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Delirium in Parkinson's disease patients. A five-year follow-up study

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Abstract

Objective: To assess the significance of delirium in parkinsonian patients in a 5-year follow-up case-control study with three groups of patients: Parkinsonian and Delirium (PDG), Parkinsonian (PG) and Control (CG). Methods: Comparisons of Short Test of Mental Status (STMS) and Unified Parkinson's Disease Rating Scale-motor section (UPDRS(m)) between groups were performed using analysis of variance with repeated measurements. Comparisons of survival functions and Cox regression models were used to analyse the time until death. Results: STMS and UPDRS(m) mean scores were statistically different between PDG group and the other two groups ($p<0.001$) and between PDG and PG groups ($p<0.001$), respectively. Including all groups, PG's patients (HR = 0.29; 95% C.I. = 0.09–0.93) and CG's patients (HR = 0.13; 95% C.I. = 0.03–0.60) had less hazard to die than PDG's patients; patients with a STMS basal score >33 (HR = 0.37; 95% C.I. = 0.13–0.99) had less hazard to die than patients with a score ≤ 33. Finally, including PDG and PG groups, patients with basal UPDRS(m) score >17 (HR = 4.88; 95% C.I. = 1.11–21.48) had higher hazard to die than patients with a score ≤ 17. Conclusion: For patients with Parkinson's, delirium is an increased risk factor for developing dementia, to have a more severe motor impairment and to death.

Keywords: Parkinson's disease; Delirium; Survival analysis; Repeated measurements

1. Introduction

Delirium is an acute organic brain syndrome presenting with whole cognitive impairment, attention disorders, reduced level of consciousness, increased or decreased psychomotor activity, and wake-sleep rhythm disorders [1–5]. The prevalence of delirium is variable due to the difference in population studied and distinct diagnostic criteria used [5], but there is consensus that this increases with aging [6], with rates as high as 60% reported in hospitalised elderly patients [7].

On the other hand, Parkinson's Disease (PD) mostly affects older people [8], and risk for postoperative delirium varying between 2.8 and 8.1 among patients with PD against controls [9], and occurrence of delirium in 5–25% of Parkinson patients treated with levodopa have been reported [10].

The mesocortical dopaminergic system has been involved in the physiopathology of delirium. This proposal has been supported by the fact that neuroleptics are useful in treating delirium [5], and additionally because dopaminergic medications are known to be likely to cause delirium [10], which determines the great complexity in handling delirium in parkinsonian patients, in which neuroleptics aggravate the disease [11].

While delirium has traditionally been considered as temporary and reversible [12], recent evidence has associated it with increased morbidity, mortality and as a risk factor for developing dementia, i.e., it can lead to catastrophic consequences [2,3,6].

This 5-year prospective comparison observational study was conducted to identify behavior in patients with PD developing delirium against a group of patients with PD and a control group.

2. Patients, materials, and methods

A consecutive series of 21 patients with PD (recorded on the Abnormal Movements Clinic, Neurology Service,

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'Carlos Andrade Marín' Hospital, a third level reference hospital) who met criteria for delirium according to the Confusion Assessment Method of Inouye et al [7], (the Confusion Assessment Method requires the presence of (i) Acute onset and fluctuating course;(ii) Inattention; (iii) Disorganized thinking; and (iv) Altered level of consciousness. The diagnosis of delirium requires the presence of features (i) and (ii) and either (iii) or (iv)).

The patients were assessed by one of the authors (MS-D), between January 1994 until December 1999 and designated as Parkinson and Delirium Group (PDG). Only those with a previous assessment (up to 3 months before the occurrence of delirium) of their higher mental functions (using the Short Test of Mental Status STMS) [13] that ruled out dementia were included; and an assessment of either the presence or absence of depression using the Hamilton scale [14] that excluded those with depression (the cut-off score was 12/13). Those in which a previous evaluation (within the last 3 months) of their parkinsonian condition through the UPDRS motor section [15] was not available were excluded as well.

Additionally, two control groups were used, one formed by 21 patients with PD, called Parkinson Group (PG), and the other one including 21 relatives (husbands or wives of patients with PD), referred to as the control Group (CG). Both patients in the PG and CG were excluded if they had, as in the case above, a score of 28 or lower on the STMS or scored with depression under the Hamilton scale (with a similar cut-off score of 12/13). For patients in the PG, those without an assessment within the last 3 months of the UPDRS motor section were excluded. The general health status in the PG, in the CG, and pre-delirium in the PDG, was similar without severe disease.

Relevant demographic and clinic variables were collected in all of them; the three groups had a total of 11 assessments: the so-called Basal Evaluation (BE) and other 10 assessments performed every 6 months. All assessments included the STMS for the three groups, the UPDRS(m), Hoehn and Yahr (H and Y) [16], Schwab and England Scale (SES) [17] for those within the PDG and PG. The BE of the PDG was the last recorded immediately before development of delirium.

The Analysis of variance (ANOVA) [18] was used to compare age mean and STMS basal scores mean between the 3 groups, and also to compare disease duration mean and the UPDRS(m) mean between PDG and PG groups. The Pearson chi-square test [19] was used to evaluate differences of proportions by gender (between all groups) and, by H and Y, SES and daily levodopa between PDG and PG groups. A p-value lower than 0.05 was accepted as statistically significant.

Comparison of the eleven assessments of STMS and UPDRS(m) mean scores collected through the five years of follow-up were performed using an ANOVA with repeated measurements [20].

To analyse the time until death between groups we compare these groups' survival functions estimated by the Kaplan-Meier method using the log-rank test [21]. We also compared the three pairs of survival functions and then we corrected the global-$\alpha = 0.05$ for multiple comparisons using Bonferroni's method ($\alpha_{\text{Bonferroni}} = 0.017$). Finally, to identify which of these factors: gender, basal age, group, basal STMS, years of illness, basal H and Y and basal UPDRS(m) were related to the time until death, we performed a first Cox regression model including the three groups and a second Cox regression model including only PDG and PG groups [21].

All statistical analysis were performed using Stata 8.0 [22].

3. Results

Delirium causes were: prostatectomy (benign hyperplasia), 4 patients; hip surgery, 8 (5 men, 3 women); dehydration, 3 (1 man, 2 women); pneumonia, 5 (3 men, 2 women); and finally, use of anti-flu medication (this patient take 4 pill (each with 2,5 mg of loratadine, 60 mg of pseudoefedrine and 500 mg od acetaminophen), 1 male patient. Delirium was the agitated type in 16 patients; in 6 patients do not have altered level of sensorium.

There were no statistically significant differences on mean age, on mean STMS basal scores and on gender between the three groups. There were no differences between PDG and PG groups on mean disease duration, on mean UPDRS(m) basal score, on H and Y, on SES and on daily doses of levodopa (Table 1).

Analysing variables collected during 5-year follow-up, values were correlated. We performed an ANOVA with

Table 1
Demographic and clinical patients' characteristics by groups

Variables	PDG ($n=21$)	PG ($n=21$)	CG ($n=21$)	P
Age (years)	67.7 (5.3)	67.5 (5.4)	67.1 (5.9)	0.9[a]
STMS	34.5 (2.0)	34.7 (1.6)	34.4 (2.1)	0.9[a]
Gender (M/F)	14/7	16/5	11/10	0.3[b]

Variables	PDG ($n=21$)	PG ($n=21$)	p
Disease duration (years)	6.05 (1.4)	6.0 (1.5)	0.8[a]
UPDRS(m)	18.4 (2.8)	19.2 (2.6)	0.4[a]
H and Y (1.5/2)	11/10	13/8	0.5[b]
S and E (70/80/90)	3/12/6	3/12/6	1[b]
Daily levodopa (mg)	n (%)	n (%)	
500	5 (23.8%)	2 (9.5%)	
625	11 (52.4%)	12 (57.1%)	
750	5 (23.8%)	7 (33.3%)	0.4[b]

$x(y)$, mean (standard deviation); x/y, absolute frequency of first class/absolute frequency of second class.

[a] Means comparison (ANOVA test); $p<0.05$ as significant.

[b] Pearson chi-square test; $p<0.05$ as significant.