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Original Research Article

Heart Rate Variability Assessment in Patients Suffering from Parkinson's Disease: A Cross-Sectional Observational Study

Meenakshi Sharma[1], Kapil Gupta[2], Sanjay Singhal[3], Himanshu Gupta[4]

[1]Sr. Professor, Department of Physiology, SMS Medical College, Jaipur
[2]Professor, Department of Physiology, SMS Medical College, Jaipur
[3]Professor, Department of Physiology, SMS Medical College, Jaipur
[4]Sr. Resident, Department of Physiology, Mahatma Gandhi Medical College, Jaipur

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Corresponding Author: Dr. Himanshu Gupta
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Abstract:

Introduction: Parkinson's disease (PD) is a common neurodegenerative disorder affecting patients in large numbers throughout the world**.** The prevalence of PD among the north Indian population is 67.71 per 100,000 individuals. Parkinson's disease (PD) is associated with autonomic nervous system dysfunction resulting in complications such as diabetes, obesity and hypertension. The objective of the present study was to assess such cardiac autonomic functions in PD patients and their subsequent comparison with healthy controls subjects via Time domain and Frequency domain parameters of heart rate variability analysis.

Methodology: The present study was conducted in the Department of Physiology, SMS Medical College, Jaipur wherein 40 PD patients (both males and females) were recruited from the Department of Neurology, SMS Medical College, Jaipur and 40 age- and gender-matched healthy subjects were selected from the hospital staff. Cardiac Autonomic functions were assessed by Time domain and Frequency domain of heart rate variability (HRV).

Results: Values of LF (ms^2), HF (ms^2) and Total power were significantly lower, whereas LF/HF Ratio was non significantly increased in cases as compared to controls. Time domain parameters (SDNN, RMSSD, Mean RR, and pNN50) decreased highly significantly in Parkinson's disease patients as compared to the healthy controls.

Statistical Analysis: Unpaired 't' test was applied for statistical analysis of data of both groups where P valve <0.05 was considered as statistically significant.

Conclusions: Our study indicated that patients with Parkinson's disease (PD) have blunted autonomic activity as evidenced by decreased values of both frequency and time domain parameters than healthy age and sex matched controls.

Key words: Parkinsonism, Heart Rate Variability, Frequency domain Parameter, Sympathetic Nervous system, Parasympathetic Nervous system

Introduction

With an ageing population globally, the burden of neurological disorders is rapidly increasing, posing a challenge to the sustainability of health systems, including in low-income and middle-income countries. [1] The burden of neurological disorders is also expected to increase in India due to the rapid demographic and epidemiological transition occurring in the country. [2]

The first and foremost description of Parkinson's disease (PD) was given by James Parkinson in early 19th century, But the knowledge about this disease has been present in India since ancient times. [3] Though the prevalence of PD in India is less compared to other countries, [4] the total burden of PD is much higher as a result of large population.

Parkinson's disease (PD) is associated with the cardinal features i.e., resting tremor, rigidity, bradykinesia, and gait disturbance. PD is an important degenerative disease because of its high prevalence and non-motor symptoms such as autonomic dysfunction [5]. Clinically significant dysfunction, such as orthostatic hypotension (OH) or postprandial hypotension, can occur in PD [6].

Orthostatic hypotension occurs in 20–50% of patients with PD and can contribute to falls and other accidental traumas [7,8]. Sympathetic failure in PD is common. OH, is one of the most frequent symptoms and the hallmark of sympathetic failure in a patient. [9] Parasympathetic dysfunction also frequently occurs in PD and it is manifested mainly as constipation, bladder disturbance, and cardiac autonomic dysfunction. These changes may reflect the pathological involvement of different components of the autonomic nervous system,

including loss of sympathetic cardiac innervation, [10] as well as deposition of Lewy bodies in sympathetic cardiac nerves and in the dorsal motor nucleus of the vagus. [11,12]

Brisinda et al. [11] evaluated autonomic nervous system dysfunction in PD and MSA in which they found Ewing's protocol scores were higher in MSA than in PD and controls.

The autonomic nervous system regulates many important functions in humans as blood pressure (BP), heart rate, thermoregulation, respiration, gastrointestinal, bladder, and sexual function.

Amidst the different noninvasive techniques for evaluating the autonomic status, HRV has emerged as a simple, noninvasive method to evaluate the sympatho-vagal balance at the Sino-atrial level and most widely performed measure of autonomic function. [13] This test generates a definite, sensitive and reproducible indirect measure of autonomic activity on cardiac function. Under frequency domain analysis (HRV frequency spectra), it is now known that HF component is attributed to parasympathetic influences on the heart and LF component is due to both parasympathetic nervous system (PNS) and sympathetic nervous system (SNS) activity. [14] Impact of the Parkinson's disease on cardiovascular function can be assessed using the HRV analysis. A better way for understanding the autonomic status short term HRV analysis is from a 5 min record of ECG.

Material and Methods

The present study was a hospital-based cross-sectional type of comparative, observational study conducted on 40 Parkinson's disease (PD) patients in the age group of 40–60 years and forty age- and gender- matched healthy controls. Diagnosed Parkinson's disease patients were recruited from the Department of Neurology, SMS Medical College and attached group of Hospitals, Jaipur, whereas Age- and gender-matched healthy controls were chosen from the employees working at SMS Medical College, Jaipur. Prior approval was obtained by the institutional ethics committee and institutional research review board. A written informed consent was obtained from all the subjects before commencing with any procedure.

Inclusion Criteria for (Case/Control) Group:

1. Diagnosed case of PD recruited from Neurology department SMS Medical College, Jaipur (for being included in Case group)
2. Apparently healthy subjects (for being included in Control group)
3. Aged 40-60 years.
4. Subjects who are cooperative and giving informed written consent.

Exclusion Criteria for both groups:

1. Acute or chronic illness (like Diabetes Mellitus, Hypertension etc.) known to affect ANS functions.
2. Person taking drugs (like Anticholinergic etc.) known to affect ANS functions
3. Smokers
4. Alcoholics.

After recording of subject information in general information section of proforma, recording of heart rate variability was done by polygraph (RMS Polyrite D, version 1.0) based on the principle of EKG. For short term analysis of HRV, ECG was recorded in the supine posture for 5 minutes after 15 minutes of supine rest in a quiet environment. The analogue ECG signals were converted to digital signal and stored in the computer offline for frequency and time domain analysis. In the frequency domain analysis, the power spectrum for HRV was calculated with the Fast Fourier Transformation (FFT) based method [14] using Kubois software.

Tools

Data collection was entered in pre organized structured proforma, which has following parts-

1. General information section: - this part of proforma include general information of subject like age, sex, address, socioeconomic status, any disease history, family history, drug history, physical examination: height, weight, BMI, resting blood pressure, resting heart rate.

2. Autonomic functions section:

Following parameters of HRV were included in the study:

A) Frequency domain HRV parameter

- Total power
- LF Power(ms^2)
- HF Power(ms^2)
- LF n.u. (normalized unit)
- HF n.u. (normalized unit)
- LF/HF ratio

B) Time domain HRV parameter

- SDNN
- Mean RR
- RMSSD
- pNN50

Statistical Analysis: Quantitative data were expressed as mean ± SD. The data were statistically analyzed using the Primer software version 6. The Unpaired 't'-test was applied for statistical analysis

of the results. Statistical significance was assigned at p value <0.05 and highly significant at p valve < 0.001.

Results

[Table 1] Shows the baseline characteristics of Parkinson's disease (PD) (Case) group and control groups. Anthropometric parameters (like Age, height, weight, and body mass index) did not show any statistically significant difference between the two groups. Values of LF (ms^2), HF (ms^2) and Total power was significantly lower ($p < 0.05$) whereas LF/HF Ratio was increased but not significantly in Parkinson's disease patients as compared to the controls [Table 2]. All time domain parameters (SDNN, RMSSD, Mean RR, and pNN50) decreased highly significantly in Parkinson's disease patients ($p < 0.001$) [Table 3].

Table 1: Anthropometric Parameters of Both Groups

Parameter	Groups (Means ± SD)		p Value	Signifi-cance
	Case Group (N-40)	Control Group (N-40)		
Age (yrs)	48.83 ± 6.44	47.9 ± 4.07	0.44	NS
Gender (M: F)	1.3 : 1	1.8 : 1		
Height (m)	1.65± 0.10	1.64 ± 0.11	0.39	NS
Weight (Kg)	61.60 ±14.40	61.05 ± 14.84	0.864	NS
BMI (Kg/m^2)	22.53± 5.01	22.63 ± 4.21	0.923	NS

Table – 1 Anthropometric parameters of Parkinson's disease (PD) (Case) group and Control group
NS- Non-significant.

Table 2: Frequency Domain Parameters of Both Groups

Parameter	Groups (Means ± SD)		p Value	Significance
	Case Group (N-40)	Control Group(N-40)		
LF (n.u.) %	61.49 ± 18.93	56.46 ± 16.12	0.205	NS
LF (ms^2)	143.13 ± 344.10	314.03± 182.50	0.003	**S***
HF (n.u.) %	38.10±18.81	43.39± 16.07	0.180	NS
HF (ms^2)	99.55± 197.44	215.20± 96.38	0.001	**S***
LF/HF Ratio	2.83 ± 3.20	1.759± 1.407	0.056	NS
Total power	473.25± 974.56	1082.83± 389.98	0.00021	**HS****

Table-2 Comparison of Frequency Domain Parameters of Parkinson's disease (PD) (Case) group and Control group

S*- Significant
HS**- Highly significant

Table 3: Time Domain Parameters of Both Groups

Parameter	Groups (Means ± SD)		p Value	Significance
	Case Group (N-40)	Control Group(N-40)		
SDNN	22.02 ± 14.61	51.68 ± 16.68	0.0001	**HS****
RMSSD	17.88 ± 18.06	48.68 ± 24.22	0.0001	**HS****
Mean RR	733.83 ± 120.37	830.97 ± 116.68	0.00	**HS****
pNN50	3.34 ± 10.94	17.43 ± 19.27	0.00	**HS****

Table-3 Comparison of Time Domain Parameters of Parkinson's disease (PD) (Case) group and Control group

S*- Significant

HS**- Highly significant

Discussion

The present study was an effort to discover the degree of autonomic dysfunction in patients of Parkinson's disease. The important findings of this study were blunting of autonomic activity with involvement of both parasympathetic and sympathetic division as evidenced by decreased values of both frequency and time domain parameters.

The pathological processes in Parkinson's disease involve both the sympathetic and parasympathetic nervous systems because Lewy bodies and neuronal degeneration have been found throughout the central autonomic network—that is, in the hypothalamus, locus coeruleus, dorsal vagal nucleus, and nucleus ambiguous, as well as in the intermediolateral column cells in the spinal cord, and in postganglionic sympathetic neurons in the prevertebral and paravertebral ganglia in addition to the dopaminergic striato-nigral pathway. [15] Thus, theoretically, cardiovascular dysregulation could relate to a central or peripheral

pathophysiology, which is also supported by our results indicating both sympathetic and parasympathetic dysfunction.

Haapaniemi TH et al. from their studies suggested that autonomic cardiovascular dysfunction in Parkinson's disease is multi-dimensional as as all the spectral components of HRV (VLF, LF and HF) were lower in Parkinson's patients than in the controls. [16]

Mastrocola C et al. after studying on 13 PD patients documented that the values of SDNN in PD are reduced significantly (about 56%) compared with the control group, while those of the LF parameter are reduced by about 75%. [17]

Alonso A et al., after conducting a prospective cohort study on PD patients found that low HRV assessed by time-domain measures (RMSSD, SDNN) is associated with increased risk of PD. No association was observed between frequency-domain measures of HRV and PD risk for which they suggested that alteration in frequency-domain measures may occur later in the course of the disease, once motor symptoms are evident whereas, time-domain measures of HRV are affected early in the pathogenesis of PD. Overall, they suggested that alterations in the cardiac autonomic system can precede the onset of motor symptoms and subsequent diagnosis of PD, and that information on HRV may help identify individuals at higher risk of developing PD. [18]

Pursiainen V et.al, after performing a study on 44 untreated PD patients showed that the impairment of the cardiovascular autonomic control mechanisms in PD is not limited to experimental reflex conditions, but causes a suppression of the HR variability that is particularly pronounced during the nighttime. In particular, the LF and HF power spectrum components of the HR variability were lower in the PD patients than in the controls. [19]

Ke JQ et. al., in their study found that sympathetic skin response (SSR) and HRV parameters (SDNN, pNN50, VLF, LF) were decreased in patients with PD. After analyzing the results of their study they suggested that both the SSR and HRV parameters are sensitive in determining the dysfunction of autonomic system not only in late but also in the early stage of PD, which can be used for early detection of autonomic dysfunction in patients with PD. [20]

The results of our study are similar to results of previous studies showing impairment of both sympathetic and parasympathetic division of autonomic nervous system suggesting a predominant dysfunction of central autonomic outflow in Parkinson's patients.

Conclusion

The findings of the present study indicate dysfunction of cardiac autonomic dysfunction as assessed by various HRV parameters. The early detection of these dysfunctions can be done by heart rate variability analysis which can result in timely detection and optimum management of severe consequences of cardiac autonomic dysfunction such as Ischemic heart disease, Peripheral vascular disease, and Myocardial infarction in PD patients.

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