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Research Report

Recognition and Treatment of Depressive Symptoms in Parkinson's Disease: The NPF Dataset

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Abstract. Depression is a major determinant of Health Related Quality of Life in PD, but there is limited data on physician recognition of depression and treatment efficacy. We used data obtained from the QII dataset of the National Parkinson's Foundation database to determine whether there was an association between depressive symptoms and utilization of antidepressants and/or mental health services (MHS) in a large cohort of PD patients. We found that prevalence of depressive symptoms remained high in the PD population despite improved physician recognition and treatment initiation.

Keywords: Parkinson's disease, depression, NPF

BACKGROUND

Parkinson's disease (PD) is a chronic neurodegenerative disease associated with a spectrum of motor and non-motor manifestations. Depression is the most common non-motor disability associated with PD, and a major determinant of Health Related Quality of Life (HRQL) [1–3]. Rates of depression in PD are frequently higher than in other similarly disabled populations, with the prevalence of depression reported anywhere from 20% to 90% of patients [4, 5]. The etiology of depression in PD is multifactorial, and not a purely reactive process to disability [6]. Despite the high prevalence, physician recognition of depression in the PD population is as low as 10–20% [7, 8]. Even in those patients where depression is recognized, the optimal approach to treatment remains uncertain and the relative efficacy of various approaches to treatment have not been established [9]. Currently, pharmacotherapy constitutes the first line treatment for depression in PD, although a recent meta-analysis demonstrated that only nine randomized placebo controlled trials employing standardized outcome measures of treatment efficacy could be identified [10]. While there is recently published class I evidence [11] that SSRIs and SNRIs (serotonin-norepinephrine reuptake inhibitors) are effective in treating depression in this population, large-scale, longitudinal data is lacking. Furthermore, concerns about safety and polypharmacy in this population have led to some emerging interest in non-pharmacological alternatives to the treatment of depression. Dobkin et al. [12] reported the significant positive effects of 10 weekly sessions of Cognitive Behavioral Therapy on depression in PD, and showed effect sizes that were larger than many of the antidepressant trials. There is a need for more data to verify these results, evaluate them longitudinally, and compare them to pharmacologic interventions and other mental health services.

The National Parkinson's Foundation (NPF) has launched a quality improvement initiative project (QII)

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to establish and validate the care practices that lead to the best clinical outcomes across 20 NPF Centers of Excellence [13, 14]. All PD patients followed at participating centers are eligible to participate. The NPF-QII database includes longitudinal data on demographics, disease severity, comorbidities, quality of life, pharmacological treatment, and allied health care and mental health care utilization, in a large cohort of patients followed in a naturalistic setting. This study aims to explore the utilization of antidepressants and mental health services (MHS) in the NPF-QII cohort, to determine whether there is an association between depressive symptoms and utilization of treatments, and to assess the impact and comparative efficacy of different treatment approaches longitudinally. In this study, MHS referred to counseling by a social worker or mental health professional. We anticipated that physicians would be more likely to refer to mental health services or initiate antidepressants in patients with more significant depressive symptoms, and that treatment would result in measurable improvement in depressive symptoms.

METHODS

Data was obtained from the NPF-QII database for which a detailed description of the design has been previously published [13, 14]. The emotional wellbeing domain of the Parkinson's Disease Questionnaire (PDQ-39e) was used as a proxy measure of depressive symptoms. PDQ-39e has been shown to correlate with other validated markers of depression such as BDI [15, 16]. It includes 6 questions (17–22) scored from 0 (least severe) to 24 (most severe). An emotional subscore $\geq$10 was used as a cut-off for depressive symptoms. This cutoff was chosen because a separate analysis of a subset of 412 patients from the NPF-QII database demonstrated a strong correlation between PDQe score $\geq$10 and BDI score in a range consistent with depression ($r = 0.66$, unpublished data courtesy of Michael Okun et al.). Baseline demographics and clinical characteristics between those utilizing antidepressants and/or MHS and "non-users" were compared. The association between utilization and PDQ-39e was analyzed with a case-mix adjustment based on propensity scores (probabilities of utilizing service) predicted by baseline covariates. The propensity score was used as an independent variable to adjust for imbalance between the utilization group and non-use group. Patient ID was used as a random effect in the model. The model indicates that the utilization of antidepressants and/or MHS has a positive correlation with the PDQ-39e scores ($p < 0.0001$).

RESULTS

7031 patients were included in the cohort at the time of data analysis. Baseline characteristics are provided in Table 1. 23% had a PDQe subscore $\geq$10 ($n = 1616$), and among these patients 33% ($n = 539$) were utilizing antidepressants, 6% ($n = 104$) were utilizing MHS, 14% ($n = 224$) were using both, and 47% ($n = 749$) were using neither. PDQe subscore was significantly correlated with use of antidepressants and mental health services at baseline (p-value <0.0001). The odds of utilization of antidepressants and/or MHS at entry into the study among those with PDQe score $\geq$10 were 3 times (OR 2.98) that of those with score <10. The association between level of PDQe score and use of antidepressants or MHS remained significant after the adjustment of the propensity scores (p-value <0.0001), which were estimated based on baseline covariate characteristics.

The subsequent analysis focused on those patients who started new treatment with antidepressants and/or MHS during the study observation time period (from baseline study entry until visit 2 at least 12 months later). Of the 4653 patients who were not receiving any depression-focused care at study initiation ("non-users"), 2.4% were prescribed an antidepressant ($n = 111$), 1.0% were referred to MHS ($n = 48$), and 0.3% were prescribed both ($n = 14$). Among those with a PDQe score $\geq$10, 9.3% ($n = 70$) started a new treatment (medication, MHS, or both), compared to 2.6% ($n = 103$) of those with a score <10. As expected, those patients with higher PDQ-39e scores were more likely to receive new services. This is summarized in Fig. 1.

In terms of the longitudinal assessment of treatment efficacy, the analysis was restricted to patients whose follow-up data was available ($n = 2709$). Among these patients only 3.9% ($n = 105$) were prescribed a new antidepressants or MHS. Ninety two percent of those with a new service or drug had a propensity score in the top quartile. Overall, there was no significant difference between those who received a new service or drug and those who did not, in terms of the change of PDQe score ($p = 0.387$) after adjustment of propensity scores. Among those with a propensity score in the top quartile, the difference in the proportion of patients who improved from PDQe $\geq$10 to PDQe <10 was not significant ($p = 0.406$), with 15.6% of new users improved compared to 12.0% of continued non-users.

Table 1

Baseline characteristics comparison between those who used and who did not use antidepressants and/or mental health care services in QII cohort. All factors are highly associated with the utilization of antidepressants and/or mental health service with p-values < 0.05. From the table those who did not use service (before visit) tend to be older, more likely living at home, more likely having spouse/partner as regular care partner, having shorter disease duration, less likely having motor fluctuations, more likely having HY stage 1–2, smaller number of comorbidities, shorter TUG, better in cognition, better in PDQ39 and PDQ39e, and lower in MCSI.

		Overall ($N = 7031$)	Utilization of anti-depressants and/or mental health care services			
			Antidepressants ($N = 1695$, 24.1%)	Mental health service ($N = 245$, 3.5%)	Both ($N = 438$, 6.2%)	Neither ($N = 4653$, 66.2%)
Demographic Variables						
Age of onset		58.2 ± 11.4	57.7 ± 11.6	55.0 ± 11.5	56.1 ± 11.4	58.7 ± 11.3
Gender	Male	4423	971 (57.3%)	139 (56.7%)	244 (55.7%)	3069 (66.0%)
	Female	2608	724 (42.7%)	106 (43.3%)	194 (44.3%)	1584 (34.0%)
Social Variables						
Living Situation	At Home	6759	1607 (94.8%)	235 (95.9%)	398 (90.9%)	4519 (97.1%)
	Skilled Care	213	71 (4.2%)	10 (4.1%)	30 (6.8%)	102 (2.2%)
	Other	59	17 (1.0%)		10 (2.3%)	32 (0.7%)
Regular Care Partner	No	1030	219 (12.9%)	48 (19.6%)	70 (16.0%)	693 (14.9%)
	Spouse/Partner	5348	1270 (74.9%)	167 (68.2%)	310 (70.8%)	3601 (77.4%)
	Other Relative	383	120 (7.1%)	17 (6.9%)	26 (5.9%)	220 (4.7%)
	Paid Caregiver	220	72 (4.2%)	10 (4.1%)	24 (5.5%)	114 (2.5%)
	Other	50	14 (0.8%)	3 (1.2%)	8 (1.8%)	25 (0.5%)
Diagnosis Variables						
Disease Duration		8.9 ± 6.3	10.0 ± 6.5	9.6 ± 5.9	9.2 ± 5.9	8.5 ± 6.3
Motor Fluctuations	No	3648	761 (44.9%)	106 (43.3%)	201 (45.9%)	2580 (55.4%)
	Yes	3383	934 (55.1%)	139 (56.7%)	237 (54.1%)	2073 (44.6%)
Hoehn and Yahr Stage	1	746	105 (6.2%)	13 (5.3%)	43 (9.8%)	585 (12.6%)
	2	3909	834 (49.2%)	150 (61.2%)	213 (48.6%)	2712 (58.3%)
	3	1831	560 (33.0%)	63 (25.7%)	128 (29.2%)	1080 (23.2%)
	4	545	196 (11.6%)	19 (7.8%)	54 (12.3%)	276 (5.9%)
Clinical Variables						
Number of comorbidities		1.8 ± 1.4	2.0 ± 1.4	1.9 ± 1.5	2.1 ± 1.4	1.7 ± 1.3
Standardized TUG		−0.1 ± 1.0	0.1 ± 1.0	0.0 ± 1.0	0.0 ± 1.0	−0.1 ± 0.9
Immediate Word Recall		4.3 ± 1.0	4.2 ± 1.0	4.3 ± 1.0	4.3 ± 1.0	4.4 ± 0.9
Delayed Word Recall		3.0 ± 1.4	2.9 ± 1.4	3.0 ± 1.3	3.1 ± 1.4	3.0 ± 1.4
Verbal Fluencey		18.1 ± 6.6	17.3 ± 6.6	18.4 ± 6.8	17.9 ± 6.7	18.3 ± 6.5
Moca Estimate		24.4 ± 3.6	24.0 ± 3.7	24.5 ± 3.5	24.4 ± 3.8	24.5 ± 3.5
PDQ-39						
PDQ-39e Category	<10	5415	1156 (68.2%)	141 (57.6%)	214 (48.9%)	3904 (83.9%)
	≥10	1616	539 (31.8%)	104 (42.4%)	224 (51.1%)	749 (16.1%)
PDQ39 Emotion	All	6.1 ± 4.9	7.5 ± 4.9	8.9 ± 4.9	9.9 ± 5.4	5.1 ± 4.4
	PDQ39e <10	4.0 ± 2.8	4.8 ± 2.7	5.4 ± 2.5	5.5 ± 2.7	3.6 ± 2.7
	PDQ39e ≥10	13.3 ± 3.1	13.4 ± 3.1	13.6 ± 3.0	14.1 ± 3.6	13.0 ± 3.0
PDQ39 Summary Score (%)	All	25.3 ± 16.0	30.3 ± 16.4	31.5 ± 15.5	33.0 ± 17.0	22.4 ± 14.9
	PDQ39e <10	19.7 ± 11.8	23.3 ± 12.3	23.3 ± 11.7	22.7 ± 11.9	18.4 ± 11.4
	PDQ39e ≥10	43.7 ± 13.9	45.4 ± 13.6	42.8 ± 12.7	42.9 ± 15.3	42.9 ± 13.8
MCSI						
MCSI Index (%)		19.1 ± 12.7	21.6 ± 13.9	22.3 ± 13.8	24.0 ± 14.7	17.6 ± 11.6

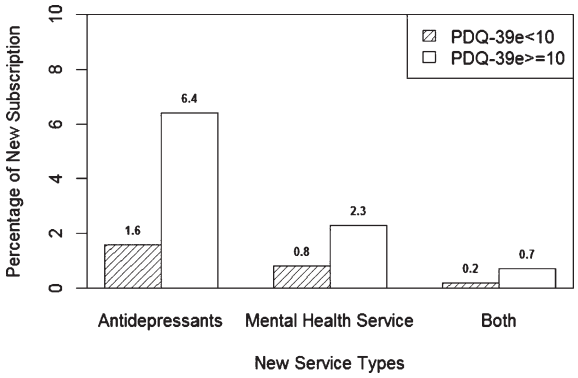

Fig. 1. Percentage of patients prescribed a new service among those not receiving depression-focused care at study initiation. Among 4653 patients, 2.4% were prescribed an antidepressant ($n = 111$), 1.0% were referred to MHS ($n = 48$), and 0.3% were prescribed both ($n = 14$). Those with higher PDQ-39e scores (i.e. scores ≥ 10) were more likely to be started on antidepressants, referred to mental health services, or both.

DISCUSSION

Our study confirms the high prevalence of depressive symptoms (23% of 7031 patients) in a large cohort of PD patients. While the NPF-QII dataset does not include a validated depression screening scale, PDQ-39e can be used as a proxy measure of depressive symptoms, as it has been shown to correlate with other validated markers of depression such as BDI [15, 16]. Furthermore, the prevalence of depressive symptoms in our cohort is consistent with prior studies in this population, further validating the use of PDQe as a surrogate measure of depressive symptoms.

In a previous analysis of baseline data from this cohort, antidepressant use and referral to counseling were among several factors found to be associated with worse HRQL [13]. Our current study demonstrates higher rates of physician recognition of depressive symptoms in this population than was previously reported, as reflected by the fact that 54% of patients with PDQe ≥ 10 were utilizing antidepressants, MHS, or both, at study entry. While this finding is reassuring, it cannot be generalized to the PD population at large because this cohort is obtained from NPF Centers of Excellence (COE) where awareness of PD related depression is expected to be higher. In addition, even at COEs, 46% of patients who scored in the "depressed" range were untreated.

The fact that a substantial proportion of "users" of MHS or antidepressants entered this study with PDQe scores ≥ 10 deserves further discussion because it can yield two possible conclusions: 1) Physicians are better at recognizing depressive symptoms and initiating treatment when the symptoms are more severe and therefore more apparent; 2) Depressive symptoms remains prevalent in this population despite treatment, calling into question the treatment efficacy. The first conclusion is problematic because 46% of those with PDQe score ≥ 10 (i.e. more severe depressive symptoms) were not receiving treatment at baseline. Whether this can be blamed on poor recognition by physicians, personal preferences, or other factors unaccounted for cannot be easily determined by this retrospective study. Furthermore, a limitation of this dataset is that it does not contain information regarding medication compliance or patient preferences with regard to antidepressant use. The second conclusion is difficult to assess without factoring in duration of treatment or baseline severity of depressive symptoms, although we did attempt to use our longitudinal data to investigate this. A significantly higher percentage of those with greater severity of depressive symptoms were started on antidepressants and/or MHS during the study (9.3% compared to 2.6% of those with score <10), confirming that physicians do recognize some depressive symptoms in this population. Importantly, this still leaves 90.7% of "non-users" with scores ≥ 10 who were not initiated on an antidepressant or referred to MHS. Among those who were recognized and started on treatment, those with a highest propensity for services were most likely to receive them. This suggests that physicians recognize depressive symptoms in patients who are more likely to utilize treatment. The efficacy of the treatments will have to be addressed in the prospective analysis once the longitudinal data on a larger cohort of the subjects who were newly started on treatment becomes available.

CONCLUSIONS

The NPF-QII cohort is the largest cohort of PD patients reported to date, and provides data collected in a naturalistic rather than experimental setting which better reflects real practice. Analysis of this dataset demonstrates that prevalence of depressive symptoms remains high in the PD population despite improved physician recognition and treatment initiation. Further longitudinal data will be necessary to determine the impact of antidepressant use and MHS on depression, to compare the relative efficacy of treatments in this population, and to determine whether a synergistic effect of medication and MHS may be present. In the interim, physicians should be vigilant about systematic

screening for depression as part of the routine assessment of all PD patients.

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CONFLICT OF INTEREST

Danny Bega, MD has no conflicts of interest to disclose. Sam Wu, PhD has no conflicts of interest to disclose. Qinglin Pei has no conflicts of interest to disclose. Peter Schmidt, PhD has no conflicts of interest to disclose. Tanya Simuni, MD has served as a consultant and received honorarium from Novartis, Ibsen, General Electric, UCB Pharma, TEVA, IMPAX, Merz, Boehringer Ingelheim, National Parkinson Foundation, and GSK (terminated April 2009). She has also received research support from NIH, MJ Fox Foundation, TEVA, IMPAX, National Parkinson Foundation, Northwestern Memorial Foundation.

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