearing loss was due to age and that she needed to use a hearing aid.

Physical examination revealed no pathologic findings. Apart from her high ALP levels, the patient's vitamin D and parathyroid hormone (PTH) levels, as well as thyroid, liver, and kidney function test results, were within normal limits (Table 1). ALP isoenzyme electrophoresis showed her rate of bone ALP was 95% (normal limits:23-75%). The patient's cranial x-ray radiography demonstrated an increase in diploe distance and a sclerotic pattern in the calvarium (Figure 1). Whole-body bone scintigraphy following administration of 20 mCi teknetium-99m methylene diphosphonate (Tc-99m MDP) demonstrated a diffuse increase in radioactive substance involvement of the calvarium (Figure 2). Her serum osteocalcin concentration was 110.5 ng/mL (normal limits: 15-45 ng/mL) and her spot urinary deoxypyridinoline (DPD) level was 29.3 nM/mM creatine (normal limits: 5-20 nM/mM creatine).

Table 1— Laboratory Test Results.

Parameter	Result	Normal Range
Alkaline phosphatase (ALP) (U/L)	381	40-150
Bone ALP (%)	95 (361 U/L)	23-75
Parathyroid hormone (PTH) (pg/mL)	45	12-65
25(OH) Vitamin D (ng/mL)	32	30-150
Thyroid stimulating hormone (μU/L)	2.59	0.56-5.57
Uric acid (mg/dL)	3,5	2.6-6.0
Aspartate aminotransferase (U/L)	16	5-34
Alanine aminotransferase (U/L)	9	0-55
Gamma-glutamyl transferase (U/L)	11	9-36
Direct bilirubin (mg/dL)	0.1	0-0.5
Total bilirubin (mg/dL)	0.3	0.2-1.2
Urea (mg/dL)	34	21-43
Creatinine (mg/dL)	0.6	0.4-1
Hemoglobin (g/dL)	13.2	12.3-15.3
Erythrocyte sedimentation rate (mm/hour)	12	0-20



Figure 1— Increased diploe distance and a sclerotic image in the calvarium from the lateral cranial x-ray radiography.

Hearing loss was evaluated by high resolution computed tomography (HRCT) imaging of the temporal bone and audiological analysis. HRCT showed bilateral external auditory canals, middle ear and mastoid air cells and a cochlear structure; the ossicular chain was intact (Figure 3). Audiological

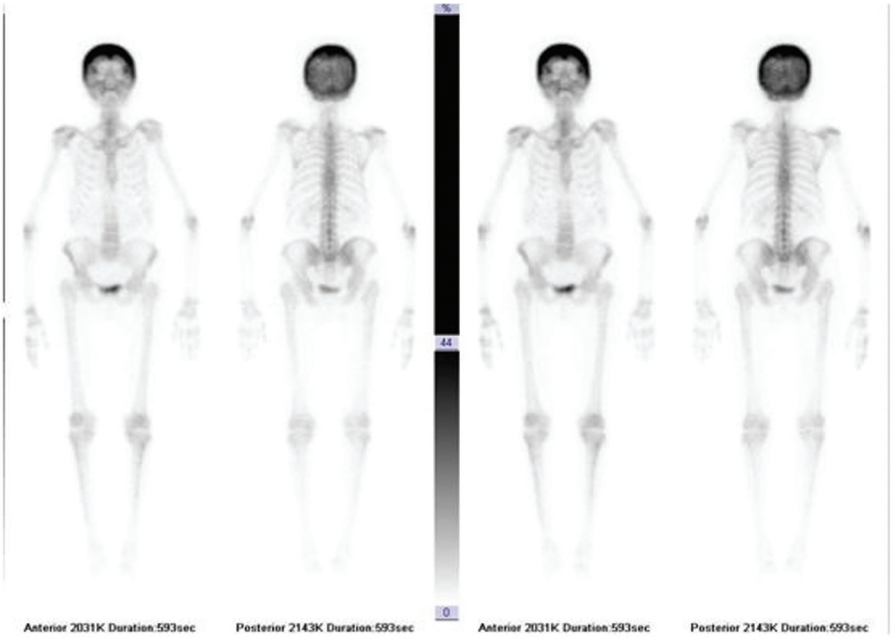


Figure 2— Diffused increase in radioactive substance involvement of the calvarium upon whole-body Tc-99m MDP bone scintigraphy.



Figure 3— Temporal bone HRCT image: Intact ossicular chain, normal cochlear structure.

examination at 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz revealed moderate (35 decibel) bilateral sensorineural hearing loss. A bilateral type-A tympanogram was obtained. Acoustic reflexes could be obtained in both ears, with no associated tinnitus or vestibular dysfunction.

The patient was diagnosed with Paget's disease with hearing loss as a first symptom. She was started on treatment with zoledronic acid (5 mg single dose, intravenous). At a three month follow-up visit, her ALP level (109 U/L) had returned to within the normal range, her serum osteocalcin concentration was 32 ng/mL, and her spot urinary DPD value was 12.2 nM/mM creatine. Audiologic examination showed a mild improvement in hearing, of about 5-decibels.

Discussion

Paget's disease is the second most commonly encountered metabolic bone disease after osteoporosis. Its incidence increases with age, affecting about 1-2% of older white men (>55 years). The prevalence of the disease varies with ethnicity and geographic location. Although relatively common in the United Kingdom, the United States of America and New Zealand, few cases have been reported in the Scandinavian countries, in Asia and on the Indian subcontinent (1).

Genetic predisposition may be the most important factor in disease etiology, with about 15% of patients having a family history of disease. Paget's disease demonstrates an autosomal dominant inheritance in most families, with increased penetrance during the sixth and seventh decades of life (2).

The most important genetic alterations associated with the development of Paget's disease are mutations in the Sequestosome 1 (SQSTM1) gene, which has been reported in both familial and sporadic cases of Paget's disease (3).

Most patients with Paget's disease are asymptomatic and may remain asymptomatic throughout their lifetimes. Some patients are incidentally diagnosed when assessed for other health conditions, by, for example, the discovery of an increased serum ALP or abnormal radiography findings. In contrast, many other patients may remain asymptomatic for many years, delaying the diagnosis of the disease. The average time from the appearance of first symptoms to diagnosis has been reported to range from four to nine years (5).

Large population studies have demonstrated that Paget's disease is associated with back pain, osteoarthritis, hip arthroplasty, knee arthroplasty, fracture(s), and an increased risk of hearing loss (6). Since some of these symptoms, such as back pain, osteoarthritis, and hearing loss are frequently observed in older individuals, Paget's disease may be overlooked. Our patient was not diagnosed with Paget's disease until two years after her first complaints of hearing loss and after several visits to other hospitals. A proper diagnosis of Paget's disease was delayed in this patient, because her hearing loss was associated with older age.

About 30% of patients with Paget's disease are symptomatic, with bone pain the most common complaint. Pain typically occurs at rest and increases at night. Other common complaints due to complications of this disease include pain associated with secondary osteoarthritis, pathologic fractures, bone deformities and hearing loss. Less frequently reported complications include hypercalcemia (together with immobilization), heart failure, osteosarcoma, and paraplegia (1).

Hearing loss has been reported in approximately half of Paget's disease patients with skull involvement (1). Hearing loss may appear as conductive, sensorineural or mixed-type, with mixed-type bilateral hearing loss most frequently associated with Paget's disease. Hearing loss is accompanied by vertigo in 25% of patients and by tinnitus in 20% (4). Although several abnormalities of the external, middle and inner ear have been described in patients with hearing loss, the mechanism of hearing loss is not well understood, and its cause cannot be described in most patients (7). The bilateral sensorineural hearing loss in patient was not accompanied by any pathological finding in the HRCT of the temporal bone.

Bone pain is the most frequent indication for treatment of patients with Paget's disease, with other indications including hearing loss, spinal cord compression, skull involvement and hypercalcemia. Bisphosphonate therapy, the treatment of choice, rapidly inhibits the process of Paget's disease development and maintains long-term disease control. Bisphosphonates have been found to reduce bone turnover and improve histology, suggesting that these agents may prevent the complications of the Paget's disease (5).

Bisphosphonate therapy has been reported to induce rapid regression of symptoms in patients with spinal stenosis associated with Paget's involvement. Bisphosphonates, however, are expected to have little effect on complications such as hearing loss (7). Improvements in hearing and decreased progression of hearing loss have previously been reported in patients treated with bisphosphonates, both in case reports and retrospective studies. However, a recent prospective non-controlled study found that bisphosphonate treatments did not significantly improve hearing loss (8).

The oral bisphosphonates alendronate and risedronate, and the intravenous agents, pamidronate and zoledronate, were recently approved for the treatment of Paget's disease. The use of oral bisphosphonates is very limited, due to low response rates to treatment, the absence of sustained remission and the frequently encountered gastrointestinal side effects. Zoledronic acid is the treatment of choice due its early reduction of bone turnover, a sustained response for up to 24 months, and lower rates of gastrointestinal side effects (9). Intravenous zoledronic acid (5 mg single dose) was deemed preferable in our patient due to her two-year history of the disease. Although an auditory test after 3 months showed mild improvement in hearing, the difference was not statistically significant.

In conclusion, most patients with Paget's disease are diagnosed late in the course of disease, after many years of asymptomatic disease. Paget's disease should be considered in patients presenting with hearing loss as the solitary symptom, without other symptoms such as bone pain, bone deformity and pathologic fractures. Paget's disease should be suspected in older patients who present with hearing loss. ALP analysis and CT scanning of the skull may contribute to the early diagnosis of Paget's disease. Furthermore, bisphosphonate treatment may result in improved hearing loss in patients with Paget's disease.

Conflict of Interest

The authors declare that they have no conflict of interests.

REFERENCES

1. Ralston SH, Layfield R. Pathogenesis of Paget disease of bone. Calcif Tissue Int 2012;91(2):97-113. (PMID:22543925).
2. Cody JD, Singer FR, Roodman GD, et al. Genetic linkage of Paget disease of the bone to chromosome 18q. Am J Hum Genet 1997;61(5):1117-22. (PMID:9345096).
3. Rea S, Walsh J, Ward L, Magno A, et al. Sequestome 1 mutations in Paget's disease of bone in Australia: Prevalence, genotype/phenotype correlation, and a novel non-UBA domain mutation [P364S] associated with increased NF-B signaling without loss of ubiquitin binding. J Bone Miner Res 2009;24(7):1216-23. (PMID:19257822).
4. Young CA, Fraser FD, Mackenzie IC. Detection of hearing impairment and handicap in Paget's disease of bone using a simple scoring system: A case control study. Bone 2007;40(1):189-93. (PMID:16962839).
5. Langston AL, Ralston SH. Management of Paget's disease of bone. Rheumatology 2004;43(8):955-9. (PMID:15187244).
6. Van Staa TP, Selby P, Leufkens HG, Lyles K, Sprafka JM, Cooper C. Incidence and natural history of Paget's disease of bone in England and Wales. J Bone Miner Res 2002;17(3):465-71. (PMID:11878305).
7. Monsell EM. The mechanism of hearing loss in Paget's disease of bone. Laryngoscope 2004;114(4):598-606. (PMID:15064610).
8. Donáth J, Krasznai M, Fornet B, Gergely P Jr, Poór G. Effect of bisphosphonate treatment in patients with Paget's disease of the skull. Rheumatology 2004;43(1):89-94. (PMID:12923287).
9. Reid IR, Hosking DJ. Bisphosphonates in Paget's disease. Bone 2011;49(1):89-94. (PMID:20832512).

Turkish Journal of Geriatrics
2014; 17 (2) 210-213

Özlem BİLİR[1]
Gökhan ERSUNAN[1]
Özcan YAVAŞİ[1]
Kamil KAYAYURT[1]
Atıf BAYRAMOĞLU[2]

Case Report

MAD HONEY POISONING PRESENTING AS TRANSIENT ISCHEMIC ATTACK

Abstract

Mad honey poisoning is a clinical state resulting from the ingestion of honey produced in the Black Sea region of Turkey. This honey is produced from the nectar of the Rhododendron Ponticum plant. Grayanotoxin is responsible for this cholinergic syndrome, presenting with either one or a combination of two or more of lightheadedness, weakness, diaphoresis, nausea, vomiting, salivation, depressed cognitive function, syncope, blurred vision, paresthesia in the perioral region or extremities, cyanosis and convulsions shortly following ingestion of mad honey. Hypotension and bradycardia are the most commonly seen signs of toxicity. Symptoms usually respond well to intravenous fluid replacement and atropine, and relieve within 24 hours. In this paper, we report a case of mad honey poisoning in a 67 years old patient who presented with weakness on his right side, mimicking transient ischemic attack.

Key Words: Honey; Poisoning; Toxicology; Ischemic Attack, Transient.

Olgu Sunumu

GEÇİCİ İSKEMİK ATAK ŞEKLİNDE ORTAYA ÇIKAN DELİ BAL ZEHİRLENMESİ

Öz

Deli bal zehirlenmesi Türkiye'nin Doğu Karadeniz bölgesinde üretilen balın yenmesinden kaynaklanan klinik bir durumdur. Bu bal, Rhodendron Ponticum bitkisinin nektarından üretilir. Deli bal yenmesini takiben, sersemlik hissi, güçsüzlük, terleme, bulantı, kusma, tükrük salgılama, kognitif fonksiyonlarda baskılanma, senkop, bulanık görme, ağız çevresinde veya ekstremitelerde parestezi, siyanoz veya konvulziyondan biri veya iki ya da daha fazlasının birlikte görülmesiyle ortaya çıkan bu kolinerjik sendromdan grayanotoksin sorumludur. Hipotansiyon ve bradikardi en sık görülen zehirlenme bulgularıdır. Semptomlar genellikle intravenöz sıvı replasmanı ve atropine iyi cevap verir ve 24 saat içinde düzelir. Bu yazı kapsamında, sağ tarafında güçsüzlükle başvuran 67 yaşındaki hastada, geçici iskemik atağı taklit eden deli bal zehirlenmesi olgusu sunulmuştur.

Anahtar Sözcükler: Deli Bal; Zehirlenme; Toksikoloji; Geçici İskemik Atak.

İletişim *(Correspondance)*

Özcan YAVAŞİ
Recep Tayyip Erdoğan Üniversitesi Eğitim ve Araştırma Hastanesi, Acil Tıp Kliniği RİZE

Tlf: 0464 217 03 66
e-posta: ozcanyavasi@yahoo.com.tr

Geliş Tarihi: 18/11/2013
(Received)

Kabul Tarihi: 06/02/2014
(Accepted)

[1] Recep Tayyip Erdoğan Üniversitesi Eğitim ve Araştırma Hastanesi, Acil Tıp Kliniği RİZE
[2] Atatürk Üniversitesi Tıp Fakültesi Acil Tıp Anabilim Dalı ERZURUM

Introduction

Honey has both medicinal and poisonous properties. The toxic effect is associated with grayanotoxin in honey. Grayanotoxin containing honey, called "mad honey" is one of the oldest biological agents (1). Plants containing grayanotoxin, are found in different geographical regions in the world such as Turkey, Japan, Nepal, Brazil and North America. The intoxication signs occur after the ingestion of honey produced from the flower and nectar of Rhododendron Ponticum, which is also called 'mountain flower' in Turkey. As these toxins taken from rhododendron type plants cannot be detoxified by bees, they are directly blended into the honey, resulting in intoxication (2). Besides its nutraceutical values, there is a general belief that mad honey can act as an aphhrodisiac, or as a treatment for gastritis, peptic ulcer, weakness, arthritis, diabetes, and hypertension and is commonly used in alternative medicine (1,3,4). This makes it attractive for elderly patients who are on multidrug medication for several accompanying diseases. Here we report a case of mad honey poisoning in a 67 years old patient who presented with weakness on his right side, mimicking transient ischemic attack.

Case Report

A 67 year old male patient was presented at our emergency department by emergency medical staff with complaining of weakness on his right extremities. From the history taken from his relatives it was learnt that he developed a sense of fainting, nausea, vomiting, and loss of consciousness following ingestion of a spoonful of honey. 14 years and 9 months ago he had developed ischemic stroke, but he had been performing his daily activities without any sequela. His vital signs were as follows: arterial blood pressure, 60/40 mmHg; heart rate, 40 beats/minute; respiratory rate, 10/minute; and oxygen saturation, 89%. His general status was poor, non-cooperating, and non-oriented, with a Glasgow coma scale (GCS) score of 9 (E2,M5,V2). His pupils were isocoric but pinpoint. His neurological examination revealed 3/5 motor deficits on right upper and lower extremities and a positive Babinsky sign on the right. This unstable patient was monitorized, an intravenous line placed, and oxygen started at a rate of 4 L/minute. His ECG showed sinus bradycardia (Figure 1 A). After 1 mg intravenous Atropine, a 0.9% saline infusion was started. Following this therapy, his symptoms started to recover gradually and GCS reached 13. His new blood pressure was 110/60 mmHg and heart rate 84 beats/minute (Figure 1B). After stabilization of the patient, a cranial tomography scan was ordered but did not show any pathological findings related to the clinical status of the patient except for a widening of cortical cerebral sulci secondary to atrophy and bilateral hypodense encephalomalacic gliotic changes in the temporoparietal regions. Cranial and diffusion magnetic resonance imaging (MRI) revealed the same results. Two hours later, he was cooperating, oriented, GCS was 15, Babinsky was negative and his motor deficit recovered except for paresthesia on the right side. There were no pathological findings in laboratory tests. He was admitted to

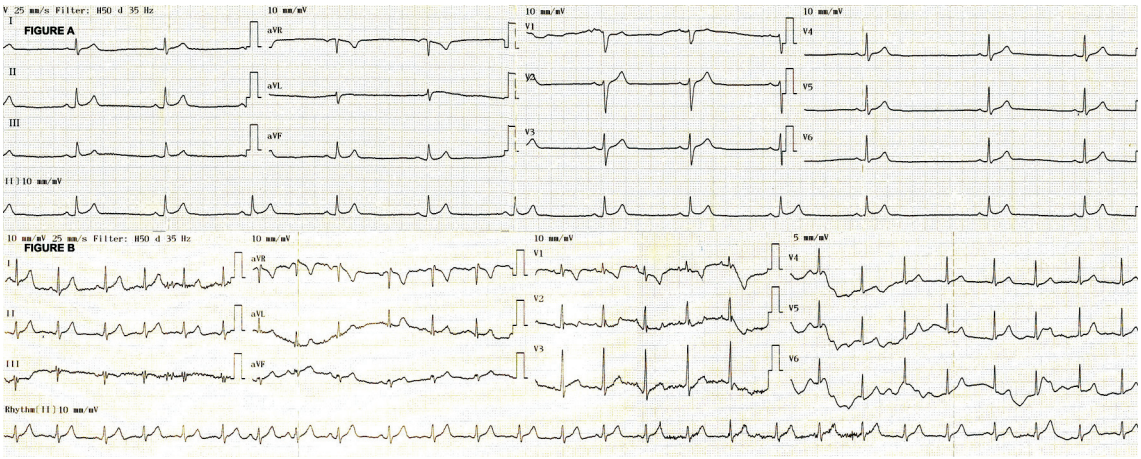


Figure 1— A, ECG trace showing sinus bradycardia at presentation. **B,** ECG trace showing normal sinus rhythm after therapy.

the intensive care unit for follow-up. His carotid artery Doppler showed only calcified plaques. After recovering from the paresthesia, the patient was discharged for ambulatory follow-up.

Discussion

Grayanotoxin-containing plants are found in different regions of the world, particularly in the eastern Black Sea region of Turkey. Although there are different forms of this toxin, the type responsible for the toxicity is Grayanotoxin I, also called andromedotoxin (2). Grayanotoxins are neurotoxins that block sodium channels in the cell membrane by affecting the conduction of action potential. The resulting effects are related to the activation and inactivation of the voltage gated sodium channels in the cell membrane. Thus, grayanotoxin inhibits inactivation of excitable cells, particularly nerve and muscle cells, by holding them in a depolarization state. In this period, calcium influx into the cell is facilitated. All events seen in the central nervous system, nerves, heart and skeletal muscles are the results of effects of the toxin on the cell membrane (5,6). The chain of events at the cellular level triggered by grayanotoxin resembles the changes in brain cells during ischemia. This is because, during ischemia and other energy deficient conditions such as hypoxia and stroke, the chain of events in neurons beginning with the insufficiency of the sodium/potassium pump is followed by cellular dysfunction, resulting from the opening of the calcium channels. Sodium/potassium pump dysfunction is often a major early pathological response, which leads to a loss in membrane potential and neuronal function (7).

The clinical picture of mad honey poisoning mimics cholinergic syndrome (6). Although this patient had meiosis, urine and gaita incontinence, nausea, vomiting, bradycardia, and hypotension as in cholinergic syndrome, actually it was a mad honey poisoning. The symptoms of intoxication are dose-related and occur acutely or after a latent period (2). The patients usually present with either one or a combination of two or more of lightheadedness, nausea, vomiting, diaphoresis, salivation, blurred vision, paresthesia in the perioral region or extremities, cyanosis shortly following ingestion. More serious forms may present with convulsion, depressed cognitive function, syncope, coordination disorder or progressive muscle weakness as in our case (1,8,9). Hypotension and bradycardia are the most commonly seen signs of toxicity (1,8-11). In the present case, besides neurological findings, hypotension and bradycardia were in the foreground. A transient ischemic attack is defined as ''a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction'' (12). As diffusion MRI of the patient did not show any acute ischemic finding, the clinical state of the patient was considered to indicate a transient ischemic attack as a result of decrease in cerebral perfusion secondary to systemic hypotension induced by mad honey poisoning. Thus, the hypotension and neurological findings in the present case were resolved by fluid replacement.

Symptoms of mad honey poisoning usually respond well to intravenous fluid replacement and atropine, and relieve within 24 hours (1,8,10,11). Close cardiac monitorization is mandatory. Although patients with mild symptoms such as lightheadedness, weakness, diaphoresis, hypersalivation, paresthesia, nausea, and vomiting can safely be discharged after 2-9 hours of monitoring, there is no consensus on the duration of hospital observation for patients that were admitted because of poisoning (6,10).

As a result of an increase in natural product consumption recently, there may be an increase in mad honey poisoning in endemic areas. Emergency physicians should include mad honey ingestion in the differential diagnosis, in addition to primary cardiac and neurological disorders while dealing with a patient with unexplained bradycardia, hypotension and neurological symptoms in the ED and early resuscitative efforts should immediately be attempted.

References

1. Demircan A, Keles, Bildik F, et al. Mad honey sex: Therapeutic misadventures from an ancient biological weapon. Ann of Emerg Med 2009;54(6):824-9. (PMID:19683834).
2. Gunduz A, Turedi S, Uzun H, Topbas M. Mad honey poisoning. Am J Emerg Med 2006;24(5):595-8. (PMID:16938599).
3. Ajibola A, Chamunorwa JP, Erlwanger KH. Nutraceutical values of natural honey and its contribution to human health and wealth. Nutr Metab 2012;9:61. (PMID:22716101).
4. Jansen SA, Kleerekooper I, Hofman ZL, et al. Grayanotoxin poisoning: 'mad honey disease' and beyond. Cardiovasc Toxicol 2012;12(3):208-15. (PMID:22528814).
5. Maejima H, Kinashita E, Seyama I, Yamaoka K. Distinct site regulating grayanotoxin binding and unbinding to D4S6 of sodium channel as revealed by improved estimation of toxin sensitivity. J Biological Chemistry 2003;278(11):9464-71. (PMID:12524436).
6. Gündüz A, Turedi S, Russel M, Ayaz FA: Clinical review of grayanotoxin/mad honey poisoning past and present. Clin Toxicol 2008;46(5):437-42. (PMID:18568799).

7. Khatri N, Man HY. Synaptic activity and bioenergy homeostasis: Implications in brain trauma and neurodegenerative diseases. Front Neurol 2013;4:199. (PMID:24376435).
8. Bostan M, Bostan H, Kaya AO, et al. Clinical events in mad honey poisoning: A single centre experience. Bull Environ Contam Toxicol 2010;84(1):19-22. (PMID:19937314).
9. Dilber E, Kalyoncu M, Yariş N, Ökten A. A case of mad honey poisoning presenting with convulsion: Intoxication instead of alternative therapy. Turk J Med Sci 2002;32:361-2.
10. Eroğlu SE, Urgan O, Onur ÖE, Denizbaşı A, Akoğlu H. Grayanotoxin (Mad Honey) ongoing consumption after poisoning. Balkan Med J 2013;30:293-5.
11. Alp A, Şappak S, Sezer SD, et al. A rare cause of syncope among geriatric patients: Mad honey intoxication. Turkish Journal of Geriatrics 2012;15(1):115-8. (in Turkish).
12. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack. Stroke 2009;40(6):2276-93. (PMID:19423857).

Turkish Journal of Geriatrics
2014; 17 (2) 214-217

İlknur AKTAŞ[1]
Kenan AKGÜN[2]
Deniz PALAMAR[2]
Merih SARIDOĞAN[2]

Case Report

THORACOLUMBAR JUNCTION SYNDROME: AN OVERLOOKED DIAGNOSIS IN AN ELDERLY PATIENT

Abstract

Thoracolumbar junction syndrome is defined as a result of a minor intervertebral dysfunction at the thoracolumbar junction and referred pain in the low back and hip region, and can often be confused with other pathologies that may cause these symptoms.

A 65-year-old woman with nearly two years of continuous throbbing pain in the low back, right hip and groin region who was scheduled for spinal surgery with the diagnosis of spinal stenosis in the neurosurgery clinic was referred to our clinic for consultation. Physical examination revealed severe limitation of the passive and active range of motion of the lumbar spine, and pain in all directions. There was tenderness at the T_{12}-L_1, L_5-S_1 and L_4-L_5 intervertebral spaces and at the T_{12}, L_1, L_4 and L_5 spinous processes. On the right side, the maneuver of lateral pressure against the spinous process at the level of T_{12}, the pinch-roll test and the posterior iliac crest point sign were positive. Tenderness over the trochanteric region and the superior aspect of the pubis was detected on the right side. All tests were negative after a right T_{12} periapophyseal joint block using a local anesthetic, with the prediagnosis of thoracolumbar junction syndrome. The patient was diagnosed with thoracolumbar junction syndrome and treated with conservative methods.

Thoracolumbar junction syndrome is a pathology that should be considered in the differential diagnosis in elderly patients with low back, hip and groin pain.

Key Words: Low Back Pain; Iliac, Lumbar; Thoracic; Vertebrae; Aged.

Olgu Sunumu

TORAKOLOMBER GEÇİŞ SENDROMU: YAŞLI BİR OLGUDA GÖZDEN KAÇAN BİR TANI

Öz

Torakolomber geçiş sendromu, torakolomber bileşkenin disfonksiyonu sonucu bel ve kalça ağrısına neden olan ve bu semptomlara neden olabilecek başka patolojilerle sıklıkla karışabilen bir sendromdur.

Yaklaşık iki yıldır sürekli zonklayıcı karakterde bel, sağ kasık ve kalça ağrısı olan 65 yaşında kadın olgu spinal stenoz tanısı ile spinal cerrahi yapılmak üzere beyin cerrahi kliniğinde iken kliniğimizden istenen konsültasyon sonucu değerlendirildi. Fizik muayenesinde tüm yönlere bel hareketleri ileri derecede kısıtlı ve ağrılıydı. T_{12}-L_1, L_5-S_1, L_4-L_5 intervertebral aralık ve T_{12}, L_1, L_4, L_5 spinöz proçesler presyonla ağrılı, sağ taraf T_{12} itme testi, deri yuvarlama testi, iliak krest nokta testi pozitifti. Sağ tarafta torakanterik ve simpizis pubis hassasiyeti mevcuttu. Torakolomber geçiş sendromu düşünülen olguya yapılan T_{12} sağ periapofizyal lokal anestetik enjeksiyonu sonrasında tüm testler negatifleşti. Torakolomber geçiş sendromu tanısı konan olgu konservatif yöntemlerle tedavi edildi.

Torakolomber geçiş sendromu, bel, kalça ve kasık ağrıları olan yaşlı olgularda ayırıcı tanıda mutlaka düşünülmesi gereken bir patolojidir.

Anahtar Sözcükler: Bel Ağrısı; İliak, Lumbar; Torasik; Vertebra; Yaşlı.

İletişim *(Correspondance)*

Deniz PALAMAR
Istanbul University, Cerrahpasa Medical Faculty,
Department of Physical Medicine and Rehabilitation
İSTANBUL

Tlf: 0533 332 18 79
e-posta: denizpalamar@gmail.com

Geliş Tarihi: 14/12/2013
(Received)

Kabul Tarihi: 23/01/2014
(Accepted)

[1] Fatih Sultan Mehmet Education and Research Hospital, Department of Physical Medicine and Rehabilitation, İSTANBUL
[2] Istanbul University, Cerrahpasa Medical Faculty, Department of Physical Medicine and Rehabilitation İSTANBUL

Introduction

The spinal junction area is the transition zone for two different spinal regions with different mobilities and different facet joint orientations (1,2). The thoracolumbar junction (TLJ) comprises the T_{10-11}, T_{11-12} and T_{12}-L_1 motion segments. There is more rotational function in the thoracic spine, mainly due to the way the facet joints are oriented. On the other hand, there is minimal rotation in the lumbar spine. But because of the tethering effect of the ribs, the thoracic spine motions mainly occur in the thoracolumbar region. TLJ is a transition zone across two different regions that have different motion abilities as well as different facet joint characteristics. These characteristics make the TLJ prone to rotational distress. Thoracolumbar junction syndrome (TLJS), sometimes described as Maigne syndrome, is a disorder that affects mostly T_{12}, L_1 and rarely T_{11}, L_2 spinal nerve roots (1-5). Low back pain is certainly the most frequently encountered pain complaint in TLJS, as well as hip and groin pain and also lower abdominal pain, pseudo-hip pain, pubic tenderness, and irritable colon symptoms that may accompany low back pain (1,2). The diagnosis is made with clinical suspicion and clinical evaluations (1-4,6). Especially in the elderly population, TLJS can be confused with lumbosacral spine problems, and may result in misdiagnosis and the application of redundant treatments.

In this report, we present a case that was scheduled for spinal surgery with hip and low back pain, and after the diagnosis of TLJS was treated with conservative treatments.

Case

A 65-year-old woman complained of continuous throbbing pain starting from the low back and spreading through the right groin and hip. Her complaints had started nearly two years before. Lumbar magnetic resonance imaging (MRI), lumbar and hip X-rays, whole body bone scintigraphy, electromyography and biochemical analysis were conducted by the physicians she was referred to. The biochemical analyses were normal, and on the lumbar MRI, a narrowing of the spinal canal at the anterior-posterior diameter due to a broad-based bulging at all levels was found. On the electromyography, mild neurogenic involvement of the muscles innervated by the L_3, L_4, and L_5 nerve roots, and in the whole body bone scintigraphy degenerative changes in the lumbar spine were revealed. On these findings, she had been diagnosed with spinal stenosis. When she did not respond to conservative treatments, surgery for spinal stenosis had been scheduled. When we evaluated the patient as a result of the consultation requested from us, she was taking tramadol 400 mg/day, gabapentin 1800 mg/day and diclofenac sodium 100 mg/day as the medical treatment. Physical examination revealed severe limitation of the passive and active range of motion of the lumbar spine, and motions were painful in all directions. There was tenderness at the T_{12}-L_1, L_5-S_1, and L_4-L_5 intervertebral spaces and at the T_{12}, L_1, L_4, and L_5 spinous processes. On the right side, the maneuver of lateral pressure against the spinous process at the level of T12, the pinch-roll test and tenderness over the posterior iliac crest point test were positive. Tenderness over the trochanteric region and the superior aspect of the pubis was detected on the right side. Her neurologic examination was normal. According to these findings, with the prediagnosis of TLJS, a right T_{12} periapophyseal joint block using a local anesthetic (2 cc of 2% lidocaine) was performed. All of the patient's tests were negative after the block (Figure 1). The patient was hospitalized in our clinic with the diagnosis of TLJS. Physical therapy modalities were applied to the thoracolumbar region. A back and abdominal muscle strengthening exercise program was organized. Her symptoms improved after the treatment. However, three weeks after the hospital admission she experienced pain, especially hip pain, exacerbated by rotational movement. With re-examination of the patient, it was seen that TLJS signs had again become positive. Spinal manipulative therapy to the thoracolumbar segment was applied. After the manipulative treatment, the patient's complaints were completely resolved and the patient was discharged with a regimen of daily activities and an exercise program to strengthen the paravertebral muscles. With a 3-year follow up period, the long-term well-being of the patient has continued.



Figure 1— Pinch-roll test were negative after the right T12 periapophyseal joint block.

Discussion

In elderly patients, low back, leg and hip pain is one of the most common problems encountered in daily practice. Clinical assessment and imaging techniques are often used for diagnosis. However, radiological studies have high false-positive rates (7-10). Therefore, despite developing technology, clinical assessment maintains its importance in terms of diagnosis and differential diagnosis (11). TLJS is one of the reasons for low back and leg pain. Low back pain is certainly the most frequently encountered pain complaint in TLJS; groin pain may accompany low back pain (1). As in our case, due to positive radiological imaging in elderly patients, there are often attempts to treat for other diagnoses such as lumbar spondylosis and coxarthrosis.

The pain pattern coincides with the distribution of the corresponding spinal nerves (T_{12}, L_1). The thoracolumbar nerve roots divide into two rami, ventral and dorsal, after exiting the intervertebral foramen (12). The T_{10} and T_{11} ventral rami are intercostal nerves and end in the abdominal wall. The T_{12} and L_1 ventral rami are subcostal and iliohypogastric nerves, respectively. They supply the lower muscles of the abdominal wall, the skin of the groin area and the lateral surface of the hip. They are responsible for pseudovisceral pain and groin pain. The perforating lateral cutaneous branch, which supplies the skin of the upper lateral part of the thigh, is responsible for pseudotrochanteric pain (2,12,13). The posterior ramus branches into medial and lateral branches. The medial branch is a motor branch and innervates the multifidus and interspinous muscles.

The lateral branch gives cutaneous innervation to the subcutaneous tissues of the lumbar and buttock area, facet joints, and supraspinous and interspinous ligaments. These cutaneous branches pierce the thoracolumbar fascia and pass through the subcutaneous tissues of the lumbar and buttock area as distal as the greater trochanter, in some cases (1,13). This branch is responsible for pain in the lower lumbar and crista iliaca region. Pseudovisceral pain is felt in the lower abdomen, groin and testicles, and symptoms of irritable bowel may be seen (1,14). This syndrome can mimic intestinal, urological, and gynecological problems, and can result in misdiagnosis and improper treatment of the patient. TLJS has been reported as a frequently overlooked cause of testicular, buttock and lower abdominal pain (15-17). Trochanteric pain can mimic hip pathologies such as coxarthrosis and trochanteric bursitis. As well, as in cases with pain radiating to the leg, TLJS can mimic sciatalgia. Pain mainly increases with motion. Hip flexion and adduction is often painful. The trochanteric region is frequently painful with palpation (1). In our case, radiating pain to the hip and leg suggested sciatalgia. With the absence of pathology at the hip joint and MRI findings of spinal stenosis, the patient had a diagnosis of spinal stenosis. Maigne has reported that, of 350 patients seen in a back pain clinic, 40% were found to have pain of thoracolumbar origin (1). Another study conducted by Akgun et al. also found that 39.6% of patients admitted with mechanical low back pain were found to have pain from TLJS (18). TLJS is often seen in the population aged over 50 (1). This may be due to a decrease in paravertebral muscle strength and also a dysfunction due to a degenerative process in that region. Likewise, our case was a 65-year-old woman with degenerative changes in the lumbar region. Rotational strains have an important role in the etiology because the lateral flexion and rotation movements occur mainly at the TLJ. Although TLJS is commonly seen in elderly patients, it is reported to be a potential cause of back pain in athletes, often caused by repetitive extension and rotational movements (19). In our case, due to repetitive rotational movements, the patient's complaints were exacerbated again after the treatment of TLJS with a periapophyseal joint block. After manipulative therapy to the thoracolumbar segment, dysfunction was improved.

The diagnosis is made on purely clinical grounds. Classic signs are: a positive iliac-crest point test, a positive pinch-roll test, localized tenderness over a certain spinous process at the TLJ and tenderness over the involved apophyseal joint. Pain and deep tenderness are located at the level of the iliac crest at a point, which is consistently located seven centimeters from the midline. For the posterior iliac crestal point sign; pressure at this point causes a sharp pain similar to the patient's complaint. This sign requires careful and precise localization. Once the irritated nerve is located, deep pressure and gentle movement produce marked tenderness. The opposite iliac crest is examined in a similar manner and is commonly unaffected. The skin and subcutaneous tissues of the lower lumbar and upper gluteal region are examined with the pinch-roll test. Referred pain is accompanied by hyperalgesia of the skin and subcutaneous tissues in the involved dermatomes. This hyperalgesia or hypersensitivity can be revealed by gently grasping a fold of skin between the thumbs and forefingers, lifting it away from the trunk and rolling the subcutaneous surfaces against one another in a pinch and roll fashion. On the involved side the skin overlying the buttock and iliac crest is found to be tender when compared to the opposite side (1-4,6).

For clinical examination of the TLJ to show the involvement of the particular segment two maneuvers has been defined. The first maneuver is friction pressure over the facet

joints. For this maneuver pressure is applied deeply, and longitudinally approximately 1 cm lateral to the spinous process and is followed by a slow, gentle friction movement by the palpating finger. Tenderness is elicited over one or two joints ipsilateral to the lower back pain. The other maneuver for the examination of the TLJ is lateral pressure on the spinous processes. The pressure is applied with the thumb slowly and tangentially at each level. The test is performed from left to right, and then repeated from right to left. In the case of TLJS, pain will usually be felt in one direction only. This maneuver imparts rotation to the vertebra. Ipsilateral rotation is frequently tender at the involved level (1-4).

The diagnosis is confirmed by a periapophyseal joint block. For the examination of these signs and for the diagnostic block placing the patient in a forward flexed position, across the examining table, in order to open up the spine into flexion and gap the posterior elements is suitable. This is a very convenient and comfortable position to examine the spine from the TLJ to the sacrum, because the lordosis is reversed (1).

In the majority of cases, TLJS is particularly responsive to spinal mobilization and manipulation therapy (1-4). Long-acting corticosteroid injections can sometimes be preferable to manipulation. For those with contraindications for spinal manipulative therapy or corticosteroid injections, electrotherapy is beneficial. Regulation of activities of daily living, and especially the avoidance of the rotational movements, is critical. A targeted exercise program is essential. Radiofrequency electrocoagulation and/or surgical denervation of the involved apophyseal joint can be applied in resistant cases (1-5).

In conclusion, TLJS can often be confused with other pathologies that may cause pain in the locomotor system. The diagnosis is made with clinical suspicion and clinical evaluations. TLJS is a pathology that should be considered in the differential diagnosis, especially in elderly patients with low back, hip and groin pain.

REFERENCES

1. Maigne R. Low backs pain of thoracolumbar origin. Arch Phys Med Rehabil 1980;61(9):389-95. (PMID:6448030).
2. Maigne R. Transitional zone syndrome. In: Maigne R (Eds). Diagnosis and Treatment of Pain of Vertebral Origin-a Manual Medicine Approach. 1st edition, Williams and Wilkins, Baltimore 1996, pp 418-20.
3. Maigne R. Thoracolumbar junction syndrome. In: Maigne R (Eds). Diagnosis and Treatment of Pain of Vertebral Origin-a Manual Medicine Approach. 1st edition, Williams and Wilkins, Baltimore 1996, pp 411-16.
4. Maigne R. Low back pain of thoracolumbar origin (T11-T12-L1) (Maigne). In Maigne R (Eds). Diagnosis and Treatment of Pain of Vertebral Origin-a Manual Medicine Approach. 1st edition, Williams and Wilkins, Baltimore 1996, pp 308-20.
5. Maigne R. Segmental vertebral cellulotenoperiosteomyalgic syndrome. In Maigne R (Eds). Diagnosis and Treatment of Pain of Vertebral Origin-a Manual Medicine Approach. 1st edition, Williams and Wilkins, Baltimore 1996, pp 109-21.
6. Maigne JY, Maigne R. Trigger point of the posterior iliac crest: Painful ileolumbar ligaments insertion for cutaneous dorsal ramus pain? An anatomic study. Arch Phys Med Rehabil 1991;72(10):734-7. (PMID:1834038).
7. Torgerson WR, Dotter WE. Comparative roentgenographic study of the asymptomatic and symptomatic lumbar spine. J Bone Joint Surg Am 1976;58(6):850-3. (PMID:134040).
8. Witt I, Vestergaard A, Rosenklint A. A comparative analysis of x-ray findings of the lumbar spine in patients with and without lumbar pain. Spine (Phila Pa 1976) 1984;9(3):298-300. (PMID:6233717).
9. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331(2):69-73. (PMID:8208267).
10. Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: prevalence of intervertebral disc extrusion and sequestration, nerve root compression, end plate abnormalities and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 1998;209(3):661-6. (PMID:9844656).
11. Patel AT, Ogle AA. Diagnosis and management of acute low back pain. Am Fam Physician 2000;61(6):1779-86. 1789-90. (PMID:10750882).
12. Maigne JY, Lazareth JP, Guerin Surville H, Maigne R. The lateral cutaneous branches of the dorsal rami of the thoraco-lumbar junction. An anatomical study on 37 dissections. Surg Radiol Anat 1989;11(4):289-93. (PMID:2533408).
13. Rageot E. Syndrome of the posterior branches of spinal nerves. Anatomic, symptomatologic and therapeutic basis. J Chir (Paris) 1982;119(8-9):517-22. (PMID:6292243).
14. Kim SR, Lee MJ, Lee SJ, Suh YS, Kim DH, Hong JH. Thoracolumbar junction syndrome causing pain around posterior iliac crest: a case report. Korean J Fam Med 2013;34(2):152-5. (PMID:23560215).
15. Sebastian D. Thoracolumbar junction syndrome; a case report. Physioter Theory Pract 2006;22(1):53-60. (PMID:16573246).
16. Ozturk G, Geler Kulcu D, Aydog E. Thoracolumbar Junction Syndrome: A case report. J PMR Sci 2013;16:126-9.
17. Doubleday KL, Kulig K, Landel R. Treatment of testicular pain using conservative management of the thoracolumbar spine: A case report. Arch Phys Med Rehabil 2003;84(12):1903-5. (PMID:14669201).
18. Akgun K, Aktas I, Cakmak B. Importance of the thoracolumbar junction (Maigne) syndrome in low back pain. Eur J Pain 2006;10:105.
19. Fortin JD. Thoracolumbar syndrome in athletes. Pain Physician 2003;6(3):373-5. (PMID:16880885).

Turkish Journal of Geriatrics
2014; 17 (2) 218-222

Feyza ÜNLÜ ÖZKAN[1]
Cem NAZİKOĞLU[2]
İlknur AKTAŞ[1]
Mustafa BULUT[3]
Işıl ÜSTÜN[4]

Case Report

FEMORAL NEUROPATHY AFTER DIAGNOSTIC CORONARY ANGIOGRAPHY

Abstract

Femoral neuropathy has been reported with different conditions including hip replacement, obstetric and gynecological procedures, and abdominal and urological explorative laparatomies. Isolated lesions of the femoral nerve is rare; most cases of femoral neuropathy result from positioning or compression during abdominal or pelvic surgery. Femoral neuropathy can be seen as a consequence of hematoma formation from misguided femoral catheterizations. We report a 65 year old case with severe femoral neuropathy following diagnostic angiography caused by the sandbag placed on the groin for homeostasis. This condition should be kept on mind when a patient presents with difficulty in walking with a recent history of diagnostic catheterization.

Key Words: Aged; Coronary Angiography; Femoral Neuropathy.

Olgu Sunumu

TANISAL ANJİOGRAFİ SONRASINDA GELİŞEN FEMORAL SİNİR NÖROPATİSİ

Öz

Femoral sinir nöropatisinin kalça protezi uygulanması, obstetrik ve jinekolojik işlemler, abdominal ve ürolojik eksploratris laparatomiler gibi farklı koşullar sonrası geliştiği bildirilmiştir. Femoral sinirin izole lezyonları nadir olmakla beraber femoral sinir nöropatisi olgularının büyük çoğunluğu abdominal ve pelvik cerrahiler sırasında hastanın pozisyonlanmasına veya kompresyon uygulanmasına bağlı olarak görülmektedir. Anjiografi sırasında ya da sonrasında kateterizasyon komplikasyonu sonucunda hematoma bağlı olarak da femoral sinir nöropatisi gözlenebilir. Bu sunumda 65 yaşındaki bir hastada diagnostik koroner anjiografi sonrası kasık bölgesine hemostaz amacıyla kum torbası uygulanması sonucunda gelişen femoral sinir nöropatisi olgusu sunulmuştur. Bu durum, yürüme güçlüğü şikayeti ile başvuran hastalarda akılda bulundurulmalıdır ve hastalar yakın geçmişte diagnostik kateterizasyon öyküsü açısından da akılda tutulmalıdır.

Anahtar Sözcükler: Yaşlı; Koroner Anjiografi; Femoral Nöropati.

İletişim ***(Correspondance)***

Cem NAZİKOĞLU
Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi,
Kritik Yoğun Bakım Kliniği, İSTANBUL

Tlf: 0216 578 30 00
e-posta: cemnazikoglu@gmail.com

Geliş Tarihi: 24/01/2014
(Received)

Kabul Tarihi: 19/02/2014
(Accepted)

[1] Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi, Fiziksel Tıp ve Rehabilitasyon Kliniği İSTANBUL
[2] Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi, Kritik Yoğun Bakım Kliniği İSTANBUL
[3] Kartal Koşuyolu Yüksek İhtisas Hastanesi, Kardiyoloji Kliniği İSTANBUL
[4] Bağcılar Eğitim Araştırma Hastanesi, Fiziksel Tıp ve Rehabilitasyon Kliniği İSTANBUL

Introduction

Femoral neuropathy (FN) has been reported with different conditions including hip replacement surgery, and abdominal and urological explorative laparatomies (1-4). Isolated lesions of the femoral nerve are rare, whereas FN arising from lesions of the lumbar plexus or L2-4 nerve roots is more common. Most cases of FN result from prolonged positioning in the lithotomy position during labor, gynecologic or urologic procedures (5). FN can be seen as a consequence of retroperitoneal hemorrhage, often from excessive anticoagulation or hematoma formation from misguided femoral catheterizations (6-8). We report a case of FN at the inguinal level after diagnostic angiography and discuss the clinical evaluation of a patient with a femoral nerve lesion, in the context of a review of the literature.

Case

A 65 year old female referred with the complaint of buckling of the knee during walking. Her medical history revealed that she had had a diagnostic coronary angiography and stayed in the intensive care unit (ICU) for 3 weeks after the procedure. Her difficulty in walking was discovered when she was mobilized in the ICU. She was evaluated by an orthopedic surgeon and magnetic resonance imaging (MRI) of her left knee was planned. MRI revealed rupture in the anterior cruciate ligament and degenerative changes in the knee joint. She was referred to physical medicine and rehabilitation for treatment. She had no prior history of difficulty in walking before the angiography. She had diabetes mellitus type 2, which was under control by the oral antidiabetic drugs. She had no other systemic or metabolic illness. Besides the oral antidiabetics, she was on antihypertensive (losartan) and lipid lowering (atorvastatin) medication. She denied any kind of infection before or after the procedure. On physical examination, mild quadriceps atrophy was noticed in her left leg. On manual muscle testing, left hip flexion was 5/5, knee extension was 2/5, knee flexion, ankle dorsiflexors and plantar flexors were 5/5. Muscle testing on the right leg was normal. On sensory examination, diminished sensation on the left anterior thigh and medial calf was detected. Deep tendon reflexes were otherwise normal except for absent knee jerk on the left. Physical examination findings suggested a femoral nerve lesion.

EMG examination revealed subacute axonal femoral neuropathy at the inguinal ligament on the left. Compound muscle action potential (CMAP) amplitude recorded from the left rectus femoris muscle was reduced when compared to the right side. There was also marked reduction in the sensory nerve action potential (SNAP) amplitude of the left saphaneous nerve. Bilateral peroneal and tibial motor and sural sensory nerve conduction studies were in normal range. Needle EMG revealed marked fibrillation potentials and positive sharp waves in vastus medialis and vastus lateralis with reduced recruitment of normal configuration motor unit potentials. Iliopsoas muscle, adductors and tibialis anterior muscles were normal. Normal nerve conduction study of peroneal, tibial and sural nerves excluded the diagnosis of polyneuropathy. EMG findings were confined to the femoral innervated vastus medialis and lateralis so L2-4 radiculopathy was also excluded. No spontaneous activity was recorded at the iliopsoas muscle and normal recruitment was observed so lesion was localized to the inguinal ligament, above which femoral nerve gives supply to iliopsoas muscle. Findings were interpreted as subacute axonal femoral neuropathy at the inguinal ligament.

There had been no hemorrhagic complications after the angiography nor catheterization misguidance during the procedure. Ultrasonography examination revealed that there was no hematoma or pseudoaneurysm formation in the groin region. Sandbag application in the groin region was thought to have caused compression of the femoral nerve at the inguinal ligament. Electrical stimulation was applied to the quadriceps muscle and patient was enrolled in a rehabilitation program for 6 weeks and kept on the quadriceps strengthening exercises. At the third month EMG evaluation, no spontaneous activity was recorded at the quadriceps muscle and there's only slight reduction in the recruitment with high amplitude, polyphasic and long duration MUAPS. The patient was able to walk independently.

Discussion

The femoral nerve is derived from the lumbar plexus and receives innervation from L2, L3 and L4 nerve roots. In the pelvis, the femoral nerve emerges from behind the psoas muscle; it sends muscular branches to the iliopsoas muscle and then runs beneath the inguinal ligament. In the thigh, the femoral nerve sends muscular branches to the sartorius and pectineus muscles and is the most important supply to the quadriceps femoris muscle. The femoral nerve continues along the medial border of the calf as the saphanous nerve. It supplies sensation to the anterior and medial thigh as well as

the medial calf, which is the sensory territory of the saphenous nerve (9).

Patients with FN present with difficulty in walking due to quadriceps weakness and dragging of the leg due to iliopsoas weakness. The quadriceps is a strong muscle with four heads, so it is sometimes difficult to detect subtle weakness in mild lesions of the femoral nerve. Asking the patient to arise from the floor from a kneeling position may be helpful in detecting mild cases. In more severe cases, quadriceps atrophy may be seen. Weakness of hip flexion is an important sign of FN; it indicates involvement of the iliopsoas muscle, localizing the lesion proximal to the inguinal ligament (10). Sensory disturbance in the anterior and medial thigh is seen. Sensory disturbance in the medial calf, extending to the medial malleolus in the saphaneous nerve territory may also be encountered. Examination of deep tendon reflexes is important, as the patellar reflex is depressed or absent in FN. EMG examination is important in diagnostic evaluation. EMG reveals the extent and severity of the neuropathy and aids in differentiating it from lumbar plexopathy and L2-4 radiculopathy.

Most femoral neuropathies result from gynecologic, urologic and orthopedic surgery, or are due to retroperitoneal or groin hematomas after catheterization (1-8). Compressive femoral neuropathy after diagnostic transfemoral angiography is a rarely reported condition that has serious implications, especially in elderly patients to whom diagnostic angiographies are frequently applied. Probably having type 2 diabetes mellitus for years gave rise to the susceptibility in our patient to nerve compression syndromes. Although no polyneuropathy was detected on EMG examination we know that diabetic patients are more vulnerable to any kind of nerve lesions. Findings in only femoral innervated muscles and normal peroneal and tibial nerve conduction studies lead us to the diagnosis of FN. Because there was no history of viral infection or any other condition leading to neuropathy and because of the localization and time course of the pathology we accused the sandbag applied to the inguinal region as the causative agent of FN in our case. Severe lesions of the femoral nerve lead to walking disability. Sometimes mild femoral nerve lesions with subtle muscle weakness may present only with frequent falls, which lead to additional serious problems like fractures, especially in elderly patients.

In a study of 9585 cardiac catheterizations, Kent et al. (11) reported 20 patients (0.21%) with femoral neuropathy, which were mostly due to local hematoma or pseudoaneurysm. Pressure applied to the puncture site for hemostasis is reported as a rare cause. The reason for FN in our case was pressure applied by the sand bag over the groin. Ultrasonographic examination revealed that there was no hematoma or pseudoaneurysm formation in the groin region. Reported cases are mostly mild demyelinating lesions; however, severe cases leading to walking difficulty and requiring long periods of rehabilitation, as in our case, may also be encountered.

This condition should be kept in mind when a patient presents with difficulty in walking and a recent history of diagnostic catheterization. Initiation of an early rehabilitation program is as important as the early diagnosis of neuropathy for the prevention of muscle atrophy and joint damage due to knee instability. These aspects are particularly important in the elderly, in whom sarcopenia and degenerative changes in the joints coexist. Electrophysiological evaluation is important for diagnosis and follow-up. Confounding factors, such as the anterior cruciate ligament rupture and gonarthrosis in our case, should be evaluated carefully. EMG is one of the most useful tools in differential diagnosis.

In conclusion, FN should be kept in mind when a patient presents with difficulty in walking and a recent history of diagnostic catheterization. Early initiation of a rehabilitation program is important for recovery and for the prevention of unwanted additional problems like falling and its consequences, especially in elderly patients.

REFERENCES

1. Kannan S, Ho KM. Femoral nerve palsy after femoral vein cannulation. Anesth Analg 2000;90:1246-7. (PMID:10781494).
2. Celebrezze JP, Pidala MJ, Porter JA, et al. Femoral neuropathy: an infrequently reported postoperative complication. Report of four cases. Dis Colon Rectum 2000;43:419-22. (PMID:10733127).
3. Unwin A, Scott J. Nerve palsy after hip replacement: medicolegal implications. Int Orthop 1999;23:133-7. (PMID:10486021).
4. Keating JP, Morgan A. Femoral nerve palsy following laparoscopic inguinal herniorrhaphy. J Laparoendosc Surg 1993;3:557-9. (PMID:8111106).
5. Al Hakim M, Katirji MB. Femoral neuropathy induced by the lithotomy position: A report of 5 cases and a review of the literature. Muscle Nerve 1993;16:891. (PMID:8355719).
6. Kuruvilla A, Kuruttukulam G, Francis B. Femoral neuropathy following cardiac catheterization for balloon mitral valvotomy. Int J Cardiol 1999;71:197-8. (PMID:10574409).
7. Yu Chien-Ching, Shih Ying-Ju, Tsai Su-Ju. Femoral nerve injury following transfemoral angiography: A case report. Tw J Phys Med Rehabil 2008;36(4): 227-34.

8. Barçin C, Kurşaklioğlu H, Köse S, Işik E.Transient femoral nerve palsy after diagnostic coronary angiography. Anadolu Kardiyol Derg 2009;9(3):248-9. (PMID:19520660).
9. KL Moore. Anatomy of pelvis and perineum, In: Keith L. Moore. Clinically oriented Anatomy. 3rd Edition, Williams & Wilkins, USA 1992, pp 326-434.
10. Preston DC, Shapiro BE. Femoral Neuropathy, In: Electromyography and Neuromuscular Disorders. Clinical-Electrophysiological Correlations. 2nd edition, Elsevier Philadelphia 2005, pp 355-64.
11. Kent KC, Moscucci M, Gallagher SG, Di Mattia ST, Skilman JJ. Neuropathy after cardiac catheterization: incidence, clinical patterns and long term outcome. J Vasc Surg 1994;19:1008-13. (PMID:8201701).