Depression and care-dependency in Parkinson's disease: Results from a nationwide study of 1449 outpatients

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Abstract

Parkinson's disease (PD) is frequently compounded by neuropsychiatric complications, increasing disability. The combined effect of motor and mental status on care-dependency in PD outpatients is not well characterized. We conducted a cross-sectional study of 1449 PD outpatients. The assessment comprised the Montgomery-Asberg Depression Rating Scale (MADRS) and the diagnostic criteria for dementia. PD severity and treatment complications were rated using Hoehn and Yahr staging and the Unified Parkinson's Disease Rating Scale (UPDRS) IV. The acknowledged level of care-dependency was documented. Care-dependency was present in 18.3% of all patients. A total of 13.9% had dementia, 18.8% had depression, and 14.3% had both. Regression analyses revealed increasing effects of age, PD duration, and PD severity on care-dependency in all three mental-disorder subgroups with the strongest effects in patients with depression only. Depressed patients with antidepressive treatment still had significantly higher PD severity, higher MADRS and UPDRS-IV scores but were not more likely to be care-dependent than non-depressed patients. Older age, longer duration and increased severity of PD contribute to care-dependency in patients with untreated depression. Treatment of depression is associated with lower rates of care-dependency.

Keywords: Depression, Parkinson's disease, Dementia, Care

1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder among the elderly, characterized by progressing motor impairment leading to increasing physical disability [1]. It can also be accompanied by neuropsychiatric complications such as dementia or depression, aggravating the course of the disease in 25-50% of all patients [2, 3]. Both motor and neuropsychiatric aspects increase risk of care-dependency. However, while the effect of

neuropsychiatric symptoms on care-dependency has been evaluated for patients with dementia without PD [4], the relationships among motor features, neuropsychiatric complications, and care-dependency in outpatients with PD have been neglected. Recent socioeconomic studies on PD patients have identified disease severity, dementia, and depression as substantial cost drivers in the course of the disease but have not investigated the direct links between these factors and care-dependency [5,6].

Recently, we published results from a large representative sample of 1449 PD outpatients (German Study on the Epidemiology of Parkinson's Disease with Dementia, GEPAD), providing an overview of the associations between neuropsychiatric symptoms in PD and care-dependency [7]. In the light of its amenability to various intervention strategies [8], we focus on the role of depression and its medicamentous treatment in the occurrence of care-dependency in PD outpatients with and without dementia in this paper.

2. Methods

2.1. Study design

The study design and materials of GEPAD have been described previously in greater detail [9]. In summary, GEPAD was a cross-sectional study involving 1449 outpatients with PD, randomly selected and clinically assessed by a nationwide representative sample of 315 office-based neurologists on a single study day. The assessment comprised standardized instruments including the Montgomery-Asberg Depression Rating Scale (MADRS) and the diagnostic DSM-IV criteria for dementia, obtained in a structured clinical interview [10,11]. Based on the validation studies by Leentjens et al. [12], our study criteria for depression were either a MADRS total score ≥ 14 and/or current treatment with antidepressants. In this paper, we distinguish between patients with depression (study criteria for depression fulfilled, but no dementia present), dementia (study criteria for dementia met but not for depression), or both (study criteria for depression as well as DSM-IV criteria met). The physicians recorded the current treatment status. The severity of PD was rated according to the Hoehn and Yahr staging (HY) scale. Complications in PD treatment were documented using the Unified Parkinson's Disease Rating scale (UPDRS) IV. For each patient, the physician noted the officially acknowledged level of care-dependency. In Germany, a patient's level of care-dependency is determined by an expert member of the Medical Service of the Central Association of Health Insurance Funds. It is defined using one of three severity grades: one = substantially care-dependent (average daily need for assistance at least 90 min, of which at least 45 min account for personal care such as bathing, feeding, assisting with toileting); two = severely care-dependent (average daily need for assistance at least 180 min, of which at least 120 min account for personal care); and three = most severely care-dependent (average daily need for assistance at least 300 min, of which at least 240 min account for personal care, and nocturnal assistance also becomes necessary). In this paper, care-dependency is defined as the presence of at least level one. In the absence of an officially acknowledged level of care-dependency, the physicians were also asked to state whether the patient nonetheless met criteria for care-dependency (but application pending or not made). In this paper, if not otherwise indicated, analyses on care-dependency only include patients with an officially acknowledged level.

2.2. Statistics

All scores (summary-scores and subscores) were calculated according to the corresponding scoring algorithms. Associations with 95% confidence intervals (CIs) of treatment status and PD severity and care-dependency were analyzed by regression models among patients with and without a current depression symptomatology. Logistic regression models were applied for categorical data and linear regression models for continuously distributed data. The predictive value of age, duration of PD and PD severity for care-dependency was investigated by considering the area under the receiver operating characteristics curve (AUC). Statistical inference was based on a significance level of 5%. For standard errors, CI, and /P/ values, the Huber-White sandwich estimator was implemented to take the clustered sampling design of the study into account [13]. For the detection of differences in metric and nonparametric data, we used the t-test and the Mann-Whitney test, respectively.

2.3. Ethics

The study was approved by the local Ethics Committee (August 11, 2005, No. EK140082005). Written informed consent was obtained from all participating patients or their caregivers.

3. Results

3.1. Study population

The majority of patients was male (60.5%) and had a mean age of 70.7 ± 8.4 years, with a mean PD duration of 5.5 ± 5.1 years. According to the HY stages, 44.2% of all patients had mild PD (HY I + II), 38.7% had moderate PD (HY III), and 17.1% suffered from severe PD (HY IV + V). Regarding mental status, 13.9% had dementia, 18.8% met study criteria for depression (of which 7.3% scored MADRS ≤ 13 but were currently treated with antidepressants), and 14.3% suffered concurrently from both disorders (i. e. dementia total: 28.2%, depression total: 33.1%). At the time of study conduction, 24.5% of all demented patients received antidementia treatment (acetylcholine esterase inhibitors, ChE-I).

A level of care-dependency was acknowledged for 18.3% of all patients (n = 266 of 1449), of which the majority either had level one (51.9%, n= 138) or level two (43.2%, n= 115), respectively. Thirteen patients (4.9%) had level three. One-hundred twenty-one (8.5%) patients had no officially acknowledged level of care-dependency but met criteria for care-dependency according to their attending clinicians. For 22 patients, information on care-dependency status was not available to the physician; however, they did not differ from care-independent patients (i.e., no care-dependency level acknowledged and criteria not met) regarding age (P= 0.951), HY-staging (P= 0.311), or frequency of dementia (P =0.109) or depression (P = 0.250).

Care-dependency occurred more frequently in patients aged ≥ 76 years (43.3%) than in patients at the age of 66-75 (23.7%) or ≤ 65 (13.9%), respectively. The mean ($\pm$ SD) MADRS score increased significantly with advancing levels of care-dependency, ranging from 7.7 ± 6.8 ("none") to 13.1 ± 8.3 ("one"), 14.3 ± 9.6 ("two") and 18.5 ± 11.3 ("three", total group differences P < 0.001).

3.2. Predictors for care-dependency

We used a multiple stepwise logistic regression model to calculate the effect of age, PD duration, and PD severity on caredependency. We first entered age, added PD duration (step two), and finally entered PD severity (step three). Results are displayed in Fig. 1.

In all three mental-disorder subgroups, the stepwise entry of the predictors substantially increased the AUCs. The largest AUCs were seen in patients with depression (AUCs: 0.681, 0.739, and 0.818), and the smaller in patients with dementia (AUCs: 0.603, 0.687, and 0.797) or both disorders combined (AUCs: 0.616, 0.642, and 0.782).

3.3. Depression treatment and care-dependency

Table 1 shows the associations among care-dependency, PD severity, PD treatment complications (UPDRS-IV), and depression, stratified by depression treatment status. Regardless of whether they were treated for depression or not, patients with a MADRS score ≥ 14 had more severe PD, experienced more treatment complications, and were more frequently care-dependent than patients with a MADRS score ≤ 13 . Among patients below this cut-off for depression, patients who underwent antidepressive treatment were not more care-dependent ($P = 0.794$) than the non-depressed PD group, although the former had higher HY stages ($P < 0.05$), more treatment complications ($P < 0.05$), and higher MADRS scores ($P < 0.01$). In terms of ORs, these patients had an insignificant OR for care-dependency (OR = 1.1, 95% CI: 0.66-1.73) compared to non-depressed patients. This lack of significance still held true after adjustment for dementia (18.8% vs. 23.9%, OR = 1.1, 95% CI: 0.68-1.81). These effects also applied to patients without an officially acknowledged level of care-dependency but who met the criteria for care-dependency according to the clinician (OR = 1.0, 95% CI: 0.51-2.08 and OR = 1.1, 95% CI: 0.52-2.14 after adjustment for dementia).

4. Discussion

In this paper, we analyzed the associations among PD, neuropsychiatric complications, and the degree of care-dependency, based on a large and representative sample of outpatients in Germany. According to the study criteria for dementia and depression, a large proportion of patients suffered from at least one of the disorders (47%). About one in three patients (33.1%) met the study criteria for depression.

Two important findings emerged from this work. First, in all three mental-disorder subgroups (depression, dementia, or both) age, duration of PD, and PD severity were clearly associated with care-dependency. PD severity contributed most to care-dependency, considerably increasing the AUCs at final entry in each subgroup. In patients with depression (but no dementia), the effects turned out to be strongest, revealing the largest AUCs when stepwise entering the variables considered. Thus, in these patients, care-dependency is driven more by these variables – especially age – than in patients with dementia (with and without concomitant depression).

Second, successfully treated (with antidepressants) subsyndromal patients (i.e., scoring below the MADRS cut-off for major depression while taking antidepressants) still experienced more severe motor impairments, more PD treatment complications, and higher MADRS scores than non-depressed patients. However, they were not more frequently care-dependent. This outcome was largely independent from the concurrent presence of dementia. In patients with dementia, the rates of care-dependency were increased overall, but the proportions and level of significance remained the same.

Our data underscore that dementia and depression are important contributors to the overall disease burden in PD, as previously reported [5,6,14]. In addition, the GEPAD results highlight the substantial effect of depression on care-dependency in PD, suggesting that drug therapy for depression in PD with and without dementia is always beneficial because it reduces the personal burden of the patients.

Our findings, however, should be interpreted cautiously because of a number of methodological limitations. First, it is important to note that the acknowledgment of care-dependency in Germany is mainly based on a person's incapacity to perform basic physical actions. Incapacities that result from neuropsychiatric complications and that usually increase the need for time-consuming assistance in everyday life are often taken inadequately into account. They lead, however, to a substantial degree of disability, especially for patients with mild to moderate dementia. Thus, the officially acknowledged care-dependency in our sample probably underestimates the real dependency on assistance, which relatives usually provide. Second, our results might be biased by the use of a screening tool for depression only instead of a comprehensive interview; however, because of feasibility concerns, we wanted to keep the assessment simple for the participating physicians. We are therefore unable to provide more sophisticated data on the type of depression or on previous episodes of depressive disorders. By the same token, we have not implemented a diagnostic instrument for the assessment of anxiety disorders, which are a frequent accompaniment of depression, and can equally contribute to care-dependency. Third, it should be noted that our analyses of associations between PD severity and CDP are limited by the use of the coarse-grained HY-staging instead of more sophisticated analyses based upon the UPDRS motor subscale. However, the latter one could not be implemented to the study protocol for logistical reasons, as it would have considerably prolonged the duration of assessment. Thus, to keep the study feasible for the participating office-based physicians (and their patients) during their daily routine care, we decided to omit the UPDRS III. By the same token, we lack further details regarding the patients' dementia status (e. g. duration, age at onset), as well as more detailed data about further neuropsychiatric conditions that might also contribute to care-dependency, such as anxiety disorders or psychotic syndromes. Similarly, the comprehensive documentation of these conditions would have required a considerably extended assessment. Finally, it should be considered that the prescription of antidepressants is not always a valid indicator for depression because these medications can also be prescribed for other medical conditions such as sleep disorders. However, it is noteworthy that in the GEPAD sample, the corresponding subgroup of patients featured characteristics that are rather typical for sub-syndromal patients but not for non-depressed patients (i.e., still significantly higher MADRS scores, more treatment complications and motor impairments) [15]. In any case, more detailed studies are certainly needed to develop a deeper understanding of PD, neuropsychiatric symptoms, care-dependency, and mediating factors.

Fig. 1 Impact of age, PD duration and PD severity on care-dependency in patients with depression and/or dementia, estimated by a stepwise regression analysis by first entering age (step 1), then adding duration of PD (step 2) and PD severity (step 3).

Table 1

PD severity and care-dependency among treated and untreated patients with and without current depression symptomatology (MADRS ≥ 14).

	MADRS ≥ 14			MADRS ≤ 13		
	Untreated	Treated	P-value	Untreated	Treated	P-value
PD severity, %						
Mild (HY I + II)	23.0	32.7	<0.05	52.9	42.9	<0.05
Moderate (HY III)	46.0	43.8	n.s.	35.4	43.5	<0.05
Severe (HY IV + V)	31.0	23.5	<0.05	11.7	13.7	n.s.
MADRS score, mean $\pm$ sd	17.3 $\pm$ 4.0	19.7 $\pm$ 4.6	<0.01	4.9 $\pm$ 3.6	6.9 $\pm$ 3.6	<0.01
UPDRS-IV score, mean $\pm$ sd	4.4 $\pm$ 3.6	3.6 $\pm$ 3.0	<0.05	2.0 $\pm$ 2.6	2.6 $\pm$ 2.8	<0.05
Care-Dependency, %						
Mild (Level 1)	15.7	15.8	n.s.	6.5	10.8	n.s.
Moderate (Level 2)	14.1	12.1	n.s.	6.1	3.0	n.s.
Severe (Level 3)	1.6	1.8	n.s.	0.4	0.0	—
Any	31.4	29.7	n.s.	13.0	13.8	n.s.

HY: Hoehn and Yahr staging; treated/untreated = antidepressants; n.s. = not significant.

Conflicts of interest

Oliver Riedel: None.

Richard Dodel: Professor Richard Dodel has received honoraria, travel grants and research grants from several pharmaceutical companies.

G. Deuschl: Stock Ownership in medically-related fields: none, Consultancies: none, Partnerships: none, Honoraria: Medtronic, Lundbeck, Teva, Grants: German Research Council, German Ministry of Education and Research, Medtronic. Employment: Government employee.

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I. Heuser: None.

W. Oertel: Professor Oertel has received unrestricted educational grants for clinical research projects by Novartis.

H. Reichmann: Professor Reichmann was acting on Advisory Boards and gave lectures and received research grants from Abbott, Bayer Health Care, Boehringer/Ingelheim, Cephalon, Desitin, GSK, Merck-Serono, Novartis, Orion, Pfizer, TEVA/Lundbeck, UCB Pharma, and Valeant. Peter Riederer: None.

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