National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Autonomic cardiovascular regulation in Parkinson's disease by head-up tilt test - A cross-sectional study

Raksha Jaipurkar[1], Latika Mohan[2], Rajesh Tomar[3]

[1]Department of Physiology, Armed Forces Medical College, Pune, Maharashtra, India, [2]Department of Physiology, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India, [3]58 Forward Medical Stores Depot, C/O 99 APO

Correspondence to: Raksha Jaipurkar, E-mail: rakshukarade@gmail.com

Received: April 21, 2018; **Accepted:** May 15, 2018

ABSTRACT

Background: Autonomic failure is an integral component of Parkinson's disease (PD), and orthostatic hypotension (OH) is commonly observed in advanced cases of PD. OH may be the result of underlying cardiovascular autonomic dysfunction or adverse effect of antiparkinsonian drugs. Patients may be asymptomatic during the early stage of disease but may have underlying cardiovascular dysautonomia which becomes obvious on stress. Most of the earlier studies used morphological and functional methods to evaluate cardiovascular autonomic control but were unable to evaluate during dynamic conditions. **Aims and Objectives:** The aim of the study was to evaluate cardiovascular autonomic disturbances in patients with PD using head-up tilt table test (HUTT). The objective of the study was to compare the spectral profile of heart rate variability (HRV) and blood pressure (BP) to orthostatic challenges using HUTT in patients with PD with healthy individuals. **Materials and Methods:** In this cross-sectional study, we have recorded continuous lead II ECG along with BP every 2 min in patients with PD and control group during HUTT for 10 min in supine, 45 min in 70° tilt and again 10 min in supine position which were later analyzed using Biopac software for HRV. **Results:** Symptoms indicating autonomic nervous system dysfunction were present in 65% (20) patients with PD. Postural dizziness was present in 20% (6) patients. After 5 min of tilt-up, increase in HR in patients with PD was lower than in controls. There was no significant change in diastolic BP (DBP) on tilting-up in patients with PD while DBP significantly increased in controls on tilting-up from73 ± 9 mm Hg to 80±11 mm Hg ($P < 0.00001$). The low frequency (LF) was not significantly changed in patients with PD, and it increased significantly in controls from 3.05 (2.28 to 4.70) ms^2 to 3.73 (2.69–5.03) ms^2. There was decrease low frequency/high frequency (LF/HF) in patients with PD, but the change was not significant, and there was a significant increase in LF/HF ratio from 3.43 (3.15 to 4.02) to 5.01 (4.39–5.74) in control group ($P < 0.00001$). **Conclusions**: Patients with PD suffered from symptoms of autonomic dysfunction and had cardiovascular autonomic dysfunction which becomes obvious only during stress. This will help clinicians to identify the patients of PD with cardiovascular autonomic dysfunction at an early stage and modify the treatment accordingly to prevent frequent falls.

KEY WORDS: Parkinson Disease; Autonomic Dysfunction; Heart Rate Variability; Tilt-table Test

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2018.8.0413615052018	

INTRODUCTION

Autonomic failure is an integral component of Parkinson's disease (PD), and orthostatic hypotension (OH) can be an important clue to the underlying cardiovascular autonomic failure.[1] Dr. James Parkinson in his "Essay on shaking palsy" postulated a "mysterious sympathetic influence" in patients

with PD. Symptoms of autonomic dysfunction impact quality of life more than motor symptoms.[2] However, incidence and relevance of autonomic dysfunction in patients with PD are under debate. Some of the previous studies underestimated cardiovascular autonomic nervous system (ANS) impairment, which is diagnosed in only 30% cases. However, ANS involvement increases up to 70–80%, if sexual dysfunction, swallowing and gastrointestinal disorders, bowel and bladder abnormalities, and sleep disturbances are included.[3] The cause of autonomic dysfunction in PD may be due to damage to the hypothalamus, basal ganglia, reticular formation, nucleus coeruleus, and vagal dorsal nuclei. Besides, these pre-ganglionic structures, post-ganglionic sympathetic neurons and other autonomic structures are also affected.[4] The intracranial fossa arachnoid cyst causing focal mass effect was found to be causing parkinsonian tremors.[5]

Heart rate variability (HRV) spectral analysis has been widely used in the study of ANS. There are assumptions that the neurodegenerative characteristics of PD may be associated with indices of HRV.[6] Two major types of frequencies components are observed: Low frequency (LF) (0.04–0.15Hz) and high frequency (HF) (0.15–0.4Hz) components. HF fluctuations are modulated primarily by parasympathetic tone, whereas LF bands are affected by the sympathetic and parasympathetic activity.[7]

Head-up tilt test (HUTT) is primarily a provocative test used to determine an individual's susceptibility to orthostatic intolerance.[8] In patients with PD, the associated movement disorder with OH may enhance the propensity to falls, which might result in injury.[9] Prevalence of OH varies throughout the course of PD, ranging from 40% to 60%, and resulting in symptomatic OH in approximately half of the patients.[10] OH may be the result of underlying cardiovascular autonomic dysfunction or adverse effect of antiparkinsonian drugs. Patients may be clinically asymptomatic during the early stage of disease but may have underlying cardiovascular dysautonomia. It would be clinically relevant to identify such patient which will help the physician to modify the treatment accordingly to prevent falls due to dysautonomia in addition to a movement disorder.

Most of the earlier studies used morphological and functional methods to evaluate cardiovascular autonomic control but were unable to evaluate during dynamic conditions. The present study was designed to evaluate autonomic cardiovascular disturbances in patients with PD using HUTT. We compared the spectral profile of HRV and blood pressure (BP) to orthostatic challenges using HUTT in patients with PD with healthy individuals.

MATERIALS AND METHODS

A total 33 patients with PD including 24 male and 9 female patients fulfilling the unified PD rating scale clinical criteria, visiting the neurology department consecutively were included in the study. Patients were receiving regular antiparkinson's medication. Patients with cardiovascular disease involving rhythm disturbances, diabetes, and patients on medications that affect ANS were excluded from this study. 31 age and gender-matched healthy individuals were also evaluated as controls. A written informed consent was obtained from all participants after explaining study protocol. The study was approved by Institutional Ethics Committee.

The hydraulically operated metallic head-up tilt table of foot-board support design (7' × 3') was used for the study. It was calibrated for upright angles ranging from 60° to 90° with sensors to sense specific tilt angle. Transition from supine to tilt was smooth and rapid (10–15s). The participants were gently secured by straps to prevent falling. The digital BP recorder (HEM -722 Omron, Japan) was used to record HR and BP every 2 min with the help of stopwatch during the entire test. The computer equipped with software (Biopac [acknowledge 3.9, MP100], BIOPAC Systems Inc., Santa Barbara, CA, USA) was used to record ECG and HRV analysis. Emergency tray was kept ready to meet any untoward consequence that would result from the upright tilt of subject.

All patients with PD were examined with special attention being given to symptoms and signs referring to autonomic dysfunction. Mean duration of disease in patients with PD was 3.6 ± ±2.5 years. The participants were advised to refrain from drinking beverages containing alcohol and caffeine after 2100 h on the night before the day of the test. Participants were advised to have breakfast 2 h before the start of the test. We had informed patients to follow their medication routine as per directives of treating physician to avoid non-adherence, non-compliance, and regime modification of medication. HUTT was performed on the patients and control participants in standardized environmental conditions between 8 and 10 a.m.

Continuous ECG was recorded during entire procedure of HUTT which was later analyzed by Biopac Software for HRV. The recording in supine position was done for 10 min. The tilt table was tilted up at an angle of 70° angle for 45 min and then tilted back for further recording in the supine position for 10 min. Two patients were excluded because of recurrent arrhythmias during the recording of ECG during HUTT and technical reasons during ECG recording.

In the final analysis of the linear and non-linear components of HRV, the 5 min ECG segment just before tilt, 5 min segment from 5 to 10 min of tilt and only segments with >85% sinus beats were included.

Statistical Analysis

The paired and unpaired t-test was used to compare intragroup and intergroup BP and HR parameters which

were normally distributed. This data were represented as mean ± standard deviation (SD). Mann–Whitney U-test was used to compare HRV outcomes between two groups which were not normally distributed. This data were represented as a median and interquartile range. $P \leq 0.05$ was considered statistically significant. Analysis was performed by software SPSS (version 17.0; SPSS Inc, Chicago, IL).

RESULTS

A total of 31 participants in each group, i.e., patient and control group underwent HUTT. The mean age of the patients and control groups was 60.5 ± 11 and 60 ± 11 years, respectively. There were 22 males and 9 females participants in each group. The mean height of patients with PD was 164 ± 9 cm, and that of the control group was 166 ± 9 cm. The mean weight of patients with PD was 64 ± 10 kg, and that of the control group was 66 ± 10 kg. There was no significant difference in height and weight of both groups. The mean duration of disease in patients with PD was 3.6 ± 2.5 years. Of 3 patients with PD, 23 were taking medication levodopa (300 mg), 5 were taking ropinirole (12 mg), 1 was on bromocriptine (7.5 mg), and 2 were recently diagnosed cases.

Clinical Findings

A total of 65% of patients with PD had symptoms indicating ANS dysfunction. The most common complaints were disturbances in sweating (50%), urinary function (45%), and bowel function (35%). Postural dizziness was present in 20% patients. A total of 40% of male patients had suffered from impotence. In the clinical examination, signs of motor disturbances could be found in 65% of patients with PD, the most common finding being rigidity, bradykinesia, and tremors.

Cardiovascular Response to Tilt

The baseline cardiovascular parameters HR, systolic BP (SBP), diastolic BP (DBP), pulse pressure and mean arterial pressure (MAP) were similar in both the groups as shown in Table 1. After 5 min of tilt-up there was an increase in HR of both groups; however, increase in patients with PD was lower than in controls. In patients with PD, HR was increased to 72 ± 11 bpm and in the control group to 79 ± 14 bpm which was a significant increase in both groups. The difference in HR between the test and control groups after 5 min tilt-up was highly significant ($P < 0.000012$).

There was no change in SBP on tilting-up in patients with PD and SBP was increased from 122 ± 13 mm Hg to 126 ± 14 mm Hg in control group. The difference in SBP between two groups after 5 min of tilt-up was not significant ($P = 0.33$). There was no significant increase in DBP on tilting-up in patients with PD from 74 ± 9 mm Hg to 75 ± 10 mm Hg, and there was a highly significant increase in DBP on tilting-up in control group from 73 ± 9 mm Hg to 80 ± 11 mm Hg. The difference in DBP between both groups after 5 min of tilt-up was highly significant ($P < 0.0004$). There was no significant increase in the MAP in patients with PD from supine to tilt-up, while increase MAP in control was highly significant ($P < 0.00001$). The difference in the MAP between both groups after 5 min of tilt-up was significant ($P = 0.0025$).

HRV parameters: The HRV parameters of patient and control group are shown in Table 2.

Table 1: The cardiovascular parameters of patients of PD and control group at baseline and at 5 min of tilt-up, intergroup, and intragroup comparison

Parameters	PD patients (mean±SD)	Controls (mean±SD)	*P*		
			Intergroup comparison	Intragroup comparison - before and after tilt	
				PD patients	Controls
HR baseline (bpm)	70±11	68±10	0.45	<0.001	<0.001
HR 5 min tilt (bpm)	72±11	79±14	0.04*		
HR diff (bpm)	2±4	11±9	<0.001		
SBP baseline (mm Hg)	122±15	122±13	0.96	0.8	0.01*
SBP 5 min tilt (mm Hg)	122±16	126±14	0.33		
Diff SBP (mm Hg)	−0.3±13	4±8	0.15		
DBP baseline (mm Hg)	74±9	73±9	0.83	0.2	<0.001
DBP 5 min tilt (mm Hg)	75±10	80±11	0.05*		
DBP diff (mm Hg)	1±5	7±6	<0.001		
MAP baseline (mm Hg)	89±10	89±9	0.97	0.29	<0.001
MAP 5 min tilt (mm Hg)	90±17	95±10	0.11		
MAP diff (mm Hg)	0.3±8	6±6	0.0025*		

*$P \leq 0.05$ was considered statistically significant. PD: Parkinson's disease, SD: Standard deviation, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure

Table 2: HRV parameters of patients of PD and control group

Parameters	PD patients (mean±SD)	Controls (mean±SD)	*P*		
			Intergroup comparison	Intragroup comparison - before and after tilt	
				PD patients	Controls
LF baseline (ms^2)	3.06 (2.28–4.48)	3.05 (2.28–4.70)	0.6	0.15	0.05*
LF at 5 min tilt (ms^2)	2.65 (2.16–3.55)	3.73 (2.69–5.03)	0.008*		
HF baseline (ms^2)	0.71 (0.58–1.17)	0.94 (0.62–1.19)	0.28	0.17	0.08
HF at 5 min tilt (ms^2)	0.63 (0.52–0.86)	0.75 (0.53–1.09)	0.28		
LF/HF baseline	4.22 (4.09–4.36)	3.43 (3.15–4.02)	<0.001	0.9	<0.001
LF/HF at 5 min tilt up	4.20 (4.05–4.29)	5.01 (4.39–5.74)	0.009*		
SDNN baseline (ms)	0.03 (0.02–0.05)	0.03 (0.02–0.04)	0.95	0.02*	0.3
SDNN at 5 min tilt up (ms)	0.02 (0.01–0.03)	0.03 (0.02–0.04)	0.019*		

*$P \leq 0.05$ was considered statistically significant. PD: Parkinson's disease, HRV: Heart rate variability, LF: Low frequency, HF: High frequency, SDNN: Standard deviation of normal-to-normal RR intervals

LF: There was no significant difference in baseline LF in patients with PD and controls, respectively. After 5 min of tilt-up, LF was not significantly changed in patients with PD, and it was increased significantly in controls to 3.73 (2.69–5.03) ms^2, and the difference between two groups was highly significant ($P = 0.008$).

HF: The baseline HF in patients with PD and controls was 0.71 (0.58–1.17) ms^2 and 0.94 (0.62–1.19) ms^2, respectively. After 5 min of tilt-up, HF was decreased to 0.63 (0.52–0.86) ms^2 in patients with PD and decreased to 0.75 (0.53–1.09) ms^2 in controls. These changes were not significant. The difference in HF after 5 min of tilt-up in both groups was not significant ($P = 0.28$).

LF/HF ratio: The baseline LF/HF in patients with PD and controls was 4.22 (4.09–4.36) and 3.43 (3.15–4.02), respectively; and the difference was significant ($P < 0.0009$). After 5min of tilt-up, there was decrease LF/HF in patients with PD to 4.20 (4.05–4.29), but the change was not significant; however, in controls, there was significant increase in LF/HF ratio to 5.01 (4.39–5.74) and the difference in LF/HF ratio between both groups was highly significant ($P = 0.009$).

SD of normal-to-normal RR intervals (SDNN) - There was no significant difference in baseline SDNN in both groups. After 5 min of tilt-up, there was decrease in SDNN in patients with PD to 0.02 (0.01-0.03) ms. The difference in SDNN at 5 min in both groups was highly significant ($P = 0.019$).

DISCUSSION

The main findings of our study are (1) patients with PD showed symptoms of autonomic dysfunction; (2) there was no significant difference in supine cardiovascular and HRV parameters between patients with PD and healthy individuals; and (3) patients with PD showed a blunted response in the cardiovascular and HRV parameters after 5 min of 70° tilt as compared to healthy individuals.

Nearly 65% (20) of our patients had a disturbance in sweating, micturition, and gastrointestinal function. Postural dizziness was present in 20% (6) patients. Male patients very often had sexual disturbances as well. In the clinical examination, signs of motor disturbances could be found in 65% of the patients with PD, the most common finding being rigidity, bradykinesia, and tremors. These findings are consistent with the findings of previous studies.[11,12]

During the pre-tilt period, baseline HR and BP parameters of two groups were similar; i.e., cardiac autonomic and vasomotor control of patients with PD were not different from the healthy population. Shindo *et al.* found HR and BP at rest did not differ between PD patients and normal healthy subjects.[13] Turkka *et al.* measured the serum noradrenalin and found no significant difference in baseline serum noradrenaline between patients with PD and healthy individuals.[14] Mehagnoul-Schipper *et al*. also found similar resting HR and BP between patients with PD and control group.[15] A study by Barbic *et al*. showed that in the supine position, patients with PD showed similar cardiovascular, neural modulation as in healthy age-matched controls.[16] This is consistent with findings of our study.

After 5 min of tilt-up, there was significant increase in HR, DBP, and MAP in healthy individuals than patients of PD. Our results showed that there was very highly significant change in HR difference, DBP difference and MAP difference between pre-tilt and at 5 min of tilt-up in patients with PD and healthy individuals. These results indicate patients with PD showed blunted response in HR and BP as compared to the healthy population. The abnormalities of cardiovascular autonomic dysfunction became obvious on orthostatic stress. A study by Mesec et al. also showed that cardiovascular autonomic dysfunction manifest as suppressed HR and BP

responses to various autonomic provocations.[17] Our results are also consistent with earlier reports.[1,17,18] This blunted response in HR, DBP, and MAP to tilt-up in patients with PD as compared to healthy individuals may be correlated to the common origin of sympathetic nerve supply to the heart and blood vessels, which may be impaired in patients with PD. Autonomic failure in PD, therefore, seems to reflect a "triple whammy" of cardiac and extra-cardiac noradrenergic denervation and baroreflex failure.[19] Patients of PD did not show a significant drop in BP on tilt-up to define them as cases of OH. A study by Barbic *et al*. showed in the early stage of PD, inspite of the absence of OH, spectral analysis of HRV can determine the autonomic cardiovascular abnormalities in response to orthostatic stress.[16]

Our study showed no significant difference in pre-tilt LF and HF component in patients with PD and the control group while baseline LF/HF was higher in PD patients than the control group. On 5 min of tilt-up, there was a decrease in LF and HF component in patients of PD. There was an increase in LF component and a decrease in HF component in the control group. The LF/HF ratio minimally decreased in patients with PD, and the ratio was increased in the control group after 5 min of tilt-up. The increase in LF, decrease in HF and increased LF/HF, reflects a normal response to upright tilt as reported by Pagani *et al*. as well as a study by Mukai and Hayano.[20,21] There was the very high significant difference in LF and LF/HF ratio after 5 min of tilt-up between patient of PD and control group. The decrease in LF and HF and minimal change in LF/HF ratio in patients with PD on tilt-up indicates a blunted sympathovagal response in patients with PD.[22,23]

Disagreement exists in respect of the LF component of HRV. LF reflects baroreflex function independently of cardiac sympathetic innervation.[24] Some studies suggest that LF, when expressed in normalized units, is a quantitative marker for sympathetic modulations, other studies view LF as reflecting both sympathetic and vagal activity. High-frequency power relates to respiratory sinus arrhythmia and therefore to parasympathetic cardiovagal tone.[25] Consequently, the LF/HF ratio is considered by some investigators to mirror sympatho/vagal balance or to reflect sympathetic modulations.[26] Inability to increase LF/HF ratio on tilt up in patients with PD indicates impaired sympathovagal balance. The present observation of LF/HF ratio in HRV response to orthostasis appears to be consistent with reported changes in norepinephrine concentration and muscle sympathetic nerve activity.[13,27] Studies have indicated cardiac sympathetic denervation as a result of the loss of catecholamine innervations in the nigrostriatal system in the brain and sympathetic nervous system in the heart resulting in autonomic failure in PD.[19,28]

The time domain parameter SDNN was similar in both groups at pre-tilt position. There was decrease in SDNN in patients with PD while it was maintained in healthy population on tilt up. A study by Pal *et al*. showed baseline SDNN was significantly reduced in PD patients as compared to controls confirming cardiac autonomic dysfunction in these patients.[29] Mastrocola *et al*. showed abnormalities in the diurnal HRV in patients with PD on levodopa treatment. The SDNN and LF spectral power were lower in patients with PD than healthy controls during day and night, whereas the HF spectral power was lower only during night.[30] We also found suppression in the SDNN values and all the power spectral measurements in patients with PD on tilt-up, suggesting involvement of the ANS.

The knowledge of the influence of PD medication on autonomic regulation is based on the assessment of the effects of the acute administration of a drug, of the effects of short-time medication withdrawals, or of correlations of autonomic dysfunction to medication. For ethical reasons, in the present study, patients were studied under full regimen therapy that could not be modified before the protocol was performed. Another limitation of our study is that we have not compared the data between the patients with and without orthostatic intolerance/postural dizziness as we had a small sample size.

Autonomic dysfunction in patients with PD depends on the duration and severity of the disease. In this study, we have shown that patients with PD showed autonomic symptoms and cardiovascular autonomic dysfunction which becomes obvious only on stress.

CONCLUSION

Our study showed that patients with PD suffered from symptoms of autonomic dysfunction. Postural dizziness was present in 20% patients. There was no significant difference in cardiovascular autonomic function in patients with PD and normal healthy individuals in the supine position. Patients with PD showed blunted sympathovagal balance on tilt-up that means they had cardiovascular autonomic dysfunction which becomes obvious only during orthostatic stress. This has clinical significance in early detection of cardiovascular autonomic dysfunction in patients with PD, and it may help physicians in the management of patients to prevent frequent falls due to dysautonomia besides movement disorder.

REFERENCES

1. Senard JM, Raï S, Lapeyre-Mestre M, Brefel C, Rascol O, Rascol A, *et al.* Prevalence of orthostatic hypotension in parkinson's disease. J Neurol Neurosurg Psychiatry 1997;63:584-9.
2. Parkinson J. An essay on the shaking palsy 1817. J Neuropsychiatry Clin Neurosci 2002;14:223-36.
3. Zesiewicz TA, Baker MJ, Wahba M, Hauser RA. Autonomic nervous system dysfunction in parkinson's disease. Curr Treat

Options Neurol 2003;5:149-60.
4. Ferrer I. Neuropathology and neurochemistry of nonmotor symptoms in parkinson's disease. Parkinsons Dis 2011;2011:708404.
5. Babikr WG, Abdelraheem A, Aedh AI, Alshehr H, Elhusse AB. Cerebellar ataxia and parkinsonism owing to a couple of intracranial arachnoid cysts in a patient with multiple skeletal deformities. Int J Med Sci Public Health 2016;5:1742-4.
6. Yoon JH, Kim MS, Lee SM, Kim HJ, Hong JM. Heart rate variability to differentiate essential tremor from early-stage tremor-dominant parkinson's disease. J Neurol Sci 2016;368:55-8.
7. Kasanuki K, Iseki E, Fujishiro H, Ando S, Sugiyama H, Kitazawa M, *et al.* Impaired heart rate variability in patients with dementia with lewy bodies: Efficacy of electrocardiogram as a supporting diagnostic marker. Parkinsonism Relat Disord 2015;21:749-54.
8. Grubb BP, Kosinski D. Tilt table testing: Concepts and limitations. Pacing Clin Electrophysiol 1997;20:781-7.
9. Nakamura T, Hirayama M, Hara T, Mizutani Y, Suzuki J, Watanabe H, *et al.* Role of cardiac sympathetic nerves in preventing orthostatic hypotension in parkinson's disease. Parkinsonism Relat Disord 2014;20:409-14.
10. Isaacson SH, Skettini J. Neurogenic orthostatic hypotension in parkinson's disease: Evaluation, management, and emerging role of droxidopa. Vasc Health Risk Manag 2014;10:169-76.
11. Martignoni E, Pacchetti C, Godi L, Micieli G, Nappi G. Autonomic disorders in parkinson's disease. J Neural Transm Suppl 1995;45:11-9.
12. Chaudhuri KR, Healy DG, Schapira AH. Non-motor symptoms of parkinson's disease: Diagnosis and management. Lancet Neurol 2006;5:235-45.
13. Shindo K, Watanabe H, Tanaka H, Ohashi K, Nagasaka T, Tsunoda S, *et al.* Age and duration related changes in muscle sympathetic nerve activity in parkinson's disease. J Neurol Neurosurg Psychiatry 2003;74:1407-11.
14. Turkka JT, Juujarvi KK, Lapinlampi TO, Myllyla VV. Serum noradrenaline response to standing up in patients with parkinson's disease. Eur Neurol 1986;25:355-61.
15. Mehagnoul-Schipper DJ, Boerman RH, Hoefnagels WH, Jansen RW. Effect of levodopa on orthostatic and postprandial hypotension in elderly parkinsonian patients. J Gerontol A Biol Sci Med Sci 2001;56:M749-55.
16. Barbic F, Perego F, Canesi M, Gianni M, Biagiotti S, Costantino G, *et al.* Early abnormalities of vascular and cardiac autonomic control in parkinson's disease without orthostatic hypotension. Hypertension 2007;49:120-6.
17. Mesec A, Sega S, Trost M, Pogacnik T. The deterioration of cardiovascular reflexes in parkinson's disease. Acta Neurol Scand 1999;100:296-9.
18. Kim JS, Lee SH, Oh YS, Park JW, An JY, Park SK, *et al.* Cardiovascular autonomic dysfunction in mild and advanced parkinson's disease. J Mov Disord 2016;9:97-103.
19. Jain S, Goldstein DS. Cardiovascular dysautonomia in Parkinson disease: From pathophysiology to pathogenesis. Neurobiol Dis 2012;46:572-80.
20. Pagani M, Montano N, Porta A, Malliani A, Abboud FM, Birkett C, *et al.* Relationship between spectral components of cardiovascular variabilities and direct measures of muscle sympathetic nerve activity in humans. Circulation 1997;95:1441-8.
21. Mukai S, Hayano J. Heart rate and blood pressure variabilities during graded head-up tilt. J Appl Physiol 1995;78:212-6.
22. Vianna LC, Teixeira AL, Santos TS, Rodrigues GD, Bezerra LA, Soares PP, *et al.* Symbolic dynamics of heart rate variability in parkinson's disease patients with orthostatic hypotension. Int J Cardiol 2016;225:144-6.
23. Soares FH, Rodrigues S, Lopes PF, Felipe TR, Bezerra JC, Filho NT, *et al*. Measures of heart rate variability in patients with idiopathic Parkinson's disease. J Alzheimers Dis Parkinsonism 2013;3:130.
24. Rahman F, Pechnik S, Gross D, Sewell L, Goldstein DS. LF power reflects baroreflex function, not cardiac sympathetic innervation. Clin Aut Res 2011;21:133-41.
25. Moak JP, Goldstein DS, Eldadah BA, Saleem A, Holmes C, Pechnik S, *et al*. Supine low-frequency power of heart rate variability reflects baroreflex function, not cardiac sympathetic innervation. Cleve Clin J Med 2009;76 Suppl 2:S51-9.
26. Heart Rate Variability. Standards of measurement, physiological interpretation, and clinical use. Task force of the European society of cardiology and the North American society of pacing and electrophysiology. Eur Heart J 1996;17:354-81.
27. Turkka JT. Correlation of the severity of autonomic dysfunction to cardiovascular reflexes and to plasma noradrenaline levels in Parkinson's disease. Eur Neurol 1987;26:203-10.
28. Goldstein DS, Holmes C, Li ST, Bruce S, Metman LV, Cannon RO 3rd. Cardiac sympathetic denervation in Parkinson disease. Ann Intern Med 2000;133:338-47.
29. Pal P, Ganesan M, Sriranjini S, Datta K, Sathyaprabha T. Effect of a single dose of standard levodopa on cardiac autonomic function in Parkinson's disease. Neurol India 2011;59:659.
30. Mastrocola C, Vanacore N, Giovani A, Locuratolo N, Vella C, Alessandri A, *et al.* Twenty-four-hour heart rate variability to assess autonomic function in parkinson's disease. Acta Neurol Scand 1999;99:245-7.

How to cite this article: Jaipurkar R, Mohan L, Tomar R. Autonomic cardiovascular regulation in Parkinson's disease by head-up tilt test - A cross-sectional study. Natl J Physiol Pharm Pharmacol 2018;8(9):1287-1292.

Source of Support: Nil, **Conflict of Interest:** None declared.