Cardiovascular Autonomic Impairment in Parkinson Disease

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Abstract

Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor dysfunction and several non-motor features. Dysautonomia is a significant non-motor feature as well as a neuropsychiatric symptom.

Objective: To assess cardiovascular autonomic function in Parkinson patients.

Patients and Methods: Samples were collected from Al Kadhimiya teaching hospital and Baquba teaching hospital in a period lasts from 1st January to 1st November 2013. Cardiovascular autonomic function had been tested in 44 Parkinson patients with autonomic dysfunction, 23 Parkinson patients without autonomic dysfunction and 25 healthy matched controls; using Valsalva maneuver, 30:15 ratio, and effect of posture on blood pressure.

Results: The most frequent dysautonomic symptoms in parkinson disease were fainting and dizziness (postural hypotension) with a frequency of 26.8% with a P-value 0.015. The comparison between valsalva levels in three groups of study population was significant (P-value 0.04). The comparison between 30:15 ratio in three groups of study population was not significant statistically (P-value 0.344).

Conclusion: Cardiovascular autonomic dysfunction is a common non-motor symptom associated with Parkinson's disease. It may precede the development of the cardinal motor symptoms in PD, making cardiovascular dysfunction an attractive target for early detection and potential neuroprotective strategies for PD. Valsalva maneuver and effect of changes in posture on blood pressure are affecting tests in cardiovascular autonomic study.

Keywords: Parkinson's disease; autonomic symptoms, Non-motor symptoms; cardiovascular autonomic tests, orthostatic hypotension.

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Introduction

Parkinson's disease PD is the second most common neurodegenerative disorder of the central nervous system (CNS) after Alzheimer's disease [1].

It is a progressive disease resulting primarily from the death of dopaminergic neurons in the Substantia Nigra of the ventral midbrain [2]. A variety of genetic and environmental factors underlie this loss of brain cells. However, emergent research implicates oxidative stress, inflammation, and dysfunctional mitochondria as major contributors to neurodegeneartion in PD [3].

As it is known, PD affects movement, producing motor symptoms. Non-motor symptoms, which include autonomic dysfunction, neuropsychiatric problems and sensory and sleep difficulties, are also common [4]. Autonomic dysfunction in PD is due to the complex underlying pathophysiology of the condition affecting the catecholaminergic neurones of the ANS that includes degeneration and dysfunction of the nuclei mediating autonomic functions and degeneration of cholinergic, monoaminergic, and serotoninergic nuclei [5].

The main cardiovascular symptoms of autonomic disturbance is Postural symptoms (orthostatic hypotension), it may cause considerable problems at various stages of PD particularly in the advanced stages. It is defined as a fall in systolic blood pressure (BP) of $\geq$ 20 mmHg or in diastolic BP $\geq$ 10 mmHg on either standing or head-up tilt to at least 60^{o} within 3 minutes [6].

Symptoms related to orthostatic hypotension are mainly due to reduction of blood flow to various organs, especially the brain [7].

The main categorized tests of autonomic symptoms of cardiovascular system are designated as cardiovagal innervation (parasympathetic innervation) including; heart rate (HR) response to deep breathing, Valsalva ratio, and HR response to standing (30:15 ratio). In addition, tests related to adrenergic; beat-to-beat blood pressure (BP) responses to the Valsalva maneuver, and BP and HR responses to tilt-up or active standing [8].

While Valsalva ratio is derived from the maximal HR generated by the Valsalva maneuver divided by the lowest HR following the maneuver [9].

This study aimed to assess cardiovascular autonomic function in parkinson patients.

Patients and Methods

Seventy two patients with Parkinson's disease were included in the current study. Five patients were excluded because they had diabetes mellitus and ischemic heart disease). The rest 67 patients were divided into two groups:

Parkinson patients with autonomic dysfunction group who comprise 44 patients (32 males and 12 females with age ranging from 47 years old to 73 years old.

Parkinson patients without autonomic dysfunction group include 23 patients (17 males and 6 females aged with age ranging from 45 years old to 73 years old.

In addition to Normal healthy subjects group include 25 subjects (15 males and 10 females aged with age ranging from 44 years old to 68 years old..

Methods

All patients underwent the Autonomic tests of cardiovascular system

The tests include cardiovascular autonomic function (Valsalva maneuver, Thirty: Fifteen Ratio, blood pressure vartiation) using electrocardiograph recorder (ECG-101 Biocare, China) and sphygmomanometer (Germany).

Thirty: Fifteen ratio

The patient asked to change his position from a recumbent to a standing position. Then tachycardia normally occurs and is followed after about 20 seconds by a

bradycardia that reaches a relatively stable rate at about the 30th beat after standing [10].

Response to the Valsalva maneuver

The test is performed with the subject in a semirecumbent position with a rubber clip over the nose. The subject is then requested to blow into a mouthpiece (with a calibrated air-leak) connected to a manometer and to maintain an expiratory pressure of 40 mmHg for 15 seconds while the HR is recorded [11].

The Valsalva ratio is calculated by dividing the longest inter-beat interval occurring after the maneuver by the shortest inter-beat interval during it. The highest ratio from three successive attempts, each separated by 2 minutes, is recorded [12].

Blood pressure variation (Change in Posture)

The BP is recorded with the subject supine and at rest for at least 10 minutes. The patient then stands with the arm held horizontally to avoid the hydrostatic effect of the column of blood in the dependent arm that leads to a falsely elevated BP. The BP is taken immediately on standing and then at 1-minute intervals for 5 minutes [13].

In normal subjects a slight decline in systolic pressure may occur, and diastolic pressure typically increases slightly. A decline that is greater than 20 mmHg in systolic pressure or 10 mmHg in diastolic pressure within 3 minutes of gaining an upright posture generally is regarded as abnormal. [6]. After the patient has been supine for 10 minutes, the table is tilted to an angle of at least 60 degrees, and the patient remains in this upright position for 10 minutes.

Statistical Analysis

All statistical analysis was done by using Statistical package for Social Sciences (SPSS) version 19**.**

Results

All groups including Parkinson patients with and without autonomic dysfunction and control subjects; were studied demographically. The differences between the three groups in age, gender and BMI were statistically not significant, P- value > 0.05. The total dysautonomic features in Parkinson patients with autonomic dysfunction were shown in table 1. Most common features were fainting and dizziness (postural hypotension) (26.8%), GIT problem (25.8%), followed by urinary problem (15.9%).

Table (1): Total dysautonomic features in Parkinson patients with autonomic dysfunction.

Dysautonomic features	Number	%
Dizziness and fainting (postural hypotension)	27	26.8
GIT problem	25	25.8
Urinary problem	16	15.9
Sexual dysfunction	3	2.9
Sweating abnormality	8	7.8
Pupil reaction	2	1.9
Exercise intolerance	19	18.9
Total	100	100.0

Table 2 shows comparison between valsalva levels in three groups of study population using ANOVA test. The difference was statistically significant.

Table (2): The comparison between valsalva levels in three groups of study population (ANOVA test).

Study population	Valsalva Mean ± SD	P-value
Parkinson disease with dysautonomia	1.3 ± 0.5	0.047
Parkinson disease without dysautonomia	1.4 ± 0.5	
Control group	1.5 ± 0.6	

Post hoc test compare the measurement of valsalva between each two studied groups. The differences was statistically not significant, P> 0.05 as shown in Table 3.

Table (3): The comparison between valsalva between each two groups of study population by post hoc test.

Study population	Valsalva Mean ± SD	P-value
Parkinson disease with dysautonomia **Parkinson disease without dysautonomia**	1.3 ± 0.5 1.4 ± 0.5	0.914
Parkinson disease with dysautonomia **Control group**	1.3 ± 0.5 1.5 ± 0.6	0.036
Parkinson disease without dysautonomia **Control group**	1.4 ± 0.5 1.5 ± 0.6	0.441

According to Table 4, the comparison between 30:15 ratio levels in three groups of study population using ANOVA test which show that the statistical analysis not significant, P> 0.05.

Table (4): The comparison between 30:15 ratio in three groups of study population (ANOVA test).

Study population	30:15 ratio Mean ± SD	P-value
Parkinson disease with dysautonomia	1.3 ± 0.4	0.344
Parkinson disease without dysautonomia	1.4 ± 0.4	
Control group	1.4 ± 0.3	

Post hoc test compare the measurements of 30:15 ratio between each two studied groups. The differences was statistically not significant (P> 0.05) as shown in table 5.

Table (5): Comparison between 30:15 ratio between each two groups of study population (post hoc test).

Study population	30:15 ratio Mean ± SD	P-value
Parkinson disease with dysautonomia **Parkinson disease without dysautonomia**	1.3 ± 0.4 1.4 ± 0.4	0.107
Parkinson disease with dysautonomia **Control group**	1.3 ± 0.4 1.4 ± 0.3	0.120
Parkinson disease without dysautonomia **Control group**	1.4 ± 0.4 1.4 ± 0.3	0.326

Regarding table 6, the relationship between blood pressure status and the studied population. Fifty percent of patients with Parkinson disease with dysautonomia, 30.4% of patients with Parkinson disease without dysautonomia, and only 16.0% of control group had postural hypotension, the association was statistically significant, P< 0.05 using Chi square test.

Table (6): The comparison of blood pressure in three groups of study population (Chi square test).

Blood pressure	Parkinson disease with dysautonomia (No.= 44)	Parkinson disease without dysautonomia (No.= 23)	Control (No.= 25)	P-value
Postural hypotension	22 (50.0)	7 (30.4)	4 (16.0|)	0.015
Normal blood pressure	22 (50.0)	16 (69.6)	21 |(84.0)	
Total	44 (100.0)	23 (100.0)	25 (100.0)	

Discussion

From the collected data and statistical analysis, we revealed that the most frequent dysautonomic symptoms in parkinson disease were fainting and dizziness (postural hypotension) with a frequency of 26.8%. Then gastrointestinal tract symptoms of 25.8%. This concordance with the results suggested by Jain and Goldstein [14].

Regarding the comparison between valsalva maneuver in the three groups of study population that are (Parkinson's patients with dysautonomia , parkinson's patients without dysautonomia and the control groups), the difference was statistically significant. In addition, the comparison by post hoc test between 2 groups between repeatedly, shows a significant difference in comparison between parkinson's patients with dysautonomia and control groups. These results in agreement with Leńska and his colleague [15]. This may correlates that valsalva ratio tests the changes in cardiac vagal efferent and sympathetic vasomotor activity as a result of stimulation of carotid sinus and aortic arch baroreceptors and other intrathoracic stretch receptors. These centers are affected by dopamine depletion.

The comparison between 30:15 ratio levels in three groups of study population shows; the difference was statistically not

significant. Additionally, post hoc test between them shows no significant difference. These finding are in agree with Gurevich who studied it in 22 parkinson's patients with dysautonomia [13].

The results found out by means of measurement of orthostatic blood pressure test, shows a significant difference statistically which is given also by Perez and Metzler with their colleague. They presumed pathophysiology of postural hypotension is related to the pronounced vasomotor and cardiac sympathetic dysfunction in patients with PD was caused primarily by the impairment of preganglionic or postganglionic lesions, due to the neurodegenerative process of PD [16, 17].

Conclusion

Cardiovascular autonomic dysfunction is common in patients with PD across all stages of the disease and possibly pre-date the motor development of motor symptoms. Early recognition of these symptoms by the recommended tests may go a long way with the treatment in improving the quality of life of PD patients as well as the economic burden, as postural hypotension may cause medical problems like head injury that needs investigation and medical procedures which affects the economic status of the patients.

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