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Review Article

POLYPHARMACY IN THE ELDERLY: TO PRESCRIBE, OR NOT PRESCRIBE "THAT IS THE QUESTION"

Abstract

Although its definition has not been fully accepted, polypharmacy at advanced age appears as a significant worldwide problem in terms of both elderly health and general health systems and there are still many question marks / gaps with respect to this issue. We have insufficient data on its definition and thus its prevalence and complications. Non-prescription drugs are usually ignored in the studies. Health care professionals should be aware of the risks and interventions aiming to reduce exposure and minimizing the risk associated with potentially harmful drug combinations are needed. This article addresses these issues and proposes practical recommendations regarding the rational drug use for elderly age groups.

Key Words: Polypharmacy; Aged; Therapeutics.

Derleme

YAŞLILARDA ÇOKLU İLAÇ KULLANIMI: REÇETELEMEK VEYA REÇETELEMEMEK "SORU BU"

Öz

Polifarmasi tanımı tam olarak kabul edilmese de, ileri yaşta hem yaşlı sağlığı hem de genel sağlık sistemleri açısından tüm dünyada önemli bir sağlık problemi olarak karşımıza çıkmaktadır. Ancak hala bu sorun ile ilgili pek çok soru işareti/eksik nokta bulunmaktadır. Tanımlanması ve böylece prevalans ve komplikasyonları ile ilgili veriler yetersizdir. Reçetesiz ilaçlar çalışmalarda genellikle gözardı edilmektedir. Sağlık çalışanları riskler açısından uyanık olmalı ve potansiyel zararlı ilaç kombinasyonları ile ilişkili riskler hakkında ve bu tür durumlarla karşılaşmayı azaltmak için onlara eğitimler yapılmalıdır. Bu makalede, bu sorunlar ve ileri yaş grubu için akılcı ilaç kullanımı ile ilgili pratik öneriler ele alınacaktır.

Anahtar Sözcükler: Çoklu İlaç Kullanımı (Polifarmasi); Yaşlı; Tedavi.

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INTRODUCTION

The increase in the percentage of advanced age group started to affect health systems throughout the world both socially and financially. Not only polypharmacy, but also inappropriate drug usage and related problems began to concern both the medical literature and the health insurance systems. With the increased prevalence of chronic diseases such as hypertension, arthritis, heart disease, cancer and diabetes mellitus, older individuals seem to have started using more medication. The changing physiological characteristics associated with age also require attention in the ***pharmacokinetic and pharmacodynamic*** aspects of drugs (1, 2, 3). The decline in physiological functions as part of the normal aging process may lead to altered drug disposition and sensitivity to drug effects and have important influences on the pharmacokinetic process. Multi-chronic diseases which are frequently observed among this age group require polypharmacy treatment. At the same time, chronic drug use, self-medication and noncompliance are common factors observed in the elderly. Therefore, treatment should be tailored to the individual older person. For older persons, physician's awareness and expertise is required not only in correct diagnosis, but also in treatment and follow-up.

Polypharmacy can best be defined as excessive / multiple intake of medications. Although it is a concept associated with both quantity and appropriateness of medications, there is no standard definition for it. While the United States (US) definitions relate it to indications, the European definitions relate it to the quantity of medicines (2). However, it is worthwhile to state that it describes a more complex clinical condition than being merely associated with the number of medications. Some of the authors use the terms "***experiencing problems with medicines***" and "***unnecessary or potentially inappropriate use of medication***" for the definition of polypharmacy (use of 5 or more medications) (2,3). The "***inappropriate medication***" mentioned here can be defined as ineffective use of a specific medicine or medicine class, use of a high-risk medicine instead of its safer alternative or the medicine being inappropriate for a particular disease (4). The rate of inappropriate medication use among elderly people is 40%. Use of drugs without indication, use of equivalent drugs for treating the same disease, drug interactions, inappropriate doses, and use of other drugs for treating adverse drug reactions are the subjects dealt with under the heading of polypharmacy (2,3,5).

According to some, polypharmacy may also be categorized under 2 groups: therapeutic and contra-therapeutic polypharmacy (6). Therapeutic polypharmacy involves medications that are necessary for achieving an effective treatment and are prescribed by clinicians after a careful monitoring. Examples include use of isoniazid, rifampin, ethambutol, pyrazinamide, and pyridoxine for tuberculosis, or digoxin, diuretics, and angiotensin-converting enzyme inhibitors for congestive heart failure. Contra-therapeutic polypharmacy, on the other hand, involves use of long-term and often high-dose multiple agents, which cannot be monitored, which lead to undesired or unexpected side effects during drug intake, and depends on personal or professional preferences (6).

Due to these different definitions of polypharmacy, its incidence has been reported to be between 5% and 78% (2). However, since most of the studies did not include nonprescription medications, it was stated that this ratio could be much higher, emphasizing that the elderly used prescribed medicines at a rate of 34% and over-the-counter medications at a rate of 40%. Polypharmacy was also found to be more frequent in women than in men (2).

THE NUMBER OF DRUGS

In a US study, it was observed that of women over 65 years of age, 57% used 5 or more drugs and 12% used 10 or more drugs (7). A large-scale study conducted in Europe, showed that 51% of the patients took 6 or more medications (8). The results of a study on 1944 nursing home occupants revealed that 31% of women and 23.3% of men used 3 or more drugs per day. 5.5% of the elderly people participating in the study complained about side effects of the medications they used, most frequently gastrointestinal, and polypharmacy was also shown to have a relationship with the side effects (9). A large multicenter study including elderly people admitting to outpatient clinics showed that 38.2% used 4 or more drugs (10). Another study including 1300 elderly revealed that use of 4 or more drugs was more frequent in 71-80 years age group and multiple drug use decreased with advancing age (11).

In literature, the rate of using drugs ineffectively or without indication seems to be 30-60% (3). Therapeutic duplications are also seen in treatment plans. In a study of Hajjar et al. (12), 44% of the patients were found to have used 1 or more unnecessary drugs at the time of their discharge and 25% of these were found to have started using them while they were hospitalized. The absence of indication (32%), inef-

ficacy (18%), and therapeutic duplication (2,3) were reported as the reasons of unnecessary drug use.

In the elderly, use of over-the-counter drugs also appears as another important problem. A study stated that 7% of women and 6% of men used over-the-counter drugs (9). Community-dwelling elderly patients were found to take 1 or more over-the-counter drugs at a rate of 90% and 2-4 at a rate of nearly 50% (13). Another study showed that, 47-59% of the community dwelling elderly patients were taking vitamins or minerals and 11-14% were taking herbal supplements (7). The most commonly consumed nonprescription drugs include painkillers (e.g., acetaminophen, non-steroid anti-inflammatory medicines) cold relievers, laxatives, antacids, vitamins, and nutritional supplements (7,13).

The group of medications consumed is also of interest. The most commonly prescribed drugs in the adult population in the US are cardiovascular drugs, antibiotics, diuretics, opioids, and antihyperlipidemic drugs. Use of cardiovascular drugs is reported to increase the risk of polypharmacy (2). The most frequently (26.7%) prescribed drugs were cardiovascular medications in nursing home occupants (9). Gastrointestinal and central nervous system drugs as well as nutrients / minerals are reported to be the most widely used unnecessary medication groups (12).

Interestingly, Saad and co-workers reported that geriatric consultations increased the total number of medications and the cost of medications used by elderly patients (14). In their study, the average number of medications adjusted by the geriatric consultant was 3. The most common classes of adjusted medications were pain medications (22%), nutritional supplements (13%), bowel regimens (8.5%), antipsychotics (8%), and osteoporosis medications (8%) (14).

Physiology (Pharmacokinetics and Pharmacodynamics)

Aging can be described as a decrease in functioning at the level of cells, tissues, organs, and the body, which starts from the biochemical reactions in cells with the effect of genetic constitution and external factors. The pharmacokinetic and pharmacodynamic differences in the elderly may be one of the major discussion points in the context of polypharmacy. Genetics, life style, and habits may cause these changes in the elderly to become more diverse and complex. The inhibition or induction of drug metabolism usually does not change with age (1,2,15). The composition of the body and the organ functions that contribute to elimination are more responsible for this change (15). Pharmacokinetics is significant in terms of the changes related to ***absorption*** (achlorhydria etc.), ***distribution*** (increase in liposoluble drug distribution, decrease in hydrosoluble drug distribution), ***therapeutic window*** changes, ***adverse effects***, ***metabolism***, and ***elimination*** of drugs (16,17). ***Numbers of receptors***, increased ***sensitivity to drugs***, increased ***side effects***, decrease in response to ***physiological changes***, increased ***target organ sensitivity***, ***binding capacity***, and ***biochemical reactions*** indicate pharmacodynamic changes (16,18). For example, a decrease in response to beta agonists and beta-blockers and an increase in response to opiates, benzodiazepines, or warfarine may be observed in the elderly. A decrease in the total body fluids, decreased lean body mass and body fat, decreased serum albumin levels and altered protein binding, decreased liver metabolism, decreased renal blood flow, decreased glomerular filtration rate and renal clearance associated with advanced age are all related to these physiological changes (1,2,16).

In the renal system, kidney size increases until 40-50 years of age and decreases thereafter (tubulointerstitial change associated with infarct), a decrease in creatinine clearance and glomerular filtration rates and an increase in average arterial pressure and changes in intrarenal vessels (atherosclerosis) is observed; diabetic patients are affected by these and vulnerability to infections increases with age and tumors may be encountered. A decrease in kidney mass by 25-30% and in the quantity of glomeruli by 30-40%, impairment in filtration and concentration ability, a decrease in vasopressin response, impairment in salt retention ability, an increase in dehydratation risk, a decrease in bladder capacity, an increase in residuals, frequent urinary tract infections, incontinence, and urinary obstructions are common (1,2,17,18).

In the gastrointestinal system, there is an increase in the prevalence of atrophic gastritis and aclorhidria, a decrease in motility, damage in liver, impairment in cell repair–effective drug metabolism, a decrease in the blood flow (30-40%) and volume in liver, decreased colon peristaltism, and constipation is observed (1,2,17,18). As the hepatic first-pass effect of highly cleared drugs could be reduced (due to decreases in liver mass and perfusion), the bioavailability of some drugs can be increased in the elderly. Significant changes in body composition occur with advancing age. Lipophilic drugs may have an increased volume of distribution (Vd) with a prolonged half-life, and water-soluble drugs tend to have a smaller Vd. In the elderly, hepatic drug clearance of some drugs can be reduced by up to 30% (19).

The action system of drugs in an aged body is summarized by Shepler et al.(20):

1. Drugs remain in the system for a long time due to low absorption rates,
2. Drugs become highly concentrated in different parts of the body due to impairment in the circulation system,
3. The metabolism changes due to the changes in liver and cardiac outputs,
4. Decreased renal functions affect drug excretion.

Adverse drug reactions are also seen more often. Although a general loss of appetite, falls, confusion, or urinary incontinence appear as side effects, they sometimes are perceived as the "normal" process of getting old (20).

When we consider all these changes, it becomes obvious how careful one should be when prescribing medications to the elderly. Although all these system changes are actually taught to all health professionals during their education, they are not so easy to keep in mind and to be applied to clinical practice (21). Errors occur at this point.

Predictors and Risks

Elderly people are known to be taking more drugs than the younger age group and the etiology of polypharmacy is multi-factorial. Chronic diseases and age-related changes in organs are the primary reasons for multiple drug use. Drug intake as personal preference and use of over-the-counter drugs can be cited as another factor. Moreover, complementary and supportive therapies started to become popular today throughout the world. Elderly people usually do not consider such supportive therapies as medications. Another problem is the vulnerability of the elderly. Effects of drugs, their side effects, dose regimen, storage conditions, use of similar drugs and name similarities among drugs can make it difficult for patients to trace and use drugs. Health professionals also have a supportive role in polypharmacy. Approximately 75% of patients consulting a doctor are given prescriptions (2). Since it is sometimes more difficult to provide training than to write a prescription, physicians choose the short-cut. Advertisements of pharmaceutical companies and television programs with insufficient educational content also encourage the elderly to use inappropriate drugs. ***The risk factors involved in polypharmacy*** are (2,22):

1. Patients' going to different physicians and getting many prescriptions,
2. Ease of getting non-prescription drugs,
3. Physicians' inclination towards prescribing many medicines,
4. Patients' expectations for many different drugs,
5. Use of various medicines due to additional diseases,
6. Herbal preparations and over-the-counter medications,
7. Use of drugs without any knowledge of their side effects and interactions,
8. Consulting various physicians and receiving various prescriptions,
9. Inadequate communication and coordination,
10. Replacing medication due to drug side effects (prescription cascade),
11. Prescribing medication based on symptoms rather than diagnosis,
12. Tendency to quit the medication and start with a new one,
13. Automatic prescription of drugs that are known to the patient and the physician,
14. Presence of too many medications in the market,
15. Forgetfulness of the doctor to ask and of the patient to tell about the medication,
16. Tendency to use medications obtained from acquaintances.

Having been hospitalized in the last 6 months, being female, being in depression, low level of education, and consulting 5 or more physicians a year have also been reported to increase the risk of polypharmacy (2,23). Polypharmacy was also found to be associated with advanced age, white race, education, poor health condition, use of >9 medicines, number of healthcare visits, additional insurance, and number of caregivers (3). Veehof et al., on the other hand, reported that the predictors of polypharmacy were age, cardiovascular diseases, diabetes mellitus, stomach disorders, use of drugs without full indication, and the number of medications at the start of the study (24). It was also reported to be associated with depression, hypertension, asthma, anemia, angina, diverticulosis, osteoarthritis, gout, and diabetes mellitus (2,3). Patients with cancer are also at risk today in terms of polypharmacy (4). A study showed that 92% of cancer patients used an average of 5 medications before starting cancer treatment. Supportive and complementary therapies are also commonly used by cancer patients in general (25-91%) and this is usually overlooked in studies. Not only in studies but also in clinical practice, neither the patient tells about these to the doctor, nor does the doctor ask about them. In general, problems are also experienced in relation to the follow-up of the primary treatment (4).

INAPPROPRIATE PRESCRIPTIONS

Some groups tried to develop criteria and advisory guidelines for inappropriate use of drugs. It is stressed that indication, efficacy, dose, directions, drug-drug interaction, and drug-disease interaction must definitely be considered in a medication appropriateness index (4). However, inappropriate use of drugs is frequent in clinical practice in spite of expert opinions. The rates of inappropriate drug use sometimes reach up to 50%. It was demonstrated in a study that 42% of elderly patients took their medication in an inappropriate way and 57% of them took medications with no efficacy or indication (25). In another study, the rate of potential inappropriate use of drugs was 31% and the potential of dangerous drug interactions was 10% (26). The rate of potential inappropriate use of drugs was reported to be 8-13% in ambulatory visits, 50% in nursing homes, and 17% in emergency rooms (27). The most commonly prescribed inappropriate medications included antispasmodics and platelet inhibitors. Another study showed that proton-pump inhibitors (>8 weeks, maximum dose), non-steroid anti-inflammatory drugs (>3 months), and long-acting benzodiazepines (>1 month) were prescribed as potentially inappropriate drugs (5). Non-steroid anti-inflammatory drugs and opiates were also cited as most commonly duplicated medicines (5). As the frequency of prescribing drugs increases, inappropriate use of drugs also increases. Inappropriate use of drugs was found to increase congestive heart failure, hypertension, arteriosclerotic heart disease, chronic obstructive disease, diabetes, and pleural effusion. Training of physicians and all health professionals was reported to be important in this respect (2).

A study aiming to compare the prevalence of potentially inappropriate medications using standard drug terminologies at 2 disparate institutions using electronic health records and to identify characteristics of elderly patients who have a potentially inappropriate medication on their active-medication lists showed that; female sex, polypharmacy, and number of primary care visits were significantly associated with potentially inappropriate medication prescribing (28).

A cross-sectional study was carried out on a total of 1019 participants who accepted face-to-face questionnaires in home interviews and inappropriate drug use was assessed using the Beers criteria. The study revealed that drug utilization and the prevalence of inappropriate medication use in the elderly were lower than that in reports from most developed countries. Furthermore, polypharmacy and higher age were the main risk factors for potentially inappropriate drug use in the elderly (29).

The most commonly mentioned printed tools developed for prescriptions for advanced ages are: the ***Inappropriate Prescribing in the Elderly Tool*** (IPET), the ***Beers Criteria***, the ***Medication Appropriateness Index*** (MAI), the ***Screening Tool of Older Persons' Potentially Inappropriate Prescriptions*** (STOPP), and the ***Screening Tool to alert Doctors to the Right Treatment*** (START) (22). The Canadian Consensus Panel developed the IPET in 1997 to set out adverse drug reactions and drug-disease relations. Although they recommended avoiding the use of beta-blockers in chronic obstructive lung disease and congestive heart failure, this and many other recommendations are not supported by today's evidence-based medicine (22,30). The MAI questions medications in terms of their indications rather than their appropriateness (22). Among these, the most commonly mentioned and used criteria in clinics seem to be the Beers Criteria. The Beers Criteria was developed in 1991 and modified in 1997, in 2003 and 2012 (31-33). It aims to provide guidelines to the users about inappropriate drug names and their potential side effects. It makes distinctions such as "always inappropriate" and "potentially inappropriate". Medications are also rated according to high or low number of adverse events associated with them. However, there are some points of doubt about the Beers Criteria. Some of these medications are not contraindicated; the criteria do not take into account polypharmacy, drug interactions, treatment period or different indications. Furthermore, some medications that cause frequent visits to the emergency service or have frequent side effects (warfarin, insulin, digoxin etc.) are not included in the list (27). Checklists may be helpful in detecting for discontinuing medication in elderly (34). The STOPP and START criteria that were developed to be used in Europe are viewed as being more comprehensive (22,35). The STOPP criteria attempt to classify 65 potentially inappropriate drugs according to the systems and define them in terms of drug-drug, drug-disease, falls, and therapeutic duplications. STOPP criteria identified a significantly higher proportion of patients requiring hospitalization due to potentially inappropriate medication related adverse events than Beers' criteria (35).

Besides these, the SAIL and TIDE mnemonics are noteworthy. **SAIL** stands for the first letters of **simple** as far as possible, cautious to potential **adverse effects**, complying with **indications** and necessary to be **listed** (dose, name etc.) in relation to the medications. **TIDE**, on the other hand stands for the first letters of the words stressing the significan-

ce of **time**, being cautious to **individual** reactions to drugs, potential **drug-drug interactions** and **education**. There are limited data and evidence for reviewing medications using the SAIL and TIDE criteria. The "***Brown Bag Syndrome***" was introduced thinking about the bags full of medications in the hands of patients who rush to the doctor's or the emergency room. It is recommended to check and review prescriptions and bags full of prescription or non-prescription drugs (2,36). Although no criteria may ever be globally applicable, STOPP and START make significant advances. Regional drug availability, economic considerations, and clinical practice patterns impact criteria selection (37).

Multiple medications increase the risk of inappropriate use of drugs. However, one should bear in mind that despite all these data, some drugs listed as inappropriate are included in normal treatment regimens. Medications are used in various indications as in treatment of dysautonomia and orthostatic hypotension with central-acting alpha blockers and of anxiety with benzodiazepines. However, it should be noted that use of long-acting benzodiazepines, some opiates, non-steroid anti-inflammatory drugs and prescription of more than one medication from the same class are not recommended at old age.

Adverse Drug Reactions (ADRs)

Polypharmacy increases the likelihood of drug-drug reactions, food-drug interactions and drug-disease interactions. Incidence of drug-drug interactions may be as high as 80% in older people (38). This risk becomes apparent in the advanced age group where physiologic changes are observed. ADRs were found to be associated with presence of coexisting diseases, use of specific medications (i.e. warfarin) and increased number of medications (3,39). Advanced age, malabsorption, and renal and hepatic organ problems as well as changes in the conditions specific to the patient may effect the drug interaction patterns and risks (4,38).

Nearly 20-25% of hospitalizations in the over 65-age group were observed to be associated with adverse drug reactions. In another study, the prevalence of hospitalization due to adverse drug reactions was found to be 10.7% in patients older than 60 years of age and for the age group of over 17 the medications most often blamed were the cardiovascular drug group (40). The examples given for the potentially harmful drug-drug interactions include angiotensin converting enzyme inhibitors versus potassium sparing diuretics, angiotensin converting enzyme inhibitors or angiotensin receptor blockers versus sulfamethizole / trimethoprim, warfarin versus antimicrobial agents and non-steroid anti-inflammatory drugs. These lists may be extended further (14). The likelihood of side effects increases with drug-drug interactions and concurrent use of drugs increasing or decreasing the effect of another. This risk increases especially in drugs with narrow therapeutic windows or high toxicity. Since cancer patients have previously used many drugs, contraindications, organ failures, additive toxicity and use of therapeutically similar drugs should particularly be reviewed for ADRs (4). Since pharmacologic profiles are different in cancer patients and the therapeutic window is narrow, toxic effects may be different (38). Warfarin and anti-epileptic drugs are quite risky in this respect. The overlooked supportive therapies in cancer patients and their negative effect on the anti-cancer treatment should be evaluated from this point of view.

There are various reasons for adverse drug reactions, including age- and disease-related alterations in pharmacokinetics and pharmacodynamics as well as the common practice of polypharmacy. According to the results of a study; in elderly patients registered to receive home healthcare, 14% of hospital admissions were primarily caused by ADRs. One-third of these ADRs were related to impaired renal function, generally in very old women. These ADRs may be avoided by close monitoring of renal function and adjustments to pharmacotherapy (drug selection and dose), particularly in very elderly women (41).

Mortality and Morbidity

Polypharmacy increases the risk of geriatric syndrome and negatively affects the morbidity / mortality rates. Some sources even include polypharmacy in the geriatric syndrome group. Larson et al. (42) reported that multiple drug use was associated with cognitive impairment and Ruby et al. (43) stated that multiple drug use for urologic activity was associated with the risk of urinary incontinence. Use of 2 or more psychotropic drugs increases the fall risk 2.4 to 4.5 times and use of 2 or more central nervous system drugs (opioid, hypnotic etc.) increases the fall risk 2.37 times. With the increase in the number of medications, balance problems start to occur (44).

Patients using multiple drugs had low compliance with the treatment and high mortality rates and consultancy provided by a pharmacist over the phone increased compliance with the treatment and lowered mortality rate (45). Inadequate or incomplete information increases the risks of drug inte-

ractions and side effects. Adverse drug reactions associated with inappropriate use of drugs lead to many problems. Polypharmacy appears as one of the significant reasons for hospitalization. It is known that 28% of hospitalizations are associated with incorrect drug use and 2/3 of these can be prevented. Polypharmacy was found to be associated with the increase in the prevalence of falls, prolonged hospitalization, and the increase in the rate of re-hospitalization (46). It can also cause fractures, cognitive dysfunction, postural hypotension, electrolytic disorders and cardiac failure.

Polypharmacy is also associated with the deterioration of physical and instrumental daily life activities. Drug-disease interactions and polypharmacy appear to be a risk factor not only for adverse effects but also for decreased functional condition. Benzodiazepines and anti-cholinergic drugs were reported to be associated with functional condition. The effect of antidepressant and antihypertensive drugs was found to be complex. Such functional influence may be associated with the effects of these drugs on sight, imbalance, dizziness, tension variations, alertness, and muscle strength (44). There is evidence that Beers' criteria for inappropriate medication use may have an adverse healthcare impact in the community-dwelling elderly (47).

Polypharmacy and the associated problems also cause significant increases in healthcare expenditures (48). In a study, polypharmacy was reported to be common among the patients staying in a nursing home and it was suggested that even the cardiovascular disease prevention drugs prescribed could be inappropriate due to limited life expectancy (49). Some of the causes of these increased healthcare expenditures include frequented clinical and physician visits, additional medications to treat new symptoms, repeated blood tests, visits to emergency rooms and hospitalization (2,4).

SUGGESTIONS

Prevention should be the most important step in struggling with polypharmacy. Multidimensional geriatric assessments are suggested as the most important step for prevention and treatment (4). ***Golden rules of prescribing*** are: 1-Think carefully before prescribing, 2-Prescribe with maximum knowledge about your patient and the drugs, 3-Monitor patient for efficacy and side effects, 4-Help patient make better use of medicine, 5-Review medication to discontinue, to reduce dose or to substitute with safer drug. One must consider "maximum benefit with least risk", since there is no drug which does not carry some degree of risk. According to Fialova and Onder (50);

1. Older people have substantial interindividual variability in health, disability, age-related changes, polymorbidity, and associated polypharmacy, making generalization of prescribing recommendations difficult.
2. Medication use in older adults is often inappropriate and erroneous, partly because of the complexities of prescribing and partly because of many patient, provider, and health system factors that substantially influence the therapeutic value of medications in aged people.
3. A high prevalence of medication errors in older adults results on the one hand from accumulation of factors that contribute to medication errors in all age groups, such as polypharmacy, polymorbidity, enrollment in several disease-management programs, and fragmentation of care. On the other hand, specific geriatric aspects play a role in these medication errors; these include age-related pharmacological changes, lack of specific evidence on the efficacy and safety of medications, underuse of comprehensive geriatric assessment, less availability of drug formulations offering geriatric doses, and inadequate harmonization of geriatric recommendations across Europe.
4. The dearth of geriatric clinical pharmacology and clinical pharmacy services compounds the difficulties.
5. There are gaps in research and clinical practice that lead to frequent medication errors in older adults, which must be solved by future studies and by regulatory measures in order to support errorless and appropriate use medications in these people.

Network systems specific to old age and old aged cancer patients in some countries make it easier to trace medication lists. Conflicting histories were discovered in 76% of the cases in a meta-analysis where the frequency, type, and clinical significance of drug history were explored at the time of hospitalization (51). These conflicts included drug name differences, discontinued drugs, and differences in dose and frequency. Some studies emphasize that in those for whom a geriatric assessment and treatment is being performed, it has positive effects on polypharmacy when an inappropriate drug list is sent to the doctors or by using practices such as medication grid, employing a clinical pharmacist and drug control-tracing by primary care physicians (44).

Since weekly and monthly medications, insulin, inhalers, topical drugs, patches, and ocular drops will not be in the pill box, it is stressed that care should be taken in tracing drugs.

It is stated that sources from other doctors and drugstores should also be kept in mind.

Methods considered to solve the problem or put into practice as pilot applications include provision of product information (e.g., drug interactions) in hard-copies by companies, on-line access to patient information, alerts through special programs when inappropriate drugs are prescribed, access to these systems through a personal digital assistant or a mobile phone, tracing of patients' medication profiles, assessment of the effects of accompanying diseases, reviewing potential drug-drug interactions, graduate and post-graduate education, presence of a pharmacy team, multidisciplinary approach, electronic systems, home visits or home monitoring systems (2-4).

Use of non-pharmacological treatment methods should be encouraged. A different dose and treatment calendar should be planned than those for younger age groups. Laboratory values and organ functions should be taken into consideration. Trainings should be provided for patients, their families and healthcare professionals. Appropriate follow-ups should be carried out. Since drug information is acquired after medical education through summaries of product characteristics, prescription details, self-learning, adopting senior habits, working with a clinical pharmacist and learning from the drug industry or drug representatives, it could be an important improvement to teach conservative way of prescribing during medical education. (3).

In conclusion the multidisciplinary nature of Gerontology and Geriatrics dealing with the problems of older persons in all aspects needs to become a reality in the 21st century. The elderly population needs to be productive and to have a high-quality life so as to enjoy a healthy aging. Their life expectancies and quality of life can only be improved if they have access to the health services and to social security, if the quality and quantity of the existing health services are increased and the hospital and first line treatment services are improved. Related professional groups such as physicians, pharmacists, dentists, nurses, etc. need to become more aware of these issues. The health personnel need to receive training with regard to their responsibilities towards the older persons. More effort is needed to decrease the use of drugs without control/prescription among older persons.

Mass media should be used better so as to create awareness among the population regarding the rational use of drugs. The drugs to be used by older persons should have special packaging and information which is easy to understand. The prescriptions need to be legible and clear. Moreover older patients should be provided with easy verbal explanations. They need to be encouraged and briefed to ask questions. On the part, the health personnel need to patiently and carefully inform older patients verbally and where and when necessary also in writing.

Suggestions for treatment of and study results on polypharmacy have started to be published just recently. It is strongly recommended that after graduation "continuous education programs" for medical doctors, pharmacists and nurses should include not only "appropriate prescription for the elderly" but also "avoidance of inappropriate prescription".

REFERENCES

1. Brazeau S. Polypharmacy and the elderly. The Canadian Journal of CME 2001. [Internet] Available from: http://www.stacommunications.com/journals/cme/images/cmepdf/august01/polypharmacyapvd.pdf. Accessed:12.11.2012.
2. Fulton MM, Allen ER. Polypharmacy in the elderly: a literature review. J Am Acad Nurse Pract 2005;17(4):123-32. (PMID:15819637).
3. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother 2007;5(4):345-51. (PMID:18179993).
4. Lees J, Chan A. Polypharmacy in elderly patients with cancer: clinical implications and management. Lancet Oncol 2011;12(13):1249-57. (PMID:21741307).
5. Cahir C, Fahey T, Teeling M, et al.. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. Br J Clin Pharmacol 2010;69(5):543-52. (PMID:20573091).
6. Terrie YC. Understanding and managing polypharmacy in the elderly. Pharmacy times 2004. [Internet] Available from: http://www.pharmacytimes.com/publications/issue/2004/2004-12/2004-12-9094. Accessed:12.11.2012.
7. Kaufman DW, Kelly JP, Rosenberg L, et al. Recent patterns of medication use in the ambulatory adult population of the United States: The Slone survey. JAMA 2002;287(3):337-44. (PMID:11790213).
8. Fialová D, Topinková E, Gambassi G, et al; AdHOC Project Research Group. Potentially inappropriate medication use among elderly home care patients in Europe. JAMA 2005;293(11):1348-58. (PMID:15769968).
9. Arslan S, Atalay A, Gökçe-Kutsal Y. Drug use in older people. J Am Geriatr Soc 2002;50(6):1163-4. (PMID:12110084).
10. Gokce Kutsal Y, Barak A, Atalay A, et al. Polypharmacy in the elderly: a multicenter study. J Am Med Dir Assoc 2009;10(7):486-90. (PMID:19716065).

11. Sahin G, Baydar T. Use of drugs among older persons. In: Troisi J, Gokce Kutsal Y (Eds). Aging in Turkey. International Institute on Ageing, Varitas press, Malta, 2006, pp 55-64.
12. Hajjar ER, Hanlon JT, Sloane RJ, et al. Unnecessary drug use in frail older people at hospital discharge. J Am Geriatr Soc 2005;53(9):1518-23. (PMID:16137281).
13. Stoehr GP, Ganguli M, Seaberg EC, et al. Over-the-counter medication use in an older rural community: the MoVIES Project. J Am Geriatr Soc 1997;45(2):158-65. (PMID:9033513).
14. Saad M, Harisingani R, Katinas L. Impact of geriatric consultation on the number of medications in hospitalized older patients. Consult Pharm 2012;27(1):42-8. (PMID:22231997).
15. Hines LE, Murphy JE. Potentially harmful drug-drug interactions in the elderly: A review. Am J Geriatr Pharmacother 2011;9(6):364-77. (PMID:22078863).
16. Prybys KM. Deadly drug interactions in emergency medicine. Emerg Med Clin North Am 2004;22(4):845-63. (PMID:15474773).
17. Shi S, Klotz U. Age-related changes in pharmacokinetics. Curr Drug Metab. 2011;12(7):601-10. (PMID:21495970)
18. Trifirò G, Spina E. Age-related changes in pharmacodynamics: focus on drugs acting on central nervous and cardiovascular systems. Curr Drug Metab 2011;12(7):611-20. (PMID:21495972).
19. Klotz U. Pharmacokinetics and drug metabolism in the elderly. Drug Metab Rev 2009;41(2):67-76. (PMID: 19514965).
20. Shepler SA, Grogan TA, Pater KS. Keep your older patients out of medication trouble. Nursing 2006;36(9):44-7. (PMID:16951619).
21. Harrington AR, Warholak TL, Hines LE, et al. Healthcare professional students' knowledge of drug-drug interactions. Am J Pharm Educ 2011;75(10):199. (PMID:22345718).
22. George CJ, Jacobs LG. Geriatrics medication management rounds: a novel approach to teaching rational prescribing with the use of the medication screening questionnaire. J Am Geriatr Soc 2011;59(1):138-42. (PMID:21198464).
23. Kutsal YG. Polypharmacy in elderly. Turk J Geriatr 2006; (9); Supplement: 37-44.
24. Veehof L, Stewart R, Haaijer-Ruskamp F, et al. The development of polypharmacy. A longitudinal study. Fam Pract 2000;17(3):261-7. (PMID:10846147).
25. Steinman MA, Landefeld CS, Rosenthal GE, et al. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006;54(10):1516-23. (PMID:17038068).
26. Cannon KT, Choi MM, Zuniga MA. Potentially inappropriate medication use in elderly patients receiving home health care: a retrospective data analysis. Am J Geriatr Pharmacother 2006;4(2):134-43. (PMID:16860260).
27. Bao Y, Shao H, Bishop TF, Schackman BR, Bruce ML. Inappropriate medication in a national sample of US elderly patients receiving home health care. J Gen Intern Med 2012;27(3):304-10. (PMID:21975822).
28. Buck MD, Atreja A, Brunker CP, et al. Potentially inappropriate medication prescribing in outpatient practices: prevalence and patient characteristics based on electronic health records. Am J Geriatr Pharmacother 2009;7(2):84-92. (PMID:19447361).
29. Ay P, Akici A, Harmanc H. Drug utilization and potentially inappropriate drug use in elderly residents of a community in Istanbul, Turkey. Int J Clin Pharmacol Ther 2005;43(4):195-202. (PMID:15966466).
30. Barry PJ, O'Keefe N, O'Connor KA, et al. Inappropriate prescribing in the elderly: a comparison of the Beers criteria and the improved prescribing in the elderly tool (IPET) in acutely ill elderly hospitalized patients. J Clin Pharm Ther 2006;31(6):617-26. (PMID:17176367).
31. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003;163(22):2716-24. (PMID:14662625).
32. van der Hooft CS, Jong GW, Dieleman JP, et al. Inappropriate drug prescribing in older adults: the updated 2002 Beers criteria–a population-based cohort study. Br J Clin Pharmacol 2005;60(2):137-44. (PMID:16042666).
33. Vishwas HN, Harugeri A, Parthasarathi G, Ramesh M. potentially inappropriate medication use in indian elderly: comparison of beers' criteria and screening tool of older persons' potentially inappropriate prescriptions. Geriatr Gerontol Int 2012;12(3):506-14. (PMID:22239067).
34. van Marum RJ. Discontinuing medication in elderly: A checklist may be useful. Ned Tijdschr Geneeskd 2011;155(36):A3802. (PMID:21914235).
35. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing 2008;37(6):673-9. (PMID:18829684).
36. 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).
37. Levy HB, Marcus EL, Christen C. Beyond the beers criteria: A comparative overview of explicit criteria. Ann Pharmacother 2010;44(12):1968-75. (PMID:21081709).
38. Beijnen JH, Schellens JH. Drug interactions in oncology. Lancet Oncol 2004;5(8):489-96. (PMID:15288238).
39. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriatr Pharmacother 2006;4(1):36-41. (PMID:16730619).
40. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of

prospective observational studies. Ann Pharmacother 2008;42(7):1017-25. (PMID:18594048).

41. Helldén A, Bergman U, von Euler M, et al. Adverse drug reactions and impaired renal function in elderly patients admitted to the emergency department: a retrospective study. Drugs Aging 2009;26(7):595-606. (PMID:19655826).
42. Larson EB, Kukull WA, Buchner D, Reifler BV. Adverse drug reactions associated with global cognitive impairment in elderly persons. Ann Intern Med 1987;107(2):169-73. (PMID:2886086).
43. Ruby CM, Hanlon JT, Fillenbaum GG, et al. Medication use and control of urination among community-dwelling older adults. J Aging Health 2005;17(5):661-74. (PMID:16177455).
44. Peron EP, Gray SL, Hanlon JT. Medication use and functional status decline in older adults: a narrative review. Am J Geriatr Pharmacother 2011;9(6):378-91. (PMID:22057096).
45. Wu JY, Leung WY, Chang S, et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial BMJ 2006;333(7567):522. (PMID:16916809).
46. Banerjee A, Mbamalu D, Ebrahimi S, et al. The prevalence of polypharmacy in elderly attenders to an emergency department a problem with a need for an effective solution. Int J Emerg Med 2011;4(1):22. (PMID:21635734).
47. Jano E, Aparasu RR. Healthcare outcomes associated with beers' criteria: a systematic review. Ann Pharmacother 2007;41(3):438-47. (PMID:17311835).
48. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. Am J Geriatr Pharmacother 2011;9(1):11-23. (PMID:21459305).
49. Gadsby R, Galloway M, Barker P, Sinclair A. Prescribed medicines for elderly frail people with diabetes resident in nursing homes-issues of polypharmacy and medication costs. Diabet Med 2012;29(1):136-9. (PMID:22004423).
50. Fialová D, Onder G. Medication errors in elderly people: contributing factors and future perspectives. Br J Clin Pharmacol 2009;67(6):641-5. (PMID:19594531).
51. Tam VC, Knowles SR, Cornish PL, et al. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. CMAJ 2005;173(5):510-5. (PMID:16129874).