Parkinson's disease and body mass index: too much or too little?

Doença de Parkinson e índice de massa corporal: excesso ou falta de peso?

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Parkinson's disease (PD) is the second most common degenerative disease, being characterized by the presence of motor and non-motor symptoms. The former include bradykinesia, rigidity, tremor and postural instability; the latter include depression, sleep disorders, hyposmia, constipation, cognitive dysfunction, dementia and body mass index (BMI) abnormalities[1]. The relationship between BMI and PD is very controversial. In 2010, Hawkes et al. defined a timeline for PD based on the Braak pathological staging (from stage 1 to 6) and suggested that different brain stem structures are involved in the prodromal phase (estimated to be 20 years)[2]. In stage 2, in which there is involvement of the coeruleus/subcoeruleus complex (CSC), the magnocellular portions of the reticular formation and the dorsal raphe nuclei, authors suggested that sleep disorder (REM sleep behavior disorder), depression and obesity are present[2]. A dysfunction in the CSC could cause obesity as a result of abnormalities in orexin signaling. Hu et al. studied the relationship between BMI and the risk of PD in a Finnish cohort in 2010[3]. They found that the risk of PD was twice as high in men with BMI over 30 than in those with BMI under 23, and that there was a 70% higher risk among women[3]. Palacios et al. published an interesting study in 2012 in which they investigated obesity, diabetes and risk of PD in 656 patients[4]. They concluded there is no relationship between obesity, measures of central obesity and diabetes and the risk of developing PD[4]. However, some studies suggest that patients with advanced PD present with malnutrition and lower BMI in relation to controls for several reasons, including the presence of dysphagia, dyskinesia, depression and cognitive problems[3-5]. Cassani et al. studied serum adiponectin levels in advanced-stage PD patients with body weight loss and found significantly higher levels of this protein in PD patients than in controls[6].

van der Marck et al. published a meta-analysis of BMI in PD in 2012[7]. This pooled data from seven studies and demonstrated that PD patients had a significantly lower BMI than controls, and that patients at Hoehn-Yahr stage 3 had lower BMI in comparison to patients at stage 2[7]. Fiszer et al. studied leptin and ghrelin concentrations (produced respectively in the adipose tissue and mainly in the stomach) in PD patients with weight loss[8]. The findings in this interesting study, in which plasma leptin levels were reduced and IGF-1 levels were elevated, confirm that altered plasma leptin concentrations are common in PD patients. Altered plasma concentrations of orexigenic and anorexigenic peptides (ghrelin and leptin, respectively) lead to alterations in the hypothalamic-pituitary axis[8]. However, PD patients who undergo neurosurgery for a deep brain stimulation (DBS) implant in the subthalamic nucleus can exhibit significant weight gain, underscoring the complex interaction between the hypothalamic-pituitary axis and the basal ganglia[3,5,7,9]. Markali et al. studied the role of ghrelin, neuropeptide Y and leptin in PD patients who had weight gain after DBS implant surgery[9]. They concluded that the introduction of a DBS implant in the subthalamic nucleus temporarily deregulated the hypothalamic secretion of neuropeptide Y and ghrelin, and that weight gain was therefore the result of increased production of ghrelin and leptin[9].

In the current issue of *Arquivos de Neuro-Psiquiatria*, Morales-Briceño et al. published a very interesting study about overweight PD patients[10]. The authors carried out a cross-sectional study with 177 healthy controls and 177 PD patients. Analyzing BMI, they found that overweight

and normal weight were more prevalent in the PD group than among controls. They concluded that overweight/obesity are common among Mexican patients with PD while underweight is almost negligible[10]. However, it should be noted that the PD patients in their study had a relatively short disease duration (6.3 +/- 5 years) and that the mean Hoehn-Yahr stage was 2.3 (+/- 0.9). None of the patients had DBS in the subthalamic nuclei. In the study, 65.9% of the PD patients were on dopamine agonists (83.8% on pramipexole). Although these agonists have been associated with overweight due to impulse control disorders, such as compulsive eating, the authors did not evaluate such disorders in their study[10].

Another important aspect of the study by Morales-Briceño et al. is that 90.9% of the patients had mild or moderate disease, and only 9.1% had severe disease, which potentially explains the lower frequency of underweight in this study[10]. In conclusion, the relationship between BMI and PD is still controversial, and obesity, normal weight and underweight can be present in different stages of the disease.

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