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RESEARCH

DEPRESSION AND DEMENTIA IN PARKINSON'S DISEASE

ABSTRACT

Introduction: Depression and dementia have been recognized as a common problem in PD. However there are debatable results about their nature and frequency of occurrence. Their effects on the PD clinic remain controversial. The aim of our study was to assess the frequency, risk factors, and interrelations between depression and dementia in PD patients.

Materials and Method: We evaluated retrospectively 240 idiopathic PD patients who responded well to L-dopa treatment. Severity of disease was evaluated by using UPDRS, HY and WS. HAM-D, MMSE and a socio-demographic questionnaire were also performed on all patients.

Results: Our patients (105 females, 135 males) were between 30 and 88 years of age (68.56±10.3). Depression was revealed in 43.6%, and dementia in 33.3%. Patients with dementia were older and had higher depression frequency and WS and UPDRS scores. Depressive patients had higher HY and WS scores also. Positive correlations were detected between disease duration and WS, UPDRS, HY. HAM-D had positive correlations with HY and UPDRS as well.

Conclusion: Depression and dementia were correlated with the severity of PD disability. Therefore, regular mood and cognitive state screening and appropriate treatment should be considered, especially in older PD patients with higher disease severity.

Key Words: Parkinson Disease; Psychology; Depressive Disorder; Dementia.

ARAŞTIRMA

PARKİNSON HASTALIĞINDA DEPRESYON VE DEMANS

ÖZ

Giriş: Depresyon ve demans Parkinson Hastalığı (PH) için genel bir sorun olarak bilinir. Ancak doğaları ve oluşma sıklıkları net olmayıp PH kliniğine etkileri tartışmalıdır. Çalışmanın amacı PH olanlarda depresyon ve demansın sıklığı, risk faktörleri ve etkileşimlerini değerlendirmektir.

Gereç ve Yöntem: İdiopatik PH tanı kriterlerini karşılayan ve L-dopa tedavisine iyi yanıt veren 240 hasta retrospektif değerlendirildi. Hastalık şiddeti UPDRS, Hoehn Yahr (HY) ve Webster skalaları (WS) kullanılarak yapıldı. Ayrıca Hamilton Depresyon skalası (HAM-D), Minimental test ve sosyo-demografik sorgulama her hastaya uygulandı.

Bulgular: Hastaların (105 kadın, 135 erkek) yaşları 30-88 arası (ortalama 68.56±10.3) idi. Depresyon %43.6 ve demans %33.3 sıklıkla izlendi. Kognitif yetmezliği olan hastalar daha yaşlı ve daha yüksek depresyon sıklığı ve WS, UPDRS skorlarına sahipti. Depresif hastalar da depresif olamayan hastalara kıyasla daha yüksek HY ve WS skorlarına sahiptiler. Positive korelasyonlar hastalık süresi ve WS, UPDRS, HY arasında saptandı. HAM-D skorları da HY ve UPDRS ile pozitif korelasyon göstermekteydi.

Sonuç: Depresyon ve demans PH yeti yitimi şiddeti ile koreledir. Bu nedenle düzenli duygu durum ve kognitif seviyenin irdelenmesi özellikle yaşlı ve ileri PH olan bireylerde uygun tedavinin planlanması yönüyle düşünülmelidir.

Anahtar Sözcükler: Parkinson Hastalığı; Psikoloji; Depresif Bozukluk; Demans.

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INTRODUCTION

Although cognitive dysfunction and depressive symptoms are not uncommon in Parkinson's disease (PD), frequency and the effects on disease progression are still controversial. In some studies, depression has been correlated with early disease onset, disease duration, cognitive impairment, motor disability and daily life activities (1,2), although many authors believe that these results are debatable (3,4). It is wellknown that some core features of depression, such as psychomotor retardation, anhedonia and sleep disturbance, may overlap with symptoms intrinsic to PD (5). Methodological issues of patient selection, imprecise definitions of depression, variable clinical definition of PD and study designs (cross-sectional, retrospective, and population-based) seem to be responsible for these controversial results. The aim of our study was to assess the frequency, risk factors, and interrelations between depression and dementia in the PD clinic.

MATERIALS AND METHOD

We evaluated retrospectively 240 idiopathic PD patients who fulfilled the diagnostic criteria of idiopathic Parkinson's disease (6) and who were followed up in our outpatient clinic between 2000 and 2008. Each patient was given a complete physical and neurological examination. The clinical diagnosis of PD was based on the identification of the cardinal motor signs of bradykinesia, rigidity, tremor, postural instability and asymmetric onset. Neuroimaging (cranial CT or MRI) was also performed to exclude secondary Parkinsonian syndromes (brain injury, tumour, infection, stroke, inflammatory or metabolic diseases) and neurodegenerative Parkinsonian syndromes like multisystem atrophy. Patients with a diagnosis of Parkinson plus syndromes, drug induced Parkinsonism, vascular Parkinsonism, Lewy body dementia, previous history of dementia and major depression were all excluded. Routine blood tests, B_{12}, folate, and thyroid functional tests were also performed to exclude causes of secondary dementia. Severity of PD was evaluated using the Unified Scale for Evaluation of Parkinsonism (UPDRS), Hoehn Yahr and Webster scale (WS). Depression and dementia were diagnosed based on a structured interview using DSM-IV diagnostic criteria. All individuals underwent a mental evaluation using the Mini Mental State Examination (MMSE). Depressive symptoms were assessed through the HAM-D. Moreover a socio-demographic questionnaire including age, sex, age at PD onset, disease duration, family history of PD, hemisphere dominancy, side of first symptom and therapy administered was also performed.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 14.0 was used for statistical analysis and statistical significance was defined as $p< 0.05$. Results were given as mean±standard deviation. Comparison of numeric values of all variables was performed using Mann Whitney U test or Student's t test. Chi-square tests were used for analyzing categorical variables. Kolmogorov Smirnov test was used to test the normal distribution. We used Spearman's test and Pearson's Correlation analysis for correlation analysis.

RESULTS

Our patients (105 female, 135 male) were between 30 and 88 years of age (mean 68.56±10.3). Depression and dementia were revealed as 43.6% (n=105) and 33.3% (n=80) respectively. Patients with cognitive impairment were older (71.8±8.26; 67.14±10.8, $p<0.05$) and had higher WS (14.35±6.78; 9.3±6.8, $p<0.05$) and UPDRS scores (39.2±19.1; 31±22.8, $p<0.05$) (Table 1). Depression was more frequently observed in demented patients (61.7%; 34.5%, $p<0.05$). Additionally depressed patients had more than double the frequency of dementia (47.6%; 22.9%, $p<0.05$) of patients without depression. HY scores were higher in patients with depression (2.6±0.9; 2±0.9, $p<0.05$) (Table 2). In our study neither depression nor dementia was associated with age at PD onset, disease duration, family history of PD, hemisphere dominancy or side of first symptom. Patients with a longer disease duration had higher WS ($r=0.223$, $p=0.006$), UPDRS ($r=0.278$, $p=0.002$) and HY ($r=0.198$, $p=0.035$) scores. The other positive correlations were as follows: HY scores and HAM-D ($r=0.339$, $p=0.046$); HAM-D and UPDRS ($r=0.331$, $p=0.049$). There were no statistically significant correlations between MMSE and other scale scores showing disease severity.

DISCUSSION

In this study PD patients with dementia or depression were found at a rate of 43.6% and 33.3% respectively. These results are similar to those of other studies in the literature (1-3, 7). The incidence of dementia in PD is increased by up to six times (8). In cross sectional population-based studies, dementia prevalence is reported to vary between 28 and 41% (7-9).

Table 1— Comparisons of PD Patients with and without Dementia

Parameter	Dementia (n=80)	No Dementia (n=160)	p
Age	71.8±8.26	67.14±10.8	<0.05
Gender (%females)	37	45	>0.05
Age at PD onset	64.9±9.2	62.1± 11.4	>0.05
Family history of PD (%)	38	30	>0.05
Diseae duration (years)	6.5 ±6	5.1 ±4.6	>0.05
Depression (%)	61.7	34.5	<0.05
Lateralization of first symptoms (%right side)	48	54	>0.05
Right-handed (%)	96	93.5	>0.05
Webster scale	14.35 ±6.78	9.3 ±6.8	<0.05
HY	2.5± 0.8	2.2 ±1.1	>0.05
UPDRS	39.2±19.1	31±22.8	<0.05

Values are mean±standard deviation.

Table 2— Comparisons of PD Patients with and without Depression

Parameter	Depression (n=105)	No Depression (n=135)	p
Age	68.44±10.5	68.8±10	>0.05
Gender (%females)	45.7	40	>0.05
Age at PD onset	62.8±10.9	63.1±10.8	>0.05
Family history of PD (%)	28.5	29.3	>0.05
Disease duration (years)	5.7±4.6	5.4±5.6	>0.05
Dementia (%)	47.6	22.9	<0.05
Lateralization of first symptoms (%right side)	51.2	53.4	>0.05
Right-handed (%)	95	95.2	>0.05
Webster scale scores	12.4±7.1	10±6.6	>0.05
Hoehn Yahr scores	2.6±0.9	2±0.9	<0.05
UPDRS	36.3±21.9	30.8±21.7	>0.05

Values are mean±standard deviation.

It is still controversial whether depression and cognitive impairment in PD are related to intrinsic neurobiological factors or to factors related to environmental, pschycological or disability. In several such studies an association with age is evident. In PD patients older than 80 the prevalence of dementia was 69%. Likewise prevalence was 37% versus 9% respectively in patients whose disease had begun after or before the age of 70 (7). Although there are considerable variations, and some patients may develop dementia earlier, the mean time from onset of PD to dementia is approximately 10 years (10). In the literature several baseline characteristics are reported to be associated with a high risk for dementia (5). These are old age (10-13), akinetic-rigid form (10,13), baseline motor disability, severity of motor symptoms (10,14), and in particular postural and gait disturbances, mild cognitive impairment, baseline cognitive scores (10,12,13), and visual hallucinations (10,14). Dementia is mainly characterized by impairment in attention, memory, executive and visuo-spatial functions, and behavioural symptoms such as affective changes, hallucinations, and apathy (8). Dementia was also more frequent in our older patients; however, disease duration and age at PD onset had no effect on cognitive impairment. Unfortunately we cannot comment on the clinical features of PD dementia, which were not studied in this study. Other disability geriatric scales like Geriatric Depression Scale and Instrumental Activities of Daily Living were not performed either. The advanced age, higher HY and, UPDRS scores and higher frequency of depression, were observed in our patients with dementia, but

there were no relationships between the other features including gender, age at onset, disease duration, family history of PD, hemisphere dominancy and side of the first symptom. As in the literature, depression was also observed more frequently in PD patients with cognitive impairment.

No evident associations between depression and PD disability or the severity of functional impairment are shown in the literature (15,16). On the other hand it has been shown in some studies that depression is significantly related to both illness severity and functional impairment. This is similar to our results (17-19). The presence of motor symptoms that do not respond to levodopa is also a risk factor for the appearance of major depression (15). Although depression can cause significant disability at all stages of illness, clinicians may fail to identify its presence. In PD, neurodegeneration occurs in the substantia nigra and dopaminergic neurons of the pars compacta and ventral tegmental region. In this case, the striatum, prefrontal cortex and limbic region that have projections from these anatomical structures show dopamine insufficiency, and the involvement of these connections may have an effect on depression. It has been shown that there is an association between dopaminergic insufficiency and clinical severity in PD patients (20-22). In our study there was also a correlation between depression and severity of PD disability. HAM-D scores were positively correlated with HY and UPDRS scores.

In previous studies younger patients with PD experienced twice the frequency of depression of older patients (3, 18). This result may be related to the small study groups, which included 31-34 PD patients. In a larger study, major depression was also found in 36% of 169 patients with early onset PD and in 16% of patients with late onset PD. However this significant difference disappeared when the two groups were matched for disease duration (19). As in the literature, we found no relation between depression and disease onset age.

Lateralized motor disturbances and handedness have been proven to be related to depression. It has been shown that depression in the early stages of the disease may be related to left hemisphere dysfunction, while later in the disease, depression and impairment in the activities of daily living are interrelated (17).

Likewise relationship between side of disease onset and dementia in PD has been studied before. Although there are conflicting results (23), in a study which included 108 PD patients, right-side symptoms were found to be good predictors of cognitive function (24). Motor symptoms and side of disease onset were shown to have effects on disease course and the extent of cognitive deterioration. Patients who develop tremor on the right side exhibit relative sparing of cognitive function (25). In contrast with the previous data, in our study side of first symptoms was related neither to depression nor to dementia. Methodological differences between these studies may account for this discrepancy. Our study, which included a larger group of PD patients, showed that cognitive impairment is more common in depressed patients and those of advanced age.

In conclusion, the relationship between depression and cognitive impairment is complex. Our data suggest that PD with cognitive impairment should be evaluated alongside depression inventories in order to detect and treat coexistent depression especially in older patients with higher disease severity. Because dementia and depression are common factors impairing the quality of life for PD patients, regular depression and cognitive impairment screening and especially adequate treatment of such conditions are important in PD. Further studies with larger groups may help us to have a broader view of dementia and depression in the PD clinic.

Conflict of Interest

There is no conflict of interest.

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