Overweight is more prevalent in patients with Parkinson's disease

Excesso de peso é mais frequente em pacientes com doença de Parkinson

Hugo Morales-Briceño[1], Amin Cervantes-Arriaga[2], Mayela Rodríguez-Violante[1,2], Juan Calleja-Castillo[2], Teresa Corona[2]

ABSTRACT

Underweight and malnutrition are well documented in Parkinson's disease (PD), while overweight has been less reported. We carried out a cross-sectional study including 177 healthy controls and 177 PD patients attending a tertiary care center. We recorded weight and height for all participants. A statistically significant difference was found in body mass index (BMI) between controls and PD patients (29.1±5.4 *versus* 27.2±4.7, p<0.001). In the PD Group, two patients were underweight, 32.7% were within normal range, 46.9% had overweight, and 19.2% were obese. Overweight and normal weight were more prevalent in the PD Group (p=<0.01 and <0.001, respectively) when compared to controls. In conclusion, overweight/obesity are common among patients with PD, while underweight is almost negligible.

Key words: body mass index, Parkinson disease, overweight, obesity.

RESUMO

Baixo peso e desnutrição são muito documentadas na doença de Parkinson (DP), enquanto que o excesso de peso tem sido menos relatado. Foi realizado um estudo transversal com 177 controles saudáveis e 177 pacientes com DP que frequentavam um centro terciário. O peso e a altura de todos os participantes foram arquivados. Uma diferença estatisticamente significativa no índice de massa corporal (IMC) foi encontrada entre controles e pacientes com DP (29,1±5,4 *versus* 27,2±4,7, p<0,001). No Grupo DP, dois pacientes estavam abaixo do peso, 32,7% estavam dentro do intervalo normal, 46,9% apresentavam sobrepeso e 19,2% eram obesos. Peso normal e excesso de peso foram mais prevalentes no Grupo DP (p=<0,01 e <0,001, respectivamente) em relação aos controles. Em conclusão, o sobrepeso/obesidade são comuns entre os pacientes com DP, enquanto baixo peso nessa população é quase insignificante.

Palavras-Chave: índice de massa corporal, doença de Parkinson, sobrepeso, obesidade.

Parkinson's disease (PD) is a progressive neurodegenerative disorder, and during its progression certain clinical features like dysphagia, immobility, depression, and dementia may hinder normal dietary intake, thereby contributing to malnutrition and weight loss.

The DATATOP, CALM-PD and PRESTO studies reported a prevalence of low body mass index (BMI) of 13.9, 10.1, and 15.1%, respectively. A systematic review reported that the prevalence of malnutrition in PD ranged from 0 to 24%, stating that this variation may be due to the methodology used by each author[1]. A recent meta-analysis including 12 studies with a total of 871 patients and 736 controls showed that PD patients had a significantly lower BMI than controls (1.73; 95%CI 1.11–2.35, p<0.001)[2].

Overall, a lower BMI correlates with disease severity and poor outcomes including cognitive decline and dyskinesia[3]. It has been suggested that decreased BMI during the initial six months of follow-up in PD patients might be used as a predictor of cognitive decline and dementia[4]. Finally, it has been reported that weight loss in PD is related to one-year survival rates[5].

On the other hand, obesity and weight gain have been mainly restricted to patients who have undergone deep brain stimulation, although DA have also been related to weight gain.

Mexico ranks first in obesity worldwide[6]. Given the high prevalence of obesity, we hypothesize that Mexican PD patients present more overweight and less underweight than reported on the literature. While the relationship between diabetes, obesity, hypertension and the risk of PD is still controversial[7-9], assessing this issue may help improving the understanding of PD reality in Mexico and also may provide an opportunity to study the impact of overweight in PD clinical picture.

[1]Movement Disorders Clinic, National Institute of Neurology and Neurosurgery of Mexico, Mexico City, Mexico;

[2]Clinical Neurodegenerative Disease Research Unit, National Institute of Neurology and Neurosurgery of Mexico, Mexico City, Mexico.

Correspondence: Mayela Rodríguez-Violante; National Institute of Neurology and Neurosurgery of Mexico; Insurgentes Sur 3877; Mexico City 14269 - Mexico; E-mail: mrodriguez@innn.edu.mx

Conflict of interest: There is no conflict of interest to declare.

Received 30 March 2012; Received in final form 10 July 2012; Accepted 17 July 2012

METHODS

One hundred and seventy-seven consecutive PD patients who fulfilled the Queen Square Brain Bank Criteria were recruited at the Movement Disorders Clinic, a tertiary care center in Mexico city. All patients who agreed to participate signed a written informed consent, according to the determination of the local institutional review board and Ethics Committee. One hundred and seventy-seven healthy controls matched by gender and age were also recruited among hospital visitors and patient nonblood relatives. Exclusion criteria included participants with a known diagnosis of type-2 diabetes mellitus and PD patients who had undergone deep brain stimulation surgery. Weight was measured with a calibrated balance beam scale (Seca 700), using a standardized method (fasting, without shoes, and minimal clothing). Height was measured with a telescopic height rod (Seca 220). All participants stood erect, barefoot, looking forward, against the stadiometer, after taking full inspiration. We recorded clinical and sociodemographic data for PD patients. BMI categories were determined as follows: underweight (BMI≤18.5), normal weight (BMI=18.5 to 24.9), overweight (BMI=25 to 29.9), and obesity (BMI≥30).

The levodopa equivalent daily dose (LEDD) was calculated using the following formula: LEDD=[levodopa (mg)x1 or l-dopax1.25 if receiving a Catechol-*O*-methyltransferase (COMT) inhibitor]+[bromocriptine (mg)×10]+[pramipexole (mg)×89]+[rotigotine (mg)x30]. Dopamine agonist (DA) levodopa equivalent daily doses (DA-LEDD) was defined as the LEDD for DA only.

In addition, levodopa dose, LEDD, and DA-LEDD were adjusted by body weight (milligrams per kg).

The study was approved by the Internal Review Board and Ethics Committee of the Institution.

Statistical analysis

To compare PD and Control Groups, we used *t*-tests for continuous variables as age, height, weight, and BMI. Normality of the distribution was assessed by the Kolmogorov-Smirnov test; when the normality assumption did not hold, a Mann-Whitney U Test was done as a nonparametric alternative. The χ^2 test was used for comparing nominal variables like gender. If any assumption for χ^2 use was not present, then a Fisher's exact test was performed. To compare three or more groups as in the case of BMI categories and disease severity, we used one-way ANOVA with the Bonferroni *post hoc* test; Kruskal-Wallis analysis was used as a nonparametric equivalent when necessary. Correlation analysis was carried out using the Pearson's or Spearman's correlation factor as needed. Multiple linear regressions were done using BMI as an outcome measure. A significance level of 0.05 was used throughout the study. All statistical analyses of data were performed with SPSS, version 16.0.

RESULTS

A total of 177 (43.5% female and 56.5% male) PD patients and 177 matched controls were included in the study. Healthy controls had a mean height of 1.6±0.08 m, while PD patients had 1.57±0.11 (p=0.09). Controls had a mean weight of 75.3±15.4 kg compared with 67.3±13.7 (p=0.02) in the PD Group. A statistically significant difference was found in BMI when comparing healthy controls and PD patients (29.1±5.4 *versus* 27.2±4.7, p<0.001).

In the Control Group, only three subjects (1.7%) were underweight, 33 (18.6%) had normal weight, 73 (41.2%) had overweight, and 68 (38.4%) were classified as obese.

In the PD Group, 2 (1.2%) patients were underweight, 58 (32.7%) were within normal limits, 83 (46.9%) had overweight, and 34 (19.2%) were obese. When comparing the PD Group with the Control one, the only statistically significant differences were obesity (p=<0.01) and normal weight (p<0.001) prevalence. Table compares the demographic data and anthropometric measures by gender.

The mean age of the PD sample was 64.8±12 years-old and age at diagnosis was 58.7±12.4 (mean disease duration was 6.3±5 years).

All patients were currently on anti-Parkinsonic treatment. One hundred and thirty-five patients (76.3%) were receiving levodopa (mean time of exposure of 6.2±5 years). Ninety-nine patients (65.9%) were on DA (83.8% on Pramipexole). Other treatments included amantadine (16.4%) and MAO-inhibitors (20.3%). Among patients on levodopa, the mean daily dose was 600.5±294.5 mg. Mean LEDD was 661.7±314. The DA-LEDD for those patients on Pramipexole or Rotigotine was 124.2±92.

The mean Hoehn and Yahr stage (HY) was 2.3±0.9. Ninety-one patients (51.4%) had mild disease (HY=1–2), 70 (39.5%) moderate (HY=2.5–3), and 16 (9.1%) severe disease (HY=4–5). Motor fluctuations, mainly wearing-off, were seen in 53 patients (29.9%), 31 (17.5%) showed freezing of gait, and 40 (22.6%) had peak-dose dyskinesia.

No correlation was found between BMI and age, duration of PD, total levodopa daily dose, LEDD, and DA-LEDD.

A mild inverse correlation was found between BMI and HY stage (r=-0.19, p=0.02).

Multiple linear regression using BMI as an outcome measure showed no significant covariates. Factors included in the model were age (p=0.66), gender (p=0.84), LEDD (p=0.77), levodopa daily dose (p=0.73), DA-LEDD (p=0.38), or HY stage (0.17).

Female PD patients had a slightly higher HY stage, however without reaching statistical significance (2.5±0.9 *versus* 2.2±0.9, p=0.06). No differences in BMI were found when comparing PD patients with or without dyskinesia (27.5±4.7 *versus* 27±4.6, p=0.58). Furthermore, we did not find differences regarding presence or absence of motor fluctuations.

Table. Clinical and sociodemographic characteristics of Parkinson's disease patients and controls by gender.

Demographic and anthropometric data	Female			Male		
	PD	Control	p-value	PD	Control	p-value
n	77	77		100	100	
Age (years)	65.6±12.3	65.3±12.9	0.90	64.1±12	63.2±12.4	0.78
Height (m)	1.49±0.07	1.56±0.07	0.01*	1.63±0.08	1.64±0.07	0.54
Weight (kg)	59.8±12.4	73.6±15.1	<0.001*	73.1±11.7	76.6±15.7	0.06
BMI	27±5.5	30.1±5.5	0.01**	27.3±3.9	28.3±5.2	0.11
Underweight	2 (2.6%)	2 (2.6%)	>0.9	0 (0%)	1 (1%)	>0.9***
Normal	27 (35%)	10 (13%)	0.002*	31 (31%)	23 (23%)	0.27
Overweight	34 (44.1%)	28 (36.4%)	0.41	49 (49%)	45 (45%)	0.67
Obesity	14 (18.2%)	37 (48%)	<0.001*	20 (20%)	31 (31%)	0.10

BMI: body mass index; PD: Parkinson's disease; student's *t* and χ^2 tests unless specified; *statistically significant; ** Fisher's exact test; ***Mann-Whitney U test.

DISCUSSION

According to the Organization for Economic Cooperation and Development, 30% of the Mexican population is obese[6]. The prevalence of obesity in our Control Group was 38.4%; women had higher prevalence than men (48 *versus* 31%). Participants in this study lived mostly in Mexico City and were predominantly of low incomes, both well recognized as risk factors for overweight/obesity in the Mexican population[10,11].

When comparing the BMI categories between controls and PD patients, there was a statistically significant difference in normal weight and obesity. The PD Group had a higher frequency of normal weight and less obesity.

The most likely explanation for our findings is the rightward shift of the weight distribution in Mexico. As noted, the BMI in PD patients in Mexico is lower than that of healthy controls, but still shifted to the right compared with other countries.

We can hypothesize that a higher body weight at the onset of disease may compensate for the losses produced by its progression. As a result, patients who were in the overweight category at the onset of the disease will display normal weight as the disease progresses. Conversely, patients who were obese at disease onset will progress to the overweight category; thus, the prevalence of overweight may remain comparable to healthy controls.

On the other hand, underweight was found in 1.2% of our sample. A study from North Italy that included 364 PD patients found only 3% of underweight, while 62% were overweight/obese. The authors suggested that this might be due to a high prevalence of overweight among the Italian population[12]. This finding may also apply to our population; moreover, our underweight prevalence clearly differs from the 15% reported in a North-East England PD population[13].

Beyer et al. reported an inverse correlation between BMI and disease severity[14]. Other studies have not found a correlation between BMI and severity or disease duration[15]. In our study, PD patients had a relative short disease duration (6.3±5 years), which can explain the lack of association with BMI. However, we found a low, but not statistically significant, difference in BMI regarding disease severity. Patients with moderate disease displayed a lower BMI; but since most of our sample had mild disease (68.7%, HY=1–2) we were unable to reach a conclusive result.

We found motor fluctuations in 29.9% and peak dose dyskinesia in 22.6% of our patients. It is known that disease duration is a more significant factor for developing dyskinesia than other factors, such as: gender, age of onset, body weight, absolute levodopa dose and levodopa dose per body weight kilogram[16]. We did not expect a significant prevalence of dyskinesia, as disease duration in our sample was relatively short. Nevertheless, our study did not show an effect of dyskinesia in BMI.

In regards to levodopa treatment, a cross-sectional study suggested that patients with low BMI probably receive a greater dosage of levodopa per kilogram of body weight[17]. Thus, the latter may constitute a putative factor in the occurrence of dyskinesia in these patients unless there is a concomitant reduction in levodopa dose. A correlation between daily dose of levodopa and BMI was not found, even when stratifying by levodopa dose per kilogram body weight and LEDD per kg.

In our study, 65.9% of the PD patients were on a DA (Pramipexole among 83.8%). A weak positive correlation was found between Pramipexole daily dose and BMI. Kumru et al. reported a significant weight increase in 28 PD patients after being treated with Pramipexole[18]. DA have been implicated in impulse control and compulsive behaviors in patients with PD. Specifically, compulsive eating has been reported in patients being treated with Pramipexole. Pramipexole discontinuation or dose-lowering remitted the behavior, and no further weight gain occurred[19]. Unfortunately, our study did not include any assessment of impulse control disorders, therefore we were unable to address the presence of this dopaminergic complication. Nevertheless, no correlation was found between DA-LEDD and BMI.

Finally, weight gain has also been reported as a complication of subthalamic nucleus deep brain stimulation (STN-DBS), however our study did not include patients with it.

Limitations of our study include the fact that the study population was a clinic-based, single center, non-random sample that may not be representative of the general Mexican population. This was a cross-sectional study therefore changes in BMI over time could not be assessed.

In conclusion, as expected, overweight and obesity are common among Mexican patients with PD; while underweight is almost negligible. Whether the high prevalence of overweight has an impact on other PD features, like sleep disorders and cognitive decline, should be addressed in future prospective studies.

References

1. Sheard JM, Ash S, Silburn PA, Kerr GK. Prevalence of malnutrition in Parkinson's disease: a systematic review. Nutr Rev 2011;69:520-532.
2. Van der Mack MA, Dicke HC, Uc EY, et al. Body mass index in Parkinson's disease: a meta-analysis. Parkinsonism Relat Disord 2012;18:263-267.
3. Bachmann CG, Zapf A, Brunner E, Trendwalder C. Dopaminergic treatment is associated with decreased body weight in patients with Parkinson's disease and dyskinesia. Eur J Neurol 2009;16:895-901.
4. Kim HJ, Oh ES, Lee JH, et al. Relationship between changes of body mass index (BMI) and cognitive decline in Parkinson's disease (PD). Arch Gerontol Geriatr 2012;55:70-72.
5. Walker R, Davidson M, Gray W. Gender differences in 1-year survival rates after weight loss in people with Parkinson's disease. Int J Palliat Nurs 2012;18:35-39.
6. Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. Lancet 2010;376:1775-1784.
7. Palacios N, Gao X, McCullogh ML, et al. Obesity, diabetes, and risk of Parkinson's disease. Mov Disord 2011;12:2253-2259
8. Sun Y, Chang YH, Chen HF, Su YH, Su HF, Li CY. Risk of Parkinson disease onset in patients with diabetes: a 9-year population-based cohort study with age and sex stratifications. Diabetes Care 2012;35:1047-1049.
9. Qiu C, Hu G, Kivipelto M, et al. Association of blood pressure and hypertension with the risk of Parkinson disease: the national FINRISK study. Hypertension 2011:57:1094-100.
10. Gutierrez LM, Llaca MC, Cervantes L, Velasquez Alva MC, Irigoyen ME, Zepeda M. Overweight in elderly Mexican women of a marginal community. J Nutr Health Aging 2001;5:256-258.
11. Barichella M, Marczewska A, Vairo A, Canesi M, Pezzoli G. Is underweightness still a major problem in Parkinson's disease patients? Eur J Clin Nut 2003;57:543-547.
12. Jaafar AF, Gray WK, Porter B, Turnbull EJ, Walker RW. A cross-sectional study of the nutritional status of community-dwelling people with idiopathic Parkinson's disease. BMC Neurol 2010;10:124.
13. Barichella M, Villa MC, Massarotto A, et al. Mini Nutritional Assessment in patients with Parkinson's disease: correlation between worsening of the malnutrition and increasing number of disease-years. Nutr Neurosci 2008;11:128-134.
14. Beyer PL, Palarino MY, Michalek D, Busenbark K, Koller WC. Weight change and body composition in patients with Parkinson's disease. J Am Diet 1995;95:979-983.
15. Walker RW, Howells AR, Gray WK. The effect of levodopa dose and body weight on dyskinesia in a prevalent population of people with Parkinson's disease. Parkinsonism Relat Disord 2011;17:27-29.
16. Sharma JC, Macnamara L, Hasoon M, et al. Cascade of levodopa dose and weight-related dyskinesia in Parkinson's disease (LD-WD-PD cascade). Parkinsonism Relat Disord 2006;12:499-505.
17. Zappia M, Crescibene L, Arabia G, et al. Body weight influences pharmacokinetics of levodopa in Parkinson's disease. Clin Neuropharmacol 2002;25:79-82.
18. Kumru H, Santamaría J, Valldeoriola F, Marti MJ, Tolosa E. Increase in body weight after pramipexole treatment in Parkinson's disease. Mov Disord 2006;21:1972-1974.
19. Nirenberg MJ, Waters C. Compulsive eating and weight gain related to dopamine agonist use. Mov Disord 2006;21:524-529.