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Review Article

Obesity may increase the prevalence of Parkinson's Disease (PD) while PD may reduce obesity index in patients

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Abstract

Objective: Currently, Parkinson's disease (PD) is becoming more common among younger people of ages from 30 – 40 years. The incidence is higher among patients with higher body mass index (BMI), and some reports had it that Obesity is a risk factor for PD while some reported that there is no relationship between obesity and PD. PD patient at the time of diagnosis has an above-normal BMI but which goes below normal as the disease progresses. Therefore, it is essential to explore the relationship between PD and Obesity.

Methods: 349 outpatients and inpatients with PD were selected from Jiangsu University Affiliated People's Hospital from January 2014 to December 2018, while 74 inpatients with non-cerebrovascular illness in the same period were selected as the control group. According to Hoehn-Yahr grade, Parkinson's patients were divided into three groups. The height, weight, waist and hip circumference, total cholesterol (TC), Total Glycerol (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured and recorded. The relationship between the severity of Parkinson's disease and blood lipids was evaluated.

Results: The BMI of patients with PD in the early stage was higher than that of the control group, but lower than that of the control group in the late stage, and the level of blood lipid in the patients with early PD was significantly higher than that in the control group and patients with advanced PD, especially in TG. The waist circumference and hip circumference of the patients with early PD were higher than those in the control group, but there was no statistical difference.

Conclusion: i) Obesity may increase the prevalence of PD. ii) The BMI of patients with PD shows two-way changes in different periods. iii) The BMI is higher and cholesterol is more elevated in the early stage of patients with PD, while at the advanced stage of the disease, the BMI and lipid levels of the patients showed a downward trend, which may be associated with a metabolic syndrome associated with dopamine depletion.

More Information

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Keywords: Obesity; Body Mass Index (BMI); Prevalence; The duration diagnosed with PD [DDP]

Introduction

Following Alzheimer's disease, PD is the second most common age-related neurodegenerative disorder. The motor-related symptoms include bradykinesia, rigidity, tremor, and postural instability, while metabolic imbalances, psychiatric and cognitive disorders are typical of the non-motor symptoms [1]. Among the metabolic imbalances, several reports have correlated BMI and PD [2]. Despite pieces of evidence reported a rise in insulin resistance among PD patients, the mechanistic insights of this relationship are not fully understood. A finished study emphasized on the association of over 80% of its research at high risk of PD due to history of diabetes mellitus (DM) while adjusting BMI [2-5]. Diets rich in fat have been reported to be a risk factor for PD while unsaturated fatty acids have been described to reduce PD risk. Obesity has been associated with inflammation affecting metabolism [6-8]. In the treatment of obesity, chronic use of phenetamine, a sympathomimetic agent that acts on the presynaptic vesicles in the lateral hypothalamus, stimulating β2-adrenergic receptors hence increasing the level of Norepinephrine, dopamine and serotonin, was reported to

cause PD. On the other hand, acute overdose presented typical PD symptoms such as restlessness, tremors, hyperreflexia, confusion, hallucination, and schizophrenia [9-12].

Dopamine deficiency causes some symptoms in which weight loss or gain, Gastroesophageal reflux (GERD) diseases are part of the presenting symptoms [7,13-21]. Uncontrolled weight gain causes maladaptation of the brain and the activation of inflammatory pathway affecting the hormonal milieu which together impacts negatively the central nervous system (CNS). PD patients lack enough dopamine, it is understandable that they might react negatively to proper diet during the disease [22,23].

The DDP has been reported to affect the normal metabolic balance of the patient, and disease course tends to depreciate the metabolism, bringing about tremendous weight loss as the years goes by. However, there has been no much report that relates to DDP with BMI. In this study, it was therefore examined prospectively whether DDP has a relationship with the BMI change and if obesity is a risk factor for PD.

General Information and methodology

The study had 359 outpatients and inpatients with PD that were selected from Jiangsu University Affiliated People's Hospital from January 2014 to December 2018, and 74 in-patients with a non-cerebrovascular illness in the same period were selected as the control group. As in (Table 1). All patients met the 2017 international MDS diagnostic criteria for PD, whose levodopa test was positive, and the onset of PD is known to the neurologist. Moreover, parkinsonism cannot be diagnosed with PD, and patients with severe cardiovascular and cerebrovascular diseases, severe kidney and liver insufficiency, history of extracranial injury must be excluded. The diagnosis time of Parkinson's disease was estimated by the following: The time of first visit and diagnosis of Parkinson's disease. Or the time being identified by two neurologists according to typical clinical symptoms. DDP is equal to the time from diagnosis to evaluation of PD.

Table 1: General information on patients admitted for the study.

Variable	Category of variable distribution				
DDP					
Men	Control	≤ 24 m	25 - 72 m	73 – 120 m	> 120
No of cases	29	47	68	15	25
Mean years	66.11 ± 14.52	65.35 ± 8.39	69.18 ± 10.99	69.81 ± 9.09	73.17 ± 8.17
Women	Control	≤ 24m	25 - 72 m	73 – 120 m	> 120
No of cases	45	52	57	10	10
Mean years	68.74 ± 9.73	67.48 ± 7.22	66.26 ± 12.20	77.37 ± 11.54	79.87 ± 10.66
Stage and severity of Parkinson's disease					
Men	Control	H-Y1-2	H-Y2.5-3	H-Y4-5	
No of cases	29	93	38	12	
Mean years	66.11 ± 14.52	67.13 ± 9.45	70.33 ± 10.34	78.98 ± 11.23	
Women	Control	H-Y1-2	H-Y2.5-3	H-Y4-5	
No of cases	45	98	33	10	
Mean years	68.74 ± 9.73	67.88 ± 9.82	72.56 ± 9.34	80.11 ± 9.89	

Detailed patients' history was collated such as age, sex, onset time, assessment time, UPDRS score, Webster score, Hoehn-Yahr grading score, etc. According to Hoehn-Yahr grading, patients were divided as: early-stage (1 ~ 2 grades), middle stage (2.5 ~ 3 grades), and late-stage (4 ~ 5 grades). The total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured and recorded. The relationship between the severity of PD and blood lipids was evaluated. Two staff members checked all the data respectively, and the study passed the ethical review of the ethics committee of Jiangsu University Affiliated People's Hospital.

Patient's weight and heights were obtained using an electronic height weight BMI machine with ultrasonic body weighing scale following standard protocol (that is fasting, bare feet, light clothing, erect posture, back facing the opposite side while on full inspiration). The waist circumference refers to the horizontal perimeter that is the centre of the umbilicus and the hip circumference refers to the horizontal circumference, were both taken by a standard scale soft ruler. Blood samples were collected within 24 hours after the patient's height and weight were recorded. As shown in table 1.

Statistical analysis

SPSS 16.0 statistical software was used to analyse all the indexes. Standard tests and variance homogeneity test were carried out. The mean data were expressed by mean ± standard deviation (x ± s). Two independent sample t-tests were used for mean comparison, Spearman correlation analysis for univariate analysis, variance analysis for complete random design and multiple stepwise regression analysis for multivariate analysis.

Results

Patients with PD in early stage, not DDP less than 24 m, have a BMI higher than the control group. The BMI of patients whose onset time was less than or equal to 24 months or whose severity of PD was 1-2 in Hoehn-Yahr grade was analyzed. The results showed that the BMI of patients with PD within 24 months was higher than that in patients with non-cerebrovascular disease and non-PD, but there was no significant difference. The BMI of patients with Hoehn-Yahr grade 1-2 was higher than that of the control group, which was statistical difference. Shown on table 2.

BMI of PD patients decreased in the patients of DDP more than 120 m. All the patients collected were divided into less than or equal to 24 months group, 25 - 72 months group, 73 months - 120 months group, and more than 120 months group according to the time difference between the recording

Table 2: Effect of DDP on BMI in patients with PD within 24months and early-stage (*n*).

	Control	DDP ≤ 24 m	Hoehn-Yahr 1-2
Male	22.76 ± 4.28(29)	24.57 ± 3.78(47)	25.12 ± 4.87*(93)
Female	23.08 ± 5.01(45)	24.92 ± 4.17(52)	25.77 ± 3.76*(98)

*$p < 0.05$ *vs.* group

time and the onset time. The results showed that there was no significant change in the BMI of the patients in the first few years of diagnosis of PD, but as the disease progresses, the BMI of the patients decreased after 120 months, especially in women patients. As shown on table 3A.

Patients with PD in early stage, not DDP less than 24 m, have a BMI higher than control group. The BMI of patients whose onset time was less than or equal to 24 months or whose severity of Parkinson's disease was 1- 2 in Hoehn-Yahr grade was analysed. The results showed that the BMI of patients with PD within 24 months was higher than that in patients with non-cerebrovascular disease and non-Parkinson's disease, but there was no significant difference. The BMI of patients with Hoehn-Yahr grade 1 ≤ 2 was higher than that of the control group, and there was statistical difference. Shown on table 3B.

The blood lipid level of PD patients decreased with the course of disease. Blood lipids of patients with PD at different onset stages was analyzed, and the results showed that the total blood lipids, TG, Cholesterol and LDL decreased slightly after 72 months of the onset of PD especially in 120 months, and the changes were similar both in different gender, but more significant in women, as shown on table 4.

Patients with PD in early stage, not DDP less than 24 m, have a TG higher than control group. Blood lipids were measured in normal control group, DDP patients with PD less than 24 months and PD patients in early stage, respectively. The results showed that the cholesterol level of the patients whose Hoehn-Yahr grades were 1 - 2 was only higher than that of the control group, and there were no other abnormalities. Shown on table 5.

Table 3A: Effect of different DDP on BMI in patients (*n*).

DDP	≤ 24m	25-72 m	73-120 m	> 120 m
Male	24.57 ± 3.78 (47)	24.83 ± 4.17(68)	23.67 ± 3.57(19)	21.67 ± 3.79*(25)
Female	24.92 ± 4.17(52)	25.25 ± 4.78(57)	24.37 ± 3.48(10)	22.22 ± 3.56*(10)

*p < 0.05 vs DDP ≤ 24 m group;

Table 3B: Effect of DDP on BMI in patients with PD within 24months and early-stage (*n*).

	Control	DDP ≤ 24 m	Hoehn-Yahr 1-2
Male	22.76 ± 4.28(29)	24.57 ± 3.78(47)	25.12 ± 4.87*(93)
Female	23.08 ± 5.01(45)	24.92 ± 4.17(52)	25.77 ± 3.76*(98)

*p < 0.05 *vs.* control group

Table 4: Effect of different DDP on blood lipid levels in patients (n).

DDP	≤ 24 m	24 – 72 m	72 – 120 m	>120 m
Males				
TC	4.53 ± 0.46 (47)	3.89 ± 0.37 (68)	3.43 ± 0.27(15)	3.42 ± 0.36*(25)
TG	1.82 ± 0.18(47)	1.38 ± 0.14*(68)	1.56 ± 0.11(15)	1.40 ± 0.15(25)
HDL-C	1.19 ± 0.12 (47)	1.11 ± 0.21(68)	1.51 ± 0.17(15)	1.10 ± 0.11(25)
LDL-C	2.57 ± 0.27 (47)	2.31 ± 0.24(68)	1.94 ± 0.34(15)	1.95 ± 0.17*(25)
Females				
TC	4.61 ± 0.47 (52)	4.11 ± 0.43(57)	4.51 ± 0.23(10)	3.55 ± 0.34*(10)
TG	2.03 ± 0.22 (52)	1.43 ± 0.13*(57)	1.78 ± 0.45*(10)	1.02 ± 0.17*(10)
HDL-C	1.13 ± 0.11 (52)	1.20 ± 0.14(57)	0.99 ± 0.14*(10)	0.77 ± 0.11(10)
LDL-C	2.63 ± 0.31 (52)	2.42 ± 0.25(57)	2.88 ± 0.13*(10)	2.12 ± 0.24*(10)

*p < 0.05 *vs.* ≤ 24 m group.

Waist circumference of PD patients increased slightly in early stage, but decreased with the course of disease. Measuring the waist circumference and hip circumference of PD patients with less than 24 months, 25 - 120 months and more than 120 months in DDP respectively, we found that the average waist circumference of PD patients with DDP less than 24 months was higher than that of the control group, but there was no statistical difference. As the disease progresses, the waist circumference continues to decrease in both the male and female patients, which has a significant differences, but not hip circumference. There was no significant difference in waist-hip ratio. As shown on table 6.

BMI in PD is related to DDP and severity of PD. Pearson's correlation analysis was performed on the parameters and the result is as shown as expected, BMI showed a tremendous positive correlation with weight, which indicates that the two parameters are highly dependent on each other and as one increases the other increases as well. A similar trend is also observed with HY staging and time of diagnosis (DDP) with 0.746, followed by Webster score, DDP, weight and height. Most of the other parameters showed a negative correlation which signifies that as one increases the other decreases. However, the correlation is not so high except for the DDP and BMI with -0.569, from this result it can be ascertained that there is a 50% chance that years of diagnosis affects BMI. Shown on table 7.

Discussion

The rapid growth in China's economy caused an increase in Obesity risk factors for PD [23,24], and the prevalence was estimated as 18 per 100,000 people in a survey in Shanghai, China [23]. Age-adjusted rates give a more restricted range of 72-258.8 per 100,000 people. Most of the reports recorded an

Table 5: DDP ≤ 24 months and their level of blood lipid in patients(*n*).

	Control	DDP ≤ 24	Hoehn-Yahr 1-2
Males			
TC	4.14 ± 0.7(29)	4.53 ± 0.46 (47)	4.17 ± 0.39 (93)
TG	1.01 ± 0.13(29)	1.82 ± 0.18 (47)	1.63 ± 0.27* (93)
HDL-C	1.37 ± 0.45(29)	1.19 ± 0.12 (47)	1.13 ± 0.21 (93)
LDL-C	2.31 ± 0.7(29)	2.57 ± 0.27 (47)	2.42 ± 0.25 (93)
Females			
TC	4.21 ± 0.79(45)	4.61 ± 0.47(52)	4.34 ± 0.43 (98)
TG	1.09 ± 0.15(45)	2.03 ± 0.22(52)	1.79 ± 0.28*(98)
HDL-C	1.29 ± 0.51(45)	1.13 ± 0.11(52)	1.11 ± 0.11 (98)
LDL-C	2.57 ± 0.73(45)	2.63 ± 0.31(52)	2.51 ± 0.26 (98)

*p < 0.05 *vs.* control group

Table 6: Effect of DDP on WC and HC of patients with PD (*n*).

	Control	DDP ≤ 24m	DDP 25 ~ 120m	DDP > 120m
Males				
WC	82.3 ± 8.7(29)	86.8 ± 7.9 (47)	83.2 ± 7.8 (83)	74.5 ± 5.6*#(25)
HC	89.7 ± 9.3(29)	95.3 ± 9.5 (47)	91.2 ± 9.9 (83)	84.2 ± 6.9(25)
Females				
WC	74.5 ± 7.2(45)	82.3 ± 6.7* (52)	77.5 ± 8.8 (67)	66.4 ± 5.4*#(10)
HC	91.5 ± 9.4(45)	94.1 ± 9.2(52)	90.2 ± 9.3 (67)	86.3 ± 4.8(10)

*p < 0.05 *vs.* control group; # p < 0.05 *vs.* DDP ≤ 24m group

Table 7: Pearson's correlation showing the relationship between BMI and DDP.

Height	Weight	BMI	DDP	HY	Webster
1	0.463	0.157	-0.276	-0.010	0.016
0.463	1	0.899	-0.407	-0.393	-0.051
0.157	0.899	1	-0.569	-0.651	-0.184
-0.276	-0.407	-0.569	1	0.746	0.516
-0.010	-0.393	-0.651	0.746	1	0.160
0.016	-0.051	-0.184	0.516	0.160	1

overall crude report ratio of between males and females of all ages 100 and 200 per 100,000 people [25]. The pathology of PD is yet to be understood, but some studies showed that the risk factors were age, obesity, environmental toxins, genetics, physical inactivity [2,25,26]. In recent years, more and more studies have shown that obesity is a risk factor for PD [2,6,22]. However, there is a lot of controversy about the relationship between obesity and PD because overweight, normal weight, underweight can all be present in PD which is dependent on the individual and how well managed the disease is [2,6,7,21]. China has a growing population of extreme ages, and as PD is a disease most common to these age groups understanding the aftermath effect would help to not only reduce the risk factors but also prepare us to make a timely diagnosis and prompt treatment strategy.

The BMI and DDP in patients with PD are closely related and vary with course of disease. The results show that the BMI of patients with PD in early-stage is higher than that in control group, which suggests that BMI may increase the prevalence of PD. At the same time, the BMI of patients tends to decline as the disease progress, especially in patients who have been diagnosed for more than 120 months. Blood lipid levels, such as triglycerides, cholesterol, low-density lipoproteins, also exhibit similar trends. The results suggest that as the progress of the disease, the nutritional status of the patients shows a downward trend, which may be related to the down-regulation of nutrient metabolism by the dopamine pathway. Meanwhile, the waist circumference of patients with DDP more than 120 months was smaller than those of the control group and DDP less than 24 months. Pearson's correlation analysis indicates that any of the parameters can be taken on the patients. BMI is positively correlated with body weight, and negatively correlated with disease severity, followed by DDP. The pathological basis of PD lies in the loss of dopaminergic neurons and the reduction of dopamine. In the early stage of the disease, due to the patient's less activity, the existence of compensation mechanism, the nutrition absorption is too much, so that the overweight or obese people are more. As the disease progresses, dopamine is exhausted, which leads to the decline of digestive function and poor nutritional absorption ability [13-18]. In this study, advanced patients or those with more than 10 years of onset showed decreased lipid levels and decreased BMI. It can be considered that this hyperbolic pattern of obesity index is related to the metabolic syndrome caused by dopamine depletion.

Conclusion

In summary, the study suggests that: i) Obesity may increase the prevalence of PD. ii) The BMI is higher and cholesterol is more elevated in the early stage of PD. iii) The BMI of patients with PD shows two-way changes in different periods. Attention should be paid to these metabolic diseases that not only disrupt the system but also affect the medication used decreasing the chances of proper PD management. The neurologist should work hand in hand with endocrinologist and nutritionist to follow up on PD patients for appropriate management and prognosis.

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