Journal of
Alzheimer's Disease & Parkinsonism

Soares et al., J Alzheimers Dis Parkinsonism 2013, 3:4
DOI: 10.4172/2161-0460.1000130

Research Article Open Access

Measures of Heart Rate Variability in Patients with Idiopathic Parkinson's Disease

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Abstract

The aim of this study was to verify measures of heart rate variability in patients with idiopathic Parkinson's disease. Seventy two male participants volunteered for the study, 36 with diagnosed Parkinson's disease and 36 asymptomatic individuals. We conducted ambulatory recordings of 10 minutes in orthostatic position after five minutes of rest. Data was collected with POLAR RS800CX cardiac monitor and then analyzed by Kubios HRV 2.0 software to obtain measures of time and frequency domains. We found reductions in most part of collected indexes without correlation with disease duration or drugs dosage. The reductions of collected indexes reinforce the idea that Parkinson's disease alters the autonomic nervous system modulation.

Keywords: Parkinson's disease; Heart rate; Autonomic nervous system

Abbreviations: NN: NN Interval (Inter-Beat Interval); RMSSD: Root Mean Square of Differences Between NN Intervals; SDNN: Standard Deviation of NN Intervals; PNN50: Percentage of NN Intervals Greater than 50 ms (Milliseconds); FFT: Fast Fourier Transform; LF: Low Frequency; HF: High Frequency; LF/HF: LF An HF Ratio; ECG: Electrocardiogram; HRV: Heart Rate Variability

Introduction

Parkinson's disease is a neurodegenerative morbidity that leads to motor, psychiatric and sleep disorders. In terms of motor symptoms, postural instability, shaking, rigidity, and slowness of movements are the most common symptoms. There is loss of dopamine production in midbrain neurons, resulting in loss of dopaminergic innervations in the striatum [1]. In addition to an extra pyramidal motor dysfunction, patients frequently show Autonomic Nervous System (ANS) disorders, even in early phases of the disease [2].

This disease can promote autonomic dysfunction by damage in hypothalamus, basal ganglia, formatio reticularis, cerulean and nerve vagus dorsal nuclei [3-5]. Besides those pre-ganglia structures, post-ganglia sympathetic neurons and other ANS structures are also affected [6,7].

There are assumptions that the neurodegenerative characteristics of the disease may be associated with indexes of Heart Rate Variability (HRV). Changes in ANS in Parkinson's patients include perturbations in cardiovascular regulation, hypotension, especially in orthostatic position, and sexual dysfunction [8-10].

HRV indexes in time and cardiac frequency domains have proven useful measures in predicting cardiac arrhythmias, mortality risk by cardiac artery disease and various central nervous system disturbs, such as stroke, epilepsy, brain damages and other degenerative brain disease [11].

Recently, authors evaluated the cardiovascular autonomic regulation in patients in different disease stages using short duration measures and reinforced the method efficacy as non-invasive strategy [6]. Thus, the aim of this study was to verify measures of HRV in patients with idiopathic Parkinson's disease.

Materials and Methods

Seventy-two volunteer male participants were randomly selected in a university clinical center (UNP/Brazil). The sample included 36 patients with diagnosed Parkinson's disease (Parkinson Group PG) and 36 healthy individuals (Control Group=CG). We conducted measures of HRV using ambulatory recordings with 10 minutes of duration in orthostatic position, after a 5-minute rest period. The CG did not have any kind of neurologic or cardiac disorder. In addition, they did not use any kind of medication and had no genetic relation with the patients.

Heart rate variability (HRV)

We used POLAR RS800CX cardiac monitors to collect data, as there are close correlations with data obtained with electrocardiogram (ECG) [12,13]. Then, we analyzed the dataset with Kubios HRV 2.0 software. Analysis of time domain included NN intervals, SDNN, pNN50 and RMSSD. The frequency domain was analyzed by Fast Fourier Transform (FFT) and included Total Power (TP, 0-0.4 Hz), High Frequency (HF, 0.15-0.4 Hz), Low Frequency (LF, 0.04-0.15 Hz), LF and HF ratio (LF/HF), and Very Low Frequency (VLF, 0.003-0.04 Hz) [14]. The TP express the magnitude of the HRV in a global manner. HF an LF reflect the interaction between parasympathetic, sympathetic and vagal tonus, respectively.

Statistical analysis

All measures are presented by means and standard deviation. The comparisons were conducted with t Student test for independent values ($p<0.05$). Pearson's r was used for correlations analysis ($p<0.05$).

Results and Discussion

Table 1 shows participant's anthropometric and clinical

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Received August 19, 2013; **Accepted** November 19, 2013; **Published** November 22, 2013

Citation: Soares FHR, REBOUÇAS GM, Lopes PFF, Felipe TR, Bezerra JCL, et al. (2013) Measures of Heart Rate Variability in Patients with Idiopathic Parkinson's Disease. J Alzheimers Dis Parkinsonism 3: 130. doi: 10.4172/2161-0460.1000130

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characteristics. There was no evidence of peripheral or autonomic neuropathy, including postural hypotension. Rest heart rate, Systolic Blood Pressure (SBP) or Diastolic Blood Pressure (DBP) did not differ between groups. Body weight was significantly different between groups but we have no reason to believe that it interfered with the dependent variables [15,16].

The time domain of HRV in patients revealed accentuated reductions in RMSSD, SDNN, NN, pNN50 in comparison with CG in accordance with the literature [17]. The frequency domain revealed consistent reductions in LF, HF and LF/HF in PG, in contrast with elevations on the same indexes in the CG. There was no correlation between age and time or frequency domains in any group (Table 2).

Parkinson's is a slow-progression disease and is, in general, related with shaking, rigidity in body members, as long as rigidity in muscles and slowness of movements. Some evidences suggest that a combination between genetic and environmental factors may be placed as causes of those symptoms [18,19].

In addition, the deregulation of cardiovascular control may be related with the peripheral or central physiopathology of the Parkinson's disease [20]. Our findings support this hypothesis, once there were significant differences in HRV indexes between groups, denoting dysfunctions in the balance between sympathetic and parasympathetic control in cardiac activity.

Earlier studies with Parkinson's patients, using tests in cardiovascular reflexes, have demonstrated repressed responses of cardiac frequency for different stimuli, such as normal and deep breathing and Valsalva maneuver. Those findings describe autonomic responses, during only a limited period of time, with large individual variability, promoting a limited view of the autonomic mechanisms in control of cardiac activity [9,21,22].

	Parkinson Group	Control Group	*p*
	(n = 36)	(n = 36)	
	Mean ± SD	Mean ± SD	
Age (yr)	61.2 ± 3.9	58.9 ± 4.1	0.066
Body Weight (kg)	72.3 ± 6.6	78.8 ± 4.1	0.041
Stature (cm)	173.5 ± 3.9	175.7 ± 3.5	0.89
Time with disease (yr)	6.2 ± 2.9	-	-
Time with medication (yr)	4.7 ± 2.5	-	-
L-3,4-dihydroxyphenylalanine (mg/d)	250 ± 170.5	-	-
Rest heart rate (bpm)	76.5 ± 11.2	71.3 ± 13.8	0.058
Seated SBP (mmHg)	118 ± 2.3	120 ± 2.9	0.8
Seated DBP (mmHg)	76 ± 1.1	78 ± 1.5	0.712

Table 1: Participant's anthropometric, clinical and physiological characteristics.

Measures of Time Domain			
	Parkinson Group (n=36) Mean ± SD	Control Group (n=36) Mean ± SD	P
NN	343.2 ± 95.9	597.1 ± 111.7	0.001
PNN50	0.6 ± 1.3	2.7 ± 1.4	0.003
SDNN	40.7 ± 13.3	66.2 ± 19.2	0.009
RMSSD	6.2 ± 2.4	15.3 ± 3.9	0.004
Measures of Frequency Domain			
	Parkinson Group (n=36) Mean ± SD	Control Group (n=36) Mean ± SD	p
VLF	317.1 ± 93.9	338.5 ± 123.7	0.033
LF	34.6 ± 6.7	69.3 ± 11.8	0.003
HF	10.9 ± 3.9	18.2 ± 3.8	0.003
LF/HF	4.7 ± 1.1	7.9 ± 2.2	0.031

Table 2: Measures of HRV and statistical comparisons between groups.

The present study demonstrates that the investigated parameters of time domain were significant lower in Parkinson's patients suggesting an involvement ANS in the physiopathology of the disease.

Studies have demonstrated that a deficiency in cardiovascular autonomic control occurred in the beginning of the disease [23,24]. Researchers evaluated patterns of tonic cardiovascular control by lower results for SDNN and reported deregulation in new patients, even not treated, and advanced ones [25].

Our investigation corroborates with those studies concerning autonomic alterations. However, our findings do not support an association with disease duration.

Studies that utilized traditional HRV measures of the time domain and 24h spectral analysis concluded that the autonomic dysfunction was directly related with the duration and seriousness of the disease, age and drug use [17,26]. However, we did not find association among HRV parameters, age, time of drug use or medication dose.

Failure or deregulation of noradrenergic sympathetic innervations is potentially important, as orthostatic hypotension could be associated with dysfunctions in this system. Orthostatic hypotension itself could contribute for susceptibility for falling, and other traumatic accidents in patients, and its treatment, after an early diagnosis, may be important for Parkinson's disease patient's quality of life [27].

Here we advocate that HRV test is a valid, noninvasive, method that seems to be useful to evaluate autonomic dysfunctions as soon as they appear. We also demonstrate that HRV analysis, using time and frequency domains, in short duration (10 minutes), represents an alternative to more expensive and time demanding 24h analysis using ECGs.

Conclusions

Reductions in HRV indexes, associated with the disease, reflect loss of sympathetic and parasympathetic balance, which may be result of structural damage caused by Parkinson's disease. HRV, as non-invasive technique, might represent a strong indicator of neuronal regulatory activity. Its use can represent a useful tool, not only for research, but also for early diagnosis and clinical behavior of Parkinson's disease.

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