CNS Neuroscience & Therapeutics

LETTER TO THE EDITOR

CNS Neuroscience & Therapeutics

Decreased Anti-Parkinson's Therapy during Hospitalization due to Infectious Diseases is Associated with Worse Prognosis

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Received 29 December 2015; revision 1 March 2016; accepted 6 March 2016

doi: 10.1111/cns.12545

Parkinson disease (PD) is a multisystem disease characterized with various motor and nonmotor symptoms [1]. Patients with PD are at increased risk for both pneumonia and urinary tract infections (UTI) [2] as a result of various autonomic abnormalities. Indeed, pneumonia and UTI are leading causes for PD patients' hospitalizations, mainly during the advanced stages of disease [3]. Previous publications stressed that medication errors are common right after hospital admission and necessitated recommended frequent consultations with professional neurologists [4]. The investigators of this study hypothesized that patients with PD might have worse prognosis when hospitalized due to infections due to dopaminergic treatment under-dose. These assumptions were confirmed in a previous analysis of a smaller cohort [5]. The main clinical outcomes were in-hospital mortality and worse discharge destination after hospitalizations (defined as worse in any case that the patient arrived from home and was discharged to a nursing home, rehabilitation facility, or was referred to chronic hospitalization).

This was a follow-up, retrospective study of consecutive PD patients diagnosed with either pneumonia, UTI, or both and hospitalized to internal medicine departments (IMD) in one large tertiary medical center through 2008–2013. The follow-up study doubled the patient population included in a previous publication [5]. All the data collected for this study was originally documented in the electronic medical record on patient's admission, compiled into an electronic sheet and was analyzed by SAS (Ver. 9.1). The study was approved by the institutional ethics/review board (head, Prof D. Haratz). Patients had to fulfill the following inclusion criteria: (1) diagnosis of idiopathic Parkinson disease, (2) active dopaminergic therapy, prior to hospitalization, (3) over 30 years of age, and (4) hospitalized to IMD due to pneumonia, UTI, or both. Patients were excluded due to: (1) dementia, (2) active therapy, prior to hospitalization, with antipsychotic medications, (3) state post-deep brain stimulation or other cranial neurosurgical intervention, (4) other neurodegenerative diseases or extrapyramidal disorders, and (5) any degree of immune compromise.

Anti-Parkinson drugs' dosing was taken into account as follows: the L-dopa equivalent was calculated for each dose as previously published and was then summed in order to describe a daily dosage—the L-dopa equivalent daily dose (LEDD) [6]. LEDD reduction was evaluated using multivariate logistic regression with the aforementioned main clinical outcomes and was adjusted to potentially confounding parameters: (1) gender, (2) age, and (c) plasma creatinine levels. Statistical significance was assumed only when p values were lower than 0.05 in accord with confidence intervals of 95%, as generally accepted. The medical records of 1171 consecutive PD patients were reviewed. About 995 patients were excluded, 684 of which due to dementia. A total of 205 patients were included in our analysis, of which 107 (52.2%) were

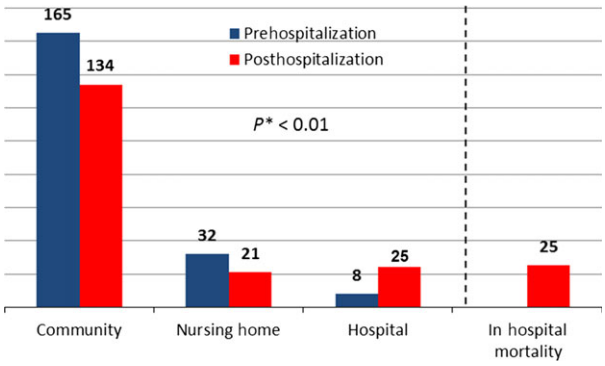

Figure 1 Shift of discharge destination: pre- and posthospitalization.

Table 1 Baseline Patients' characteristics

	In-hospital mortality		Discharge destination	
	Alive	Dead	Same	Worse
Pneumonia n (%) (n = 107)	92 (45)	15 (7.3)	75 (36.5)	17 (8.3)
UTI n (%) (n = 122)	109 (53.2)	13 (6.3)	95 (46.3)	14 (6.8)
Male n (%) (n = 132)	114 (55.6)	18 (8.8)	96 (46.8)	18 (8.7)
Female n (%) (n = 73)	66 (32.2)	7 (3.4)	57 (27.8)	9 (4.4)
Creatinine (mg/dL) Mean (SD) 1.4 (0.7)	1.4 (0.6)	1.9 (1.4)	1.3 (0.6)	1.5 (0.6)
Mean Age (years) (SD) 80.0 (7.8)	79.7 (8)	82.3 (5.4)	80.2 (7.0)	76.8 (12.2)
Relative change in LEDD (mean, %)	−19%	−36%	−17%	−30%

diagnosed with pneumonia and 122 (59.5%) patients had UTI. Twenty-four (9.6%) patients had both types of infection. Seventy-three patients were female (35.9%), and the mean age was 80 ± 7.7 years. Among patients with PD admitted due to pneumonia, 13 patients (12.3%) deteriorated to respiratory insufficiency necessitating mechanical (invasive) ventilation. The rate of in-hospital mortality in our study of patients with PD was 12.2%.

Upon admission, 104 (50.7%) patients had lower LEDD values when compared with their regular medications. Mean LEDD values were found to be significantly lower at the beginning of hospitalization when compared to LEDD values prior to hospitalization (441.9 mg vs. 595 mg; $P < 0.001$). At the end of hospitalization, there was a significant change in the discharge destination: 52 patients (25.4%) were designated a worse location. Figure 1 depicts the statistically significant shift toward a worse destination after hospitalization. The mean duration to next hospitalization among patients with decreased LEDD values upon admission was significantly shorter (131.2 vs. 156.7 days, $P = 0.045$). Analysis by in-hospitalization mortality showed that relative LEDD reduction was significantly associated with increased risk of mortality (OR = 3.25, 95% CI 1.04 – 10.1; $P = 0.042$), (Table 1). Also, relative LEDD reduction upon admission was significantly associated with worse destination upon discharge (OR = 2.6, 95% CI 1.08 - 6.25; $P = 0.03$), (Table 1).

The present study expands the current literature regarding prognostic factors associated with PD patients' deterioration and survival. It further reinforces the findings of a previous, smaller cohort analysis published earlier [5]. Decreased dopaminergic treatment was found to be a widespread phenomenon during PD patients' hospitalizations, occurring in more than half of the population (50.7%). As we hypothesized, decreased anti-Parkinson treatment is associated with increased risk for in-hospital mortality, worse discharge destination, and shorter time until next hospitalization.

It was previously demonstrated that medications are often prescribed incorrectly or utterly withdrawn during hospitalization; Krähenbühl-Melcher and co. made an extensive review of studies published between 1990 and 2005 regarding drug-related problems in hospitals and established that medication errors occurred in a mean of 5.7% of all drug administration cases, omission errors in 22.1% of total medication administration, and administration at an incorrect timing in 34.5% of the cases [7].

Previous studies demonstrated that anti-Parkinson medication administration is often delayed, decreased, or utterly neglected during acute admissions, potentially due to lack of staff knowledge [8]. Consistently, inappropriate withholding of PD medication is common in patients with PD admitted to surgical departments [6].

Our study's result are consistent with a previous paper which described the profile of hospitalized patients with Parkinson's disease, suggesting that 26% of patients with PD are being discharged to a worse location after acute hospitalization [9]. Nonetheless, neither an association between drug-related problems and change in discharge destination nor a comparison between arrival and discharge destinations was presented before. The endpoints influenced in this study by decreased anti-Parkinson medication dosing should be considered as major outcomes: both in-hospital mortality due to infection and shorter duration until rehospitalization serve as outcomes in huge clinical trials of newly launched medications. Our study results imply that such catastrophic outcomes are partially avoidable in less expensive, more common means, that is, correct and timely dosing. Consecutively, the authors of this study side with previous papers stressing the need for staff education programs and the necessity of guidelines regarding the management of patients with PD upon admission to IMD, potentially affecting their prognosis [10].

Study limitations: We included into our multivariate logistic regression only selected variables, considered to have a high impact on clinical outcomes. It is only prudent to assume that other demographic and clinical patients' characteristics could have a profound effect on patients' survival and discharge destinations.

Competing Interests

The authors declare that they have no competing interests.

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