Journal of the Neurological Sciences 368 (2016) 150–154

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

The high prevalence of impulse control behaviors in patients with early-onset Parkinson's disease: A cross-sectional multicenter study

L. Vela [a,*], J.C. Martínez Castrillo [b], P. García Ruiz [c], C. Gasca-Salas [d], Y. Macías Macías [a], E. Pérez Fernández [a], I. Ybot [e], E. Lopez Valdés [f], M.M. Kurtis [g], I.J. Posada Rodriguez [h], M. Mata [i], C. Ruiz Huete [j], M. Eimil [k], C. Borrue [l], J. del Val [c], L. López-Manzanares [m], A. Rojo Sebastian [n], R. Marasescu [o]

[a] Department of Neurology, Hospital Fundacion Alcorcón, Madrid, Spain
[b] Department of Neurology, Hospital Ramón y Cajal, Madrid, Spain
[c] Department of Neurology, Fundación Jiménez Díaz, Madrid, Spain
[d] M CINAC- Hospital U HM Puerta del Sur, Mostoles. Universidad CEU San Pablo, Madrid, Spain
[e] Department of Neurology, Hospital U La Paz, Madrid, Spain
[f] Department of Neurology, Hospital Clínico San Carlos, Madrid, Spain
[g] Department of Neurology, Hospital Ruber Internacional, Madrid, Spain
[h] Department of Neurology, Hospital 12 de Octubre, Madrid, Spain
[i] Department of Neurology, Hospital Puerta de Hierro, Madrid, Spain
[j] Department of Neurology, Hospital Nuestra Señora del Rosario, Madrid, Spain
[k] Department of Neurology, Hospital de Torrejón, Madrid, Spain
[l] Department of Neurology, Hospital Infanta Sofía, San Sebastián de los Reyes, Madrid, Spain
[m] Department of Neurology, Hospital de la Princesa, Madrid, Spain
[n] Department of Neurology, Hospital Príncipe de Asturias - Alcalá de Henares, Madrid, Spain
[o] Department of Neurology, Hospital de Getafe, Madrid, Spain

ARTICLE INFO

Article history:
Received 6 December 2015
Received in revised form 20 May 2016
Accepted 1 July 2016
Available online 2 July 2016

Keywords:
Parkinson's disease
Early-onset
Impulse control behavior
Impulse control disorders
Dopamine agonist
Quality of life

ABSTRACT

Introduction: In Parkinson's disease patients, impulse control disorders (ICDs) have been associated with younger age and early disease onset, yet the prevalence of ICDs in early-onset Parkinson's disease (EOPD) patients has yet to be studied. Thus, we set out to compare the prevalence of impulse control behaviors (ICBs) in a cohort of EOPD patients with that in age and gender matched healthy controls (HCs), as well as to analyze the association of these symptoms with the use of dopaminergic drugs and other clinical or demographic factors.
Methods: A cross-sectional, multicenter study was carried out on patients recruited from outpatient Movement Disorder Clinics, assessing ICBs using the short form of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP). In addition, depression and quality of life (QoL) were measured, along with other demographic and clinical variables.
Results: Of the 87 EOPD patients, 49 (58.3%) displayed an ICB, as did 28 of the 87 HCs (32.9%; $p = 0.001$). Most of the EOPD patients that displayed an ICB (91.8%) were medicated with a dopamine agonist (DA) and accordingly, DA treatment was associated with a 7-fold increased risk of developing an ICB. Patients with ICBs had a higher depression score and a worse QoL.
Conclusions: ICBs are much more prevalent in EOPD patients than in HCs and they are associated with DA intake, depression and a worse QoL.

1. Introduction

Early-onset Parkinson's disease (EOPD) has been arbitrarily defined as parkinsonism with an onset before 45 years of age [1], although 40 and 50 years of age have also been used as the threshold in some studies [2–4]. A recent community-based study indicated a 3.6% prevalence of EOPD patients in the United Kingdom [5], a condition that is frequently characterized by slower disease progression, milder cognitive decline and earlier motor complications, such as fluctuations and dyskinesias [2]. Moreover, EOPD patients usually experience more significant psychiatric and behavioral symptoms, such as depression, anxiety and obsessive-compulsive disorders, the rates of which vary from 5% to 45% [2,6,7].

In PD patients, dopamine dysregulation syndrome and impulse control disorders (ICDs) have often been associated with younger age and earlier disease onset [8–10], yet this issue has not been studied closely

* Corresponding author at: Department of Neurology, Hospital U Fundación Alcorcón, Calle Budapest 1, 28922 Alcorcón, Madrid, Spain.
E-mail address: lvela@fhalcorcon.es (L. Vela).

http://dx.doi.org/10.1016/j.jns.2016.07.003
0022-510X/

in EOPD patients. ICDs include abnormal behaviors, such as compulsive gambling, compulsive buying, abnormal sexual and eating behaviors, as well as dopamine dysregulation syndrome and other related behaviors such as punding, hobbyism and aimless wandering [11–13]. In the last few years the presence of these abnormal behaviors in PD patients has been measured with the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), a screening instrument particularly valid to discriminate ICDs [14,15]. However, at times positive responses in the QUIP are associated with milder behaviors that cannot be considered as true ICDs and indeed, many patients might experience what is defined as subsyndromal ICD [16]. Recently, rather than exclusively using the term of ICDs to refer to such behaviors, other terms like impulse control symptoms or impulse control behaviors (ICBs) or impulse control disorder symptoms have begun to be employed [17–19]. As such, and given that some of the positive responses in the questionnaire may refer to sub-clinical situations, we prefer here to refer to these behaviors as ICBs.

Since PD itself does not seem to carry an increased risk for the development of ICBs, other factors have been associated with this phenomenon, such as the use of anti-parkinsonian medications, mainly dopamine agonists (DAs) [10,12,20]. However, it remains unclear whether higher doses of dopaminergic drugs are associated with a higher risk of ICDs and if rasagiline (a monoamine oxidase inhibitor) might potentiate this risk [11,14,20–22]. Accordingly, the main aim of this study was to evaluate the prevalence of ICBs in a cohort of EOPD patients, comparing these subjects with an age and gender matched healthy control (HC) group. In addition, we analyzed the association of these symptoms with the use of dopaminergic drugs and their doses, as well as with depression and quality of life (QoL).

2. Methods

2.1. Patients

This is a cross-sectional, multicenter study designed to characterize individuals with EOPD. Patients were recruited from 14 hospitals in the greater Madrid area between March 2010 and November 2011. PD was defined according to the United Kingdom PD Society Brain Bank criteria [23], with the exception that a family history of PD was not regarded as a criterion for exclusion. EOPD was defined by an age of no later than 45 years-of-age. All patients were evaluated and followed by Movement Disorder specialists. Patients with other parkinsonisms, cognitive impairment (defined by a score below 24 in the Mini Mental State Examination -MMSE) or those unable to complete the questionnaires were excluded from the study. HC subjects with no neurological complaints were recruited, and they were matched to the patients by age and gender. The Hospital's Ethic Committees approved the study and all the participants provided their written informed consent.

2.2. Evaluations

ICBs were assessed using the QUIP-short form and a positive response for any of these behaviors was defined as a positive QUIP [14,15]. The Hoehn and Yahr scale was used to assess the motor function of PD patients and patients were evaluated with the Unified Parkinson's Disease Rating Scale (UPDRS) part III during the "ON" condition after the first morning dose of medication. The presence of dyskinesias and motor fluctuations were also registered. All patients were taking at least one antiparkinsonian drug and as such, we recorded the use of rasagiline, levodopa, COMT inhibitors and DAs, either alone or in combination. L-dopa equivalent daily dose (LEDD) was calculated according to the following formula: levodopa 100 mg = levodopa retard 75 mg = ropinirole 5 mg = rotigotine 3.3 mg = pramipexole 1 mg; Entacapone = levodopa dosage × 0.33 [24]. The total LEDD was the sum of the levodopa with or without COMT inhibitors plus the DA LEDD. The presence of depression was assessed through the Beck depression inventory (BDI), whereby patients with a score of at least 13 points out of a maximum of 63 were diagnosed as depressed [25] The QoL of all subjects (patients and controls) was assessed with the EuroQol and with the PDQ-39 in patients alone.

2.3. Statistical analysis

All statistical analyses were carried out using version 15 of the Statistical Package for the Social Sciences (SPSS) for Windows. The Kolmogorov-Smirnov test was applied to assess the normality of the quantitative variables, and the quantitative results are presented as the mean and standard deviation (SD), or as the median and interquartile range (IQR) if the data did not follow a normal distribution. Frequencies were expressed as the value "n" and as percentages. The Student's *t*-test, Chi-squared test and the Mann-Whitney *U* test were used to analyze the differences between patients and controls, and between patients with and without ICBs. A Multivariate Logistic Regression model was established to estimate the effect of DAs and rasagiline treatment, adjusted to the BDI score, years of PD evolution and unemployment. Multivariate Lineal Regression Models were used to estimate the effect of ICBs on QoL.

All p-values were two tailed and values < 0.05 were considered significant. If >10% of the data from a questionnaire or a scale were missing for any particular patient, data from that scale was excluded from the statistical analysis.

3. Results

This study was carried out on 87 patients with a mean age of 47.4 (7.9), a median disease duration of 5 (range: 2–11) years and a median UPDRS III of 16 (range: 11–23), as well as a cohort of 87 age and gender matched control subjects. The demographic and clinical features of these subjects were recorded (Table 1). With regards to treatment, 48 patients were taking rasagiline (60.6%), 55 levodopa (63%) and 70 patients (80.5%) were taking dopamine agonists (eleven patients rotigotine, pramipexole 30 patients, ropinirole 28 patients and cabergoline 1 patient). Eighteen patients were taking slow release formulations. Responses to the QUIP were obtained from 84 patients (95.4%) and 85 control subjects. When these were analyzed, the prevalence of any ICB was 58.3% in EOPD patients (CI 95%, 47.2%–69.5%) and 32.9% in the HC population (CI 95%, 22.4%–43.5%: OR, 2.9; CI 95%, 1.5–5.3; $p = 0.001$). Indeed, the number of positive QUIP responses was also significantly higher in the EOPD patients than in the controls ($p < 0.001$). All ICBs were observed more frequently in patients than in controls, but gambling, sex, buying and punding were significantly more prevalent in the patients studied (Table 2). Hobbyism was the most prevalent pathological behavior in both patients (29.3%) and

Table 1
Demographic and clinical variables in EOPD and in healthy controls.

	PD patients (n = 87)	Controls (n = 87)	p value
Sex n (% male)	53 (60.9%)	47 (54.7%)	0.443
Age (years): mean (SD)	46.9 (9.1)	45.6 (8.6)	0.312
Employment	39 (49.4%)	68 (93.2%)	<0.001
Alcohol	26 (33.8%)	54 (66.7%)	<0.001
BDI score	8 (4–14)	3 (1–6)	<0.001
BDI > 12	28 (32.9%)	4 (4.7%)	<0.001
EQ-5D median	7 (5–8)	5 (5–6)	<0.001
EQ-VAS median	70 (60–80)	90 (80–90)	<0.001

Data are presented as n (%) or as median (interquartile range - IQR) BDI: Beck Depression Inventory.
EQ-5D (from EuroQol): It is descriptive system that measures health-related quality of life on five dimensions (mobility, selfcare, usual activities, pain/discomfort, and anxiety/depression).
EQ VAS (from EuroQol): It is a 20 cm vertical visual analogue scale that generates a self-rating of health-related quality of life.