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Medication errors in Parkinson's disease inpatients in the Basque Country

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ABSTRACT

Introduction: Parkinson's disease (PD) medication errors, including both missing dopaminergic drug doses and antidopaminergic usage, have been suggested as risk factors for prolonged hospital stays. The objective of this study was to evaluate the prevalence of such errors in PD patients admitted to public acute-care hospitals in the Basque Country over a two year period and their association with clinically relevant adverse health outcomes, such as length of hospital stay and mortality.
Methods: All PD patients admitted to any of the 11 public acute-care hospitals in the Basque Country in 2011–2012 were included. Medication errors involved incorrect timing or the complete omission of administration for dopaminergic drugs, and the administration of centrally acting antidopaminergics. A logistic regression and a competing risk analysis were applied to verify whether those errors affected intrahospital mortality and length of stay.
Results: The study included 1628 patients admitted 2546 times. Medication errors, affecting almost one third of admissions and half of patients, were associated with higher mortality: inappropriately omitted dopaminergic drug doses OR = 1.92 CI 95% (1.34–2.76); inappropriate antiemetic administration OR = 2.15 CI 95% (1.36–3.39); and inappropriate antipsychotic administration OR = 1.91 CI 95% (1.33–1.73). Inappropriately omitted doses and both inappropriate antipsychotic and antiemetic administration were associated with a significant 4-day increase in median hospital stay.
Conclusion: Medication errors (missing dopaminergic drug doses and centrally acting antidopaminergic use) are not only associated with increased length of hospital stays in PD patients, but also with a higher mortality rate.

1. Introduction

Parkinson's disease (PD) patients are hospitalized more frequently, have longer admissions, and suffer more complications during hospitalization than age-matched control groups [1–3]. The reason for hospitalization is frequently unrelated to PD, and clinicians treating Parkinson's disease often rate the care received by hospitalized PD patients be of poor quality [4,5].

PD medication errors, including both the incorrect timing of levodopa administration and prescription of contraindicated drugs (mainly haloperidol and metoclopramide), are the most important risk factors for motor function deterioration during hospital admissions [6]. Maintaining a patient's strict, complex levodopa schedule may be difficult in hospital, especially when a patient with must remain *Nil per os* (NPO) for several hours perioperatively [7].

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A recent study showed that both missing levodopa doses and antidopaminergic usage result in longer hospital stays for PD patients [8]. In a previous study carried out by our group in a regional hospital serving a population of 63,940 people, we also found that inpatient pharmacotherapeutic management was far from ideal, with a high prevalence of contraindicated antidopaminergic use [9]. Furthermore, PD medication errors have even been described in "centers of excellence" (widely renowned for outstanding performance in Parkinson's research by the National Parkinson Foundation). Indeed, 94% of these centers were not confident that patients received anti-parkinson medication in a timely manner when hospitalized, 71% were not confident that hospital staff knew that anti-emetics such as metoclopramide could worsen PD motor symptoms, and 80% were not confident that physicians knew that clozapine and quetiapine were the least likely antipsychotics to worsen PD symptoms [4].

The objective of this study was to evaluate the prevalence of medication errors, considering both the use of centrally acting inappropriate antidopaminergic drugs and non-compliance with levodopa administration schedules, in all PD patients admitted to all public acute-care hospitals in the Basque Country from January 2011 to December 2012. Moreover, the relationship between medication errors and clinically relevant adverse health outcomes, such as length of hospital stay and mortality rate, was also investigated.

2. Methods

2.1. Data source and study population

To conduct this study, we linked information from different administrative healthcare databases (e-Osabide, PRESBIDE) using unique encrypted identifiers containing information about the Basque Country, an autonomous region in northern Spain with a population of 2,173,210 [10]. A unique patient identifier (known as a CIC number) is used across the entire region allowing data from different databases to be linked.

First, we obtained data on all hospitalizations from the 11 public acute-care hospitals in the Basque Country occurring over two complete years: January 2011–December 2012. Data was obtained on primary diagnosis (leading to hospitalization), as well as all secondary diagnoses as per the Modified 9th International Classification of Diseases codes (ICD-9-CM).

To identify our cohort of patients with PD admitted to acute-care hospitals, we applied the following inclusion/exclusion criteria:

We chose those admissions from acute-care hospitals where the 332.0 code was codified as the primary or secondary diagnosis during the study period. Subsequently, in order to increase sensitivity, all admissions of the same patients occurring after the first codification for PD were included (even if the 332.0 ICD-9-CM code was not used at discharge).

Patients having a code for secondary parkinsonism (332.1) at any visit were excluded, since administrative data has already shown that it is difficult to distinguish between these entities [11]. Additionally, individuals were excluded from the cohort if they had an ICD-9-CM code for primary psychiatric disorders (bipolar disorder, schizophrenia, psychotic depression) or psychosis that could require treatment with antipsychotics; the codes excluded due to their link to psychosis were: 293.81, 293.82, 297.0, 297.1, 297.2, 297.3, 297.8, 297.9, 298.0, 298.1, 298.2, 298.3, 298.4, 298.8, 298.9, 368.16, and 780.1. Patients who had an ICD-9-CM code for pituitary disorders (253*) were also excluded, because these are frequently treated with dopaminergic drugs.

Secondly, patients were required to have prescriptions for antiparkinson drugs (defined as any drug from the N04B group in the Anatomical Therapeutic Chemical (ATC) classification system) during their hospital admission. Dopaminergic medications have very limited, comparatively rare, uses other than for PD. We did not consider anticholinergics (N04A) because these are seldom used as *anti*-PD drugs [12], and are frequently prescribed to treat extrapyramidal symptoms in patients taking antipsychotics.

Next, we obtained drug prescription and administration data from computerized hospital order entry systems. Since 2011, all public hospitals (acute-care, psychiatric and long-term care) in the Basque Country have shared a single IT platform (*e-Osabide*) for inpatient pharmacotherapeutic management. In order to measure the omission of prescribed antiparkinsonian drugs, we decided to add those patients who, despite not being on a dopaminergic drug (N04B drug) while in hospital, had an active outpatient prescription for such medication. For this purpose, we collected data on all outpatient prescription medications funded by the autonomous drug benefit plan (PRESBIDE database). Only active treatments were taken into account, that is, those where the drug may be administered to the patient.

As far as the *e-Osabide* electronic administration record is concerned, there are four entry possibilities: 1) timely drug administration; 2) the dose was not administered (the reason for omission is also recorded); 3) no electronic registry of administration; and 4) the dose was administered at a different time than that prescribed.

2.2. Clinical and demographic data

Data on hospital, ward, type of admission (urgent or not), age, gender, principal diagnosis (reason for admission), admission outcome, and antiparkinson treatment were recorded. Opioid (N02A) and antidementia (N06D) drug prescription on the day of admission was also noted. The Charlson comorbidity index was calculated for each admission according to the algorithm published by Quan 2005 et al., using comorbidity ICD-9-CM codes at discharge [13]. The availability (or lack) of a neurology ward at each hospital was also recorded.

2.3. PD medication error definition

2.3.1. Centrally-acting, inappropriate antidopaminergic drugs

Any antipsychotic drug from the N05A ATC group, with the exception of clozapine or quetiapine, was considered inappropriate. Lithium, although classified as an antipsychotic by the WHO, was also excluded.

Any antiemetic drug from the A03F ATC group, with the exception of domperidone, was considered inappropriate.

2.3.2. Non-compliance with dopaminergic replacement administration schedules

Two different error types were recorded: complete omission of treatment, and omitted doses. The first group included patients with an active chronic outpatient prescription of a N04B drug who did not receive any dopaminergic replacement therapy during their hospital stay. The second group included patients with doses that were omitted because of the unavailability of the drug in time, the patient was out of the ward, or because of their NPO status and there was no alternative drug administered.

2.4. Ethical approval

The Clinical Research Ethics Committee of the Basque Country approved this study (PI201352).

2.5. Statistical analysis

Descriptive statistics were calculated to analyze the characteristics of the study population and to estimate prevalence rates. For categorical variables, an χ^2 test was applied to find out whether mortality rates were statistically different among admissions where errors were committed, or not. In the case of continuous variables, a *t*-test was used to find out if mortality was statistically different within groups.

A stepwise logistic regression model was subsequently applied to find out if medication errors were independently associated with inpatient mortality. To adjust for potential confounders, age, gender, comorbidity index, type of admission, and hospital were included in the model. The presence of a neurology ward in each center was also included as an indirect measure of "knowledge" of the disease. In addition, since dementia is a well-known risk for factor for developing delirium, antidementia drug prescription on the day of admission was also taken into account. Since it was impossible to differentiate between complete deliberate (e.g., patient on palliative care) or accidental dopaminergic drug omissions, opioid drug prescription on admission was included to counteract this possible deviation. We also registered appropriate antiemetic and antipsychotic administration, to control indication bias. A sensitivity analysis was performed to exclude those patients who died within the first 3 days during hospital stay. Results were considered to be statistically significant when $p < 0.05$.

Furthermore, in order to discover whether medication errors affected length of stay, we performed a survival analysis using a two-sided stratified log-rank test. We considered dying and discharge to be competing outcomes. Thus, a competing risk analysis was performed using Fine & Gray regression to calculate the subhazard ratios (HR) for time to discharge, adjusting for all confounding variables.

Statistical analyses were performed using SPSS software (SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) and STATA (Version 12.0Texas, Stata corporation).

3. Results

After applying all inclusion and exclusion criteria, we identified 1628 different patients, admitted a total of 2546 times to an acute-care hospital over the two year study period, yielding to 1.56 ± 0.96 admissions per patient on average (Fig. 1). Their mean age was 80.1 years, mean length of stay 8.1 days, and 53.6% of admissions were male. Table 1 shows the clinical and demographic data sorted by hospital.

Most admissions (2028/2546; 79.65%) were preceded by an emergency room visit, i.e., were unplanned. A total of 19,093 different diagnoses were coded, yielding a mean of 7.5 codes per admission. The most frequent reason for admission was PD, code 332.0 (170 admissions), followed by code 599.0 (urinary tract infection, site not specified) and code 486 (pneumonia, unspecified organism). During their hospital stay, 193 patients died, yielding a mortality rate of 11.8% (193/1628).

Antidementia drugs were used in 255 different hospital admissions, with rivastigmine being the most frequently prescribed drug. Morphine was the most frequently used opioid, being prescribed in 236 admissions.

Additional information is provided as supplementary data in Tables 1–6

3.1. Prevalence of medication error

Globally, medication errors occurred in 31.7% of admissions (807/2546) and 46% of patients (749/1628).

(Additional information is provided as supplementary material in Tables 7–11)

3.1.1. Centrally-acting, inappropriate antidopaminergic drugs

3.1.1.1. Antipsychotics. Antipsychotics were administered in 569 different admissions. 363 involved the use of inappropriate antipsychotics (14.3% of total admissions), affecting 311 different patients (19.1%) (supplementary data, Table 8). Haloperidol was the most frequently implicated drug, affecting 248 admissions (9.7%) and 223 patients (13.7%), and was prescribed "if agitation" in almost two thirds of cases.

3.1.1.2. Antiemetics. Antiemetics were administered in 464 different visits. Inappropriate antiemetics were administered in 171 different hospital admissions (6.7% of total encounters), affecting 157 patients in our cohort (9.6%) (supplementary data, Table 10). Metoclopramide was the most frequently administered inappropriate drug, being used in 164 admissions and for 151 patients.

3.1.2. Non-compliance with dopaminergic replacement administration schedules

3.1.2.1. Complete omission of treatment. In 45 admissions, corresponding to 43 patients, dopaminergic drugs were completely omitted during the hospital stay. All complete omissions occurred because the chronic outpatient dopaminergic drug was not prescribed in hospital.

3.1.2.2. Omitted doses. Of the total of 80,043 doses of dopaminergic drugs that were prescribed, 2266 were not administered (supplementary data, Table 11), 986 of cases being due to clinically unjustifiable reasons (NPO status, oral intolerance, drug not available on time or patient out of the ward). In each hospital at least one dose could not be administered because the prescribed drug was not available on time. In 88% of the admissions where the drug was not administered because of oral intolerance or NPO status, neither transdermal rotigotine nor subcutaneous apormophine was used.

3.2. Association between medication errors and mortality/length of stay

(Additional data is provided as supplementary material, Tables 14–19).

As shown in Table 2, unjustified omitted dopaminergic doses, and both inappropriate antipsychotic and antiemetic administration were associated with a higher mortality rate after adjusting for confounding variables (gender, age, comorbidity index, opiate use, dementia, appropriate antipsychotic/antiemetic use, type of admission, and presence of a neurology ward). Of note, the complete omissions of dopaminergic drugs were no longer associated with increased mortality, when the 61 patients who died within the first 3 days were excluded.

With regard to the influence of medication errors in length of stay, the results of the log-rank test performed for each variable demonstrated that inappropriate antiemetic and antipsychotic administration and inappropriately omitted dopaminergic drug doses are associated with a 4-day increase in the median length of hospital stay. Further information can be consulted in Table 17 of the supplementary data.

The results of the Fine & Gray regression (Table 3), show that HR was less than 1 for inappropriately omitted doses and inappropriate administration of both antipsychotics and antiemetics, indicating that these errors were associated with longer time to discharge after adjusting for all confounding variables. For example, as shown in Table 3, HR was 0.61 for admissions where inappropriate antiemetics were administered, which means that overall

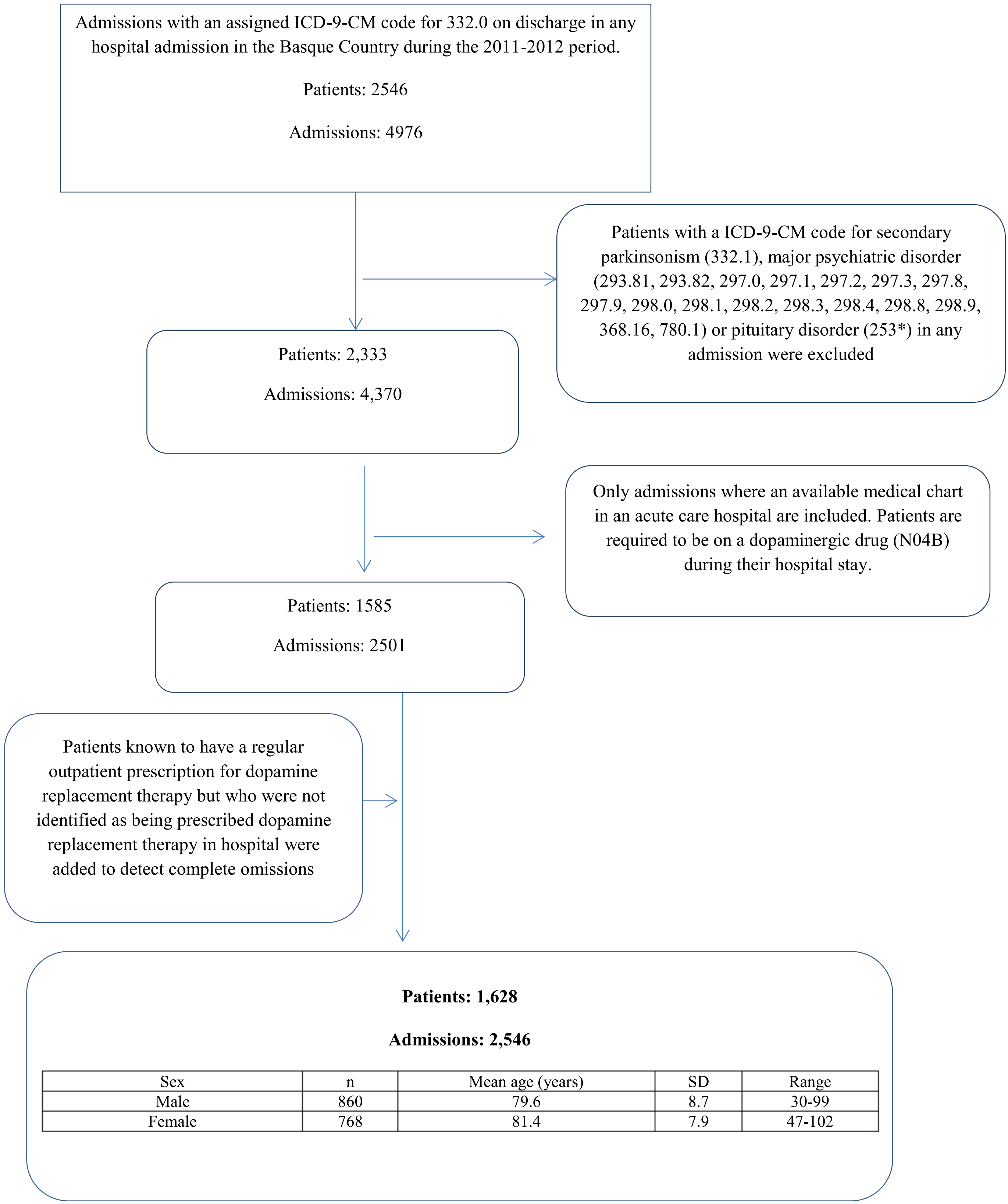

Fig. 1. Flowchart of the study population.

probability of discharge was 39% lower for this group of patients.

3.3. *Outpatient antidopaminergic prescription data*

Outpatient prescription data was available for 647 patients, 54

Table 1
Clinical and demographic data.

Hospital	Neurology ward	N. of admissions	Age mean ± SD (Range) (years);	Length of stay mean ± SD (days)	Male (%)	Charlson comorbidity index mean ± SD
Hospital 1	Yes	640	81.3 ± 8.0; (53–102)	9.0 ± 10.8	56.3	1.2 ± 1.4
Hospital 2	Yes	458	75.5 ± 10.5; (30–93)	8.0 ± 7.6	51.5	1.0 ± 1.3
Hospital3	Yes	450	81.9 ± 6.7; (49–99)	7.3 ± 6.9	50.2	1.3 ± 1.4
Hospital 4	Yes	253	80.0 ± 6.8; (51–96)	6.8 ± 8.4	64.4	1.2 ± 1.3
Hospital 5	Yes	232	81.1 ± 7.9; (51–101)	8.7 ± 7.8	50.9	1.2 ± 1.3
Hospital 6	Yes	118	80.0 ± 7.7; (52–95)	7.7 ± 8.2	47.5	0.9 ± 1.3
Hospital 7	No	104	82.9 ± 8.0; (59–98)	7.3 ± 5.8	53.8	0.8 ± 1.2
Hospital 8	No	88	82.1 ± 6.5; (64–92)	8.7 ± 10.2	55.7	1.3 ± 1.5
Hopsital 9	No	86	80.7 ± 7.0; (57–96)	8.4 ± 7.7	50.0	0.9 ± 1.5
Hospital 10	No	67	82.9 ± 6.5; (63–100)	7.9 ± 6.2	52.2	1.9 ± 1.9
Hospital 11	No	50	82.9 ± 5.8; (66–94)	9.0 ± 8.6	46.0	1.4 ± 1.6
Total		**2546**	**80.3 ± 8.4 (30–102)**	**8.1 ± 8.6**	**53.6**	**1.15 ± 1.40**

Table 2
Association between medication errors and mortality. Logistic regression results.

	Adjusted or[a] (CI 95%)	
	All patients	Excluding patients dying within first 3 days
Inappropriately omitted dopaminergic drug doses	1.92 (1.34–2.76)*	2.32 (1.58–3.39)*
Inappropriate antiemetic administration	2.15 (1.36–3.39)*	2.53 (1.57–4.08)*
Inappropriate antipsychotic administration	1.91 (1.33–2.73)*	1.99 (1.35–2.94)*
Complete levodopa omission	5.49 (2.67–11.27)*	2.62 (0.89–7.71) NS

*$p < 0.0001$.
NS: not significant.
[a] Adjusted by gender, age, comorbidity, opiate use, dementia status, appropriate antipsychotic or antiemetic use, type of admission, hospital, presence of Neurology ward.

Table 3
Association between medication errors and time to discharge. Fine & Gray regression results.

Variable	sHR (CI 95%)*
Inappropriate antipsychotic administration	0.64 (0.57–0.71)
Inappropriate antiemetic administration	0.61 (0.53–0.71)
Inappropriately omitted dopaminergic drug doses	0.64 (0.57–0.71)

*Adjusted by gender, age, comorbidity, opiate use, dementia status, appropriate antipsychotic or antiemetic use, complete dopaminergic drug omission, urgency of admission, hospital, presence of Neurology ward; $p < 0.0001$.

of whom were on antipsychotics (supplementary data, Table 12). Quetiapine was by far the most prescribed drug, being used in 36 patients. On the other hand, 77 patients were on chronic antiemetics. Domperidone was the most frequently prescribed drug in 72 patients (supplementary data, Table 13).

4. Discussion

In this retrospective observational study involving a two-year period and including all the public acute-care hospitals in the Basque Country, we have shown, for the first time, that medication errors (missing levodopa doses and centrally acting antidopaminergic use) are not only associated with longer hospital stays for PD patients, but may also contribute to increased mortality rates. Worryingly, errors affected almost one third of admissions and half of patients. Indeed, the mortality rate in our cohort (11.8% patients died) was comparatively higher than previously reported, with rates of 3.7% and 6% in Australian [2] and Italian [14] studies, respectively. The higher mortality in our cohort compared to others might be a reflection of the higher age (mean 80) of our cohort.

Our results are in line with a recently published study from a single center in Florida showing that both missing levodopa doses and dopamine antagonist usage may prolong length of stay in hospitalized PD patients [8]. The authors did not report a link with increased mortality, but the patient population was much smaller (around 300 admissions) than that studied in the present work, and was sampled from a single hospital.

Dopaminergic drug administration errors in our study were less frequent than previously reported [15,16], probably due to our stringent definition of administration errors. Interestingly, in 88% of the admissions where a dopaminergic drug was not administered because of oral intolerance or NPO status, neither transdermal rotigotine nor subcutaneous apormophine was used. Besides, it's likely that many of NPO orders were not really required since many surgical patients can be allowed to take a little fluid and medication by mouth This illustrates that there is substantial room for improvement in the implementation of published recommendations, like those for better managing PD during surgery [17].

The timely availability of antiparkinson drugs in hospital wards was a generalized problem in our setting, affecting each of the hospitals evaluated. Even in an excellent center with greater availability of drugs, 2.5% of all doses were not administered because the drug was not available on time [16]. Some authors have suggested that all possible antiparkinson drugs should be available in all hospital wards [18,19]. However this seems unfeasible, particularly in small hospitals. To this end, we have recently proposed an alternative therapeutic interchange protocol, where each unavailable drug is converted to the equivalent immediate release levodopa dose, which could be administered until the original drug is available [20]. The high percentage of PD inpatients receiving inappropriate antidopaminergics warrants concern, haloperidol and metoclopramide being by far the most prevalent drugs. This contrasts sharply with outpatient prescription data that shows quetiapine and domperidone, both considered to be appropriate choices, are, respectively, the most frequently-used antipsychotic and antiemetic drugs. With regard to antipsychotics, as PD sufferers are usually aged 65 years and over, even the most frequently used tools that employ explicit criteria to detect potentially inappropriate prescriptions in older patients (Beers and STOPP-START) dedicate a specific criterion to the use of inappropriate antipsychotics (other than clozapine or quetiapine) for this disease [21,22].

In our study haloperidol was widely prescribed for "agitation" on an "as needed" basis. Considering that PD patients have a five-fold risk of being treated for delirium when in hospital [2], the management of this syndrome in PD inpatients in our setting should be improved. In this situation, using IM/IV benzodiazepines (with close respiratory monitoring) might be preferable to haloperidol.

5. Limitations and strengths

Administrative underreporting of patient comorbidities at hospital discharge may have led to an underestimation of the number of associated diagnoses attributed to an admission, affecting the exactitude of comorbidity scores. Since our electronic prescription system only allows administration signing for entire hours, it does not allow for the detection of smaller deviations. In addition, since the implementation of the PRESBIDE (outpatient pharmacy prescription database) system was ongoing at the time of the study, outpatient prescription data was only available for 647 patients. Despite controlling for numerous potential confounders, the observational nature of our study should be taken into account when considering the relationship between medication errors and clinical outcomes. Indeed, the influence of complete dopaminergic drug omissions in mortality should be interpreted with caution considering both the low number of admissions where dopaminergic drugs were completely omitted, and the fact that we could not discriminate between deliberate (e.g., patient on palliative care) and accidental omissions. Despite the inclusion of opiate use and the ward of admission, that intended to alleviate this possible bias, a sensitivity analysis performed excluding patients who died within first 3 days (i.e. the sickest patients where a decision to withhold all treatment may well have been deliberate because they were dying) showed that complete omissions no longer were associated with an increased mortality (Table 2). Nevertheless, to our knowledge this is the largest study on inappropriate drug management in PD inpatients carried out to date. Regarding antidopaminergics, we were able to exploit administration rather than prescription data to estimate their association with mortality and length of stay. This is important since often these drugs are prescribed on an "as needed" basis.

6. Conclusion

In conclusion, our study adds to the growing body of evidence showing the deleterious effect that medication errors (antidopaminergic administration and omission of dopaminergic drug administration) might have on PD patients, prolonging length of hospital stay. For the first time, we have shown that these errors are associated with higher in-hospital mortality. It is about time that corrective measures were implemented.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.parkreldis.2016.12.028.

References

[1] V. Low, Y. Ben-Shlomo, E. Coward, S. Fletcher, R. Walker, C.E. Clarke, Measuring the burden and mortality of hospitalisation in Parkinson's disease: a cross-sectional analysis of the English Hospital Episodes Statistics database 2009-2013, Park. Relat. Disord. 21 (2015) 449–454.
[2] M. Lubomski, R.L. Rushworth, S. Tisch, Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study, J. Neurol. Neurosurg. Psychiatry 86 (3) (2015) 324–330.
[3] J.A. Temlett, P.D. Thompson, Reasons for admission to hospital for Parkinson's disease, Intern Med. J. 36 (2006) 524–526.
[4] K.L. Chou, J. Zamudio, P. Schmidt, C.C. Price, S.A. Parashos, B.R. Bloem, K.E. Lyons, C.W. Christine, R. Pahwa, I. Bodis-Wollner, W.H. Oertel, O. Suchowersky, M.J. Aminoff, I.A. Malaty, J.H. Friedman, M.S. Okun, Hospitalization in parkinson disease: a survey of national parkinson foundation centers, Park. Relat. Disord. 17 (2011) 440–445.
[5] R. Skelly, L. Brown, A. Fakis, R. Walker, Hospitalization in Parkinson's disease: a survey of UK neurologists, geriatricians and Parkinson's disease nurse specialists, Park. Relat. Disord. 21 (2015) 277–281.
[6] O.H. Gerlach, M.P. Broen, W.E. Weber, Motor outcomes during hospitalization in Parkinson's disease patients: a prospective study, Park. Relat. Disord. 19 (2013) 737–741.
[7] C.P. Derry, K.J. Shah, L. Caie, C.E. Counsell, Medication management in people with Parkinson's disease during surgical admissions, Postgrad. Med. J. 86 (2010) 334–337.
[8] D. Martínez-Ramírez, J.C. Giugni, C.S. Little, J.P. Chapman, B. Ahmed, E. Monari, A. Wagle Shukla, C.W. Hess, M.S. Okun, Missing dosages and neuroleptic usage may prolong length of stay in hospitalized Parkinson's disease patients, PLoS One 10 (2015) e0124356.
[9] S. Domingo-Echaburu, U. Lertxundi, E. Gonzalo-Olazabal, J. Peral-Aguirregoitia, I. Peña, Inappropriate antidopaminergic drug use in Parkinson's disease inpatients, Cur Drug Ther. 7 (2012) 164–169.
[10] Population in the Basque Country, Available at: http://www.eustat.es (Accessed 10 April 2016).
[11] K. Swarztrauber, J. Anau, D. Peters, Identifying and distinguishing cases of parkinsonism and Parkinson's disease using ICD-9 CM codes and pharmacy data, Mov. Disord. 20 (2005) 964–970.
[12] C.G. Goetz, G. Pal, Initial management of Parkinson's disease, BMJ 349 (2014) g6258.
[13] H. Quan, V. Sundararajan, P. Halfon, A. Fong, B. Burnand, J.C. Luthi, L.D. Saunders, C.A. Beck, T.E. Feasby, W.A. Ghali, Coding algorithms for defining Comorbidities in ICD-9-CM and ICD-10 administrative data, Med. Care 43 (2005) 1130–1139.
[14] M. Braga, M. Pederzoli, A. Antonini, F. Beretta, V. Crespi, Reasons for hospitalization in Parkinson's disease: a case-control study, Park. Relat. Disord. 20 (2014) 488–492.
[15] J.G. Hou, L.J. Wu, S. Moore, C. Ward, M. York, F. Atassi, L. Fincher, N. Nelson, A. Sarwar, E.C. Lai, Assessment of appropriate medication administration for hospitalized patients with Parkinson's disease, Park. Relat. Disord. 18 (2012) 377–381.
[16] R. Skelly, L. Brown, A. Fakis, L. Kimber, C. Downes, F. Lindop, C. Johnson, C. Bartliff, N. Bajaj, Does a specialist unit improve outcomes for hospitalized patients with Parkinson's disease? Parkinsonism and Related Disorders, Park. Relat. Disord. 20 (2014) 1242–1247.
[17] K.A. Brennan, R.W. Genever, Managing Parkinson's disease during surgery, BMJ 341 (2010) c5718.
[18] Parkinson's UK, "Get it on Time" Campaign, Available from: http://www.parkinsons.org.uk/content/get-it-time (Accessed 10 April 2016).
[19] M. Cohen, L. Smetzer, ISMP medication error report analysis delayed administration and contraindicated drugs place hospitalized Parkinson's disease patients at risk, Hosp. Pharm. 50 (2015) 559–563.
[20] U. Lertxundi, A. Isla, M.A. Solinís, S. Domingo-Echaburu, R. Hernandez, J.C. García-Moncó, A proposal to prevent omissions and delays of antiparkinsonian drug administration in hospitals, Neurohospitalist 5 (2015) 53–54.
[21] American Geriatrics Society 2015, Beers criteria update expert panel. American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults, J. Am. Geriatr. Soc. 63 (2015) 2227–2246.
[22] D. O'Mahony, D. O'Sullivan, S. Byrne, M.N. O'Connor, C. Ryan, P. Gallagher, STOPP/START criteria for potentially inappropriate prescribing in older people: version 2, Age Ageing 44 (2015) 213–218.