Hospital Mortality in Parkinson's Disease: Retrospective Analysis in a Portuguese Tertiary Centre

Mortalidade Hospitalar na Doença de Parkinson: Análise Retrospetiva num Hospital Terciário Português

ARTIGO ORIGINAL

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ABSTRACT

Introduction: Parkinson's disease is associated with high hospital mortality. Male gender, late age at onset, higher disability and the coexistence of cognitive impairment or depression have been suggested to be risk factors of death. Pneumonia and cardiovascular diseases are the leading causes of death.

Objective: To characterize the mortality (causes of hospital admission and death) of Parkinson's disease patients in a tertiary hospital, as well as demographic and clinical characteristics.

Material and Methods: Identification of hospital admissions of Parkinson's disease patients that resulted in inpatient death between 2008 and 2014. Retrospective review of medical files and inclusion of patients with disease clinically confirmed by a neurologist. Assessment of causes of death and demographic and clinical characteristics of patients.

Results: 1525 hospital admissions of Parkinson's disease patients were identified, of which 150 resulted in death. Of these, 52 patients met the inclusion criteria. Mean age at onset of Parkinson's disease symptoms was 66.8 years (± 8.7) and mean duration of disease was 12.5 years (± 7.9). Sixty-five percent of patients were in stages 4-5 of the Hoehn and Yahr scale. Thirty-three patients (63%) had dementia and eleven (21%) had depression. Infections were the leading cause of death (respiratory in 63% of cases).

Discussion: Similarly to literature, pneumonia was the leading cause of hospital death and most patients presented advanced disease stage and dementia. Contrarily to other studies, life expectancy was not reduced and cardiovascular diseases and trauma were not causes of death in our population.

Conclusions: This is the first Portuguese mortality study in Parkinson's disease. Pneumonia is the leading cause of death. Advanced disease stage and dementia were common features in these patients.

Keywords: Hospital Mortality; Hospitalization; Parkinson Disease/mortality; Portugal.

RESUMO

Introdução: A doença de Parkinson está associada a elevada mortalidade hospitalar. O sexo masculino, o início tardio da doença, o grau de incapacidade e a coexistência de deterioração cognitiva ou de depressão têm sido apontados como fatores de risco. A pneumonia e as doenças cardiovasculares são as principais causas de morte.

Objetivo: Explorar a mortalidade hospitalar (motivo de internamento e de óbito) dos doentes com doença de Parkinson num hospital terciário, assim como as características demográficas e clínicas.

Material e Métodos: Identificação das admissões hospitalares dos doentes com o diagnóstico de doença de Parkinson entre 2008 e 2014 e seleção dos doentes falecidos. Revisão retrospetiva dos processos clínicos e inclusão dos doentes com doença confirmada clinicamente por um neurologista. Avaliação das causas de óbito, características demográficas e clínicas.

Resultados: Identificámos 1 525 admissões hospitalares de doentes com diagnóstico de doença de Parkinson, das quais 150 resultaram em óbito. Destes, 52 cumpriam critérios de inclusão. A idade média do início dos sintomas de doença foi 66,8 anos (± 8,7) e a duração média da doença foi 12,5 anos (± 7,9). Sessenta e cinco por cento dos doentes encontravam-se no estádio 4-5 na escala de Hoehn e Yahr. Trinta e três doentes (63%) apresentavam demência e onze depressão. As infeções foram a principal causa de morte (respiratória em 63% dos casos).

Discussão: À semelhança da literatura, a pneumonia foi a principal causa de morte hospitalar e a maioria dos doentes apresentava estádio avançado de doença e demência. Contrastando com outros estudos, não se verificou diminuição da esperança média de vida e as doenças cardiovasculares e o traumatismo não foram causas de morte na nossa população.

Conclusões: Apresentamos o primeiro estudo português de mortalidade na doença de Parkinson. A pneumonia é a principal causa de morte hospitalar. O estádio avançado de doença e a demência foram características comuns nestes doentes.

Palavras-chave: Doença de Parkinson/mortalidade; Hospitalização; Mortalidade Hospitalar; Portugal.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder associated to high morbidity, with a relevant impact on the use of healthcare services as well as on mortality.[1,2] It is one of the most common chronic diseases of the central nervous system and 1.29/1,000 is the estimated prevalence of PD in Portugal.[3] Hospital inpatient mortality rate in patients with PD has been described as approximately 1.5 times higher than in general population.[4,5] Recent data suggest an increased mortality in PD over time, possibly due to a significant increase in average life expectancy in general population.[6] Male gender, elderly age at disease onset, disease duration, advanced stage in Hoehn and Yahr scale, high score in Unified Parkinson's Disease Rating Scale, cognitive impairment and depression all have been associated to poor outcome.[1,7,8] Leading causes of death in most studies of mortality in PD include respiratory

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infections and cardiovascular diseases.[7,9] In addition, cancer or cerebrovascular-related mortality is lower in patients with PD, possibly due to the lower prevalence of these diseases in these patients.[6,10,11]

Our study mainly aimed to identify inpatient mortality (reasons for hospital admission and cause of death) in patients with PD admitted to a tertiary hospital centre, along with their demographic and clinical characteristics.

MATERIAL AND METHODS

Patients admitted to the *Centro Hospitalar do Porto* between 1 January 2008 and 31 December 2014 who were diagnosed with Parkinson's disease – ICD-9th Edition, code 332 - were included in our study. Patients having died in Emergency or in Inpatient wards were selected for the study and their clinical records were revised; patients diagnosed with PD by a neurologist according to the Queen Square Brain Bank criteria were included in the study.[12] Patients diagnosed with atypical parkinsonian syndromes, vascular parkinsonism, drug-induced parkinsonism or other gait disorders and those lacking clinical information were excluded from the study. Patient's demographic and clinical characteristics (date of symptom onset, staging according to the Hoehn and Yahr scale, dementia and depression symptoms), reason for hospital admission, length of stay and cause of death were determined. Co-existing dementia in PD was inferred from the presence of described cognitive manifestations, from prescribed anti-dementia medication or, whenever applicable, using scores of formal neuropsychological assessment (based on Dementia Rating Scale).

Table 1 - Demographic and clinical characteristics of deceased inpatients with PD

Clinical characteristics	
Number of patients, n	52
Male/female gender, n (%)	28/24 (54/46)
Average age, years (SD)	79.7 (6.9)
Average age at disease onset, years (SD)	66.8 (8.7)
Disease duration, years (SD)	12.5 (7.9)
Average age at death, years (SD)	79.7 (6.9)
HY scale, n (%)	
1 – 2	6 (11.5)
3	10 (19.2)
4	18 (34.6)
5	16 (30.8)
Undetermined	2 (3.8)
Dementia, n (%)	33 (63)
Depression, n (%)	11 (21)

SD: standard deviation. HY: Hoehn and Yahr scale

RESULTS

In total, 1,525 patients diagnosed with PD (code 332 – ICD-9) were admitted between January 2008 and December 2014 and 150 deceased patients were identified; from these, 52 patients (24 female) met our study's inclusion criteria and, from these, 40 patients attended a movement disorders centre (36 attended our hospital) and the remaining attended a private neurologist.

Average symptom onset occurred at 66.8 years of age (± 8.7; min = 40 and max = 80) and average duration of the disease was 12.5 years (± 7.9; min = 3 and max = 42). The average age at death was 79.7 years (± 6.9; min = 62 and max = 95). Six patients (12%) presented with PD in stage 2 or lower in Hoehn and Yahr scale, while 46 (88%) presented in stage 3 to 5. Thirty-three patients (63%) presented with concomitant dementia syndrome and 11 (21%) patients with depression (Table 1). All patients were treated with levodopa (mean daily dose 830 mg), three patients were treated with dopamine agonists (ropinirole prolonged release, 8 mg/day) and one patient with anticholinergics (tri-hexi-phenidyl 5 mg/day). As regards adjuvant therapy, nine patients were treated with COMT inhibitors (entacapone, 800 mg/day), two with MAO-B inhibitors (selegiline, 5 mg/day) and two with amantadine (400 mg/day). Eleven patients were treated with antipsychotics (four with clozapine, mean daily dose 81 mg; four with quetiapine, mean daily dose 194 mg and three with cyamemazine, 25 mg/day).

Mean length of stay was 10.8 days (± 14.2; min = 1 and max = 88). Pneumonia (67% of the patients), sepsis due to urinary tract infection (12%), stroke (8%) and end-stage cancer (6%) were the main reasons for hospital admission.

Pneumonia was the major cause of death (63% of the patients), followed by nonpulmonary source of sepsis (17%), stroke (8%, two patients with cerebral infarction, one with spontaneous intracerebral haemorrhage and one patient with sub-arachnoid haemorrhage upon ruptured aneurysm) and cancer (8%, peritoneal carcinomatosis, anaplastic lymphoma of the face, cancer of the gastric cardia and small-cell lung carcinoma). Mesenteric ischaemia and pulmonary thromboembolism were less frequent causes (2% of the patients) (Table 2).

DISCUSSION

It has been assumed that patients with PD have lower life expectancy than general population. However, the

Table 2 - Causes of death of inpatients with PD

Causes of death	n (%)
Pneumonia	33 (63)
Non-pulmonary infection	9 (17)
Stroke	4 (8)
Cancer	4 (8)
Pulmonary thromboembolism	1 (2)
Mesenteric ischaemia	1 (2)

average age at death (79.7 years) in our group of patients was similar to the average life expectancy in Portugal which, according to official 2011-2013 data of the *Instituto Nacional de Estatística*, corresponds to 80.13 years.[13] An average time to death of 12.5 years was found and considered as relatively long and 65% of the patients presented in an advanced stage of the disease (4-5 in Hoehn and Yahr scale), raising the issue of quality of life and the importance of preserving patient's functionality and independence. Patients in earlier stages of PD (i.e. HY stage ≤ 2; six patients with an average age of 76 years and with an average four-year duration of the disease) died equally with pneumonia or stroke. Contribution of comorbidities and common risk factors were expected in this age group.

Pneumonia was the main cause of death, in line with different studies of mortality in PD.[7,9,10] This may be due to chest wall rigidity during motor fluctuations, to dyskinesia and to upper airway dysfunction, to which an increased risk for aspiration and a lower efficacy of expectoration is associated.[14] The risk for infections and their deadly consequences may be reduced with frequent mobilization and kinesiotherapy. None of our patients died from ischaemic heart disease, unlike different studies where cardiovascular diseases were described as one of the major causes of death in patients with PD.[6,10] Considering adverse cardiovascular effects of antipsychotic drugs, we believe that lower use of this type of drug could explain for the absence of any cardiovascular-related death in our group of patients, from whom only 20% were treated with low-dose antipsychotic drugs. Cerebrovascular diseases and cancer, which in other series were uncommon causes of death, were responsible for 16% of deaths in our group of patients, probably related to high mean age of our group of patients. Even though high admission rates occur in patients with PD due to injuries, particularly from falls, we did not find any injury-related death in our group of patients.[14]

Dementia has been considered by some authors as risk factor for death in this group of patients, which may be due to the impact of cognitive dysfunction on functional status.[1,4,8] Almost two thirds of our patients presented with dementia syndrome, corresponding to a higher prevalence than what has been described in some recent series. Oosterveld *et al.* have found the presence of dementia in 35% of the patients, while Lau *et al.* found a 31% prevalence.[1,8] In line with other studies, depression was not very frequent in our group of patients, even though it has been proved as predictive of early death in patients with PD.[15] Early treatment of comorbidities associated to increased mortality, such as dementia and depression, may improve the outcome in these patients.

Major advantages of this study regards the inclusion of patients with PD attending a neurologist, in addition to the presence of hospital records on the circumstances of death. Major limitations regard its retrospective nature and the fact of being a mono-centric study.

CONCLUSION

Our study was the first Portuguese study of mortality in PD. Our results were in line with similar studies, as regards the advanced stage of the disease and the coexistence of dementia as usual characteristics of these patients. Infections were the main cause of inpatient death in PD, with a clear predominance of pulmonary infections.

HUMAN AND ANIMAL PROTECTION

The authors declare that the followed procedures were according to regulations established by the Ethics and Clinical Research Committee and according to the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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