Original Research Article

Comparison of heart rate variability and classical autonomic function tests between type 2 diabetes mellitus and healthy volunteers

Rashmi Ramanathan[1], Mohan Jayabal[2],*, Manishankar Subramaniam[2], Vinothkumar Selvaraj[2]

[1]*Dept. of Phsiology, KMCH Institute of Health Sciences Research, Coimbatore, Tamil Nadu, India*
[2]*Dept. of Physiology, Karpagam Faculty of Medical Sciences, Coimbatore, Tamil Nadu, India*

A R T I C L E   I N F O

A B S T R A C T

Introduction: Heart rate variability is one of the diagnostic tests to assess the autonomic dysfunction in type 2 Diabetes Mellitus.

Objective: To compare the heart rate variability (HRV) and classical autonomic function tests between type 2 DM and healthy volunteers.

Materials and Methods: This study was conducted in 30 type 2 Diabetes mellitus patients and 30 healthy volunteers. Average age of diabetic patients was 48.53 ± 5.12 (mean $\pm$ SD) and that of volunteers was 47.10 ± 3.59 (mean $\pm$ SD). ECG recording was done in supine position for 5 minutes in computerized physiography. HRV analysis was done using Finland software. Classical autonomic function parameters such as deep breathing difference test, heart rate and blood pressure response to hand grip dynamometer test and valsalva ratio test were recorded in them.

Results: Statistical analysis was done using student's t-test. HRV showed statistically significant impairment between cases and controls ($p < 0.05$). Classical autonomic function test showed statistically very significant impairment between cases and controls ($p < 0.0001$).

Conclusion: HRV and Classical autonomic function tests reveals autonomic impairment in Type 2 DM, but classical autonomic function test findings showed very significant ($P < 0.0001$) impairment than HRV analysis ($P < 0.05$). So this study showed autonomic function tests are superior to HRV analysis.

1. Introduction

Type 2 DM is a metabolic disorder with high blood glucose either due to Insulin deficiency or Insulin resistance. Its incidence would be doubled by 2030.[1] Autonomic nervous system (ANS) innervates almost all organs of the body. ANS maintains homeostatic mechanism of various systems of the body. Autonomic dysfunction in diabetes is called diabetic autonomic neuropathy (DAN). DAN involves gastrointestinal, cardiovascular, genitourinary, sudomotor and metabolic systems.[2] Cardiac autonomic neuropathy (CAN) results in abnormal heart rate, orthostatic hypotension and silent MI. Decreased HRV is the initial indicator of CAN.[3] Sympathetic over activity increases heart rate and reduces cyclical beat to beat variation, whereas parasympathetic over activity decreases heart rate and increases beat to beat variation.[4]

Classical autonomic function tests and HRV are among the accepted methods for diagnosis of cardiovascular autonomic neuropathy in DM. assessment of HRV, hand grip dynamometer, valsalva technique; heart rate change to deep breath provides adequate details of sympathetic and parasympathetic function.

These clinical methods are used in diagnostic approach. The rhythm of the heart is controlled by ANS and it can be evaluated by beat to beat variation of R-R interval. Both HRV and classical autonomic function tests are non-invasive methods for assessing cardio-vagal function. HRV

* *Corresponding author.*
E-mail address: jmohan003@gmail.com (M. Jayabal).

is the most sensitive indicator for assessing sympathovagal imbalance of an individual at any given time.

2. Materials and Methods

This study was conducted in department of Physiology, PSG IMS&R. This was an observational type of study. 30 cases and 30 controls were included.

The cases were patients diagnosed with type 2 diabetes mellitus for 5 years duration in the age group between 41 to 60 years. The controls were normal healthy volunteers in the same age group. The cases were selected from diabetology OPD and endocrinology OPD according to the inclusion criteria. The controls were selected from medical OPD who were non diabetic healthy volunteers. Details of present history, treatment history were obtained.

The DATA collection tool is a protocol that has patient data, history, physical examination findings and investigation details. The subjects who fulfilled the inclusion criteria were taken for ECG recording for HRV analysis and autonomic function tests in the Physiology research laboratory, PSG IMS&R.

Heart rate variability analysis was done by recording electrocardiogram. It is a non-invasive procedure. Electrocardiograph was done for 5 minutes in a computerized physiography (NEVIQURE- Digital ECG recorder) in Lead 2. HRV analysis was done using Finland software. The resting autonomic activity was assessed by HRV. Two types of parameters are determined by HRV analysis which includes,

1. Time Domain parameters
2. Frequency Domain parameters.

2.1. Hand grip dynamometer

The subject was asked to stand for 5 minutes for the blood pressure and pulse to get stabilized and at the end of 5 minutes the subject was asked to grip the hand grip dynamometer as maximally as possible with the dominant hand and reading noted. Next the subject was asked to grip with the dominant hand at one third the maximal value and sustain at the level for one minute and the blood pressure recorded just before releasing the grip. The increase in diastolic blood pressure was noted.

2.2. Deep breathing test

In this test subject was asked to inspire deeply for 5 seconds and expire deeply for 5 seconds for 6 cycles. The ratio of shortest RR interval in inspiration to longest RR interval in expiration was calculated for each, which is called expiration-inspiration ratio (E/I ratio).

2.3. Valsalva ratio

This test was done by asking the subjects to forcefully exhale against a closed glottis into a tube connected to the sphygmomanometer and sustain the pressure at 40 mmHg for 15 seconds and ECG recorded. Valsalva ratio which is the ratio of the longest RR interval in phase 4 to the shortest interval in phase 2 was calculated.

2.4. Statistical analysis

The statistical analysis was done using SPSS software by independent Students 't' test, Analysis was done between the cases and controls. HRV and autonomic function test results were compared in both groups.

Values were expressed as Mean $\pm$ SD.

$P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Comparison of age between cases and controls

The mean age of cases was 48.53 ± 5.12 and for the controls was 47.10 ± 3.59. There was no significance in age between cases and controls as the p value was 0.2741.

3.2. Comparison of time domain measures between cases and controls

3.2.1. Mean RR

The mean RR interval of cases was 0.75 ± 0.09 and for controls was 0.80 ± 0.1. There was significant difference in mean RR between cases and controls as the p value was < 0.05.

3.3. Mean HR

The mean HR of cases was 81.16 ± 10.9 and for controls was 75.56 ± 8.9. There was significant difference in mean HR between cases and controls as the p value was < 0.05.

3.4. SDNN

The mean SDNN of cases was 27.84 ± 15.97 and for controls was 35.62 ± 16.64. The difference in SDNN between cases and controls were significant as the p value was < 0.05.

3.5. RMSSD

The mean RMSSD of cases was 20.61 ± 16.81 and for controls was 28.65 ± 18.23. The difference in RMSSD between diabetics and non - diabetics were significant as the p value was < 0.05.

3.6. Comparison of frequency domain measure between cases and controls

3.6.1. Very low frequency (VLF) power %

The mean VLF % of cases was 86.71 ± 10.70 and for controls was 78.32 ± 18.54. The difference in VLF % between cases and controls was significant as the p value was < 0.05.

3.6.2. Low frequency (LF) power %

The mean LF % of cases was 15.95 ± 13.07 and for controls was 9.88 ± 8.51. There difference in LF % between cases and controls was significant as the p value was < 0.05.

3.6.3. High frequency (HF) power %

The mean HF % of cases was 5.14 ± 6.95 and for controls was 4.82 ± 2.41. The difference in HF % between cases and controls was significant as the p value was < 0.05.

3.6.4. LF/HF Ratio

The mean LF/HF ratio of cases was 3.64 ± 1.6 and for controls was 2.14 ± 0.95. There was significant difference in LF/HF ratio between cases and controls as the p value was < 0.01.

3.7. Comparison of autonomic function tests between cases and controls

3.7.1. Diastolic blood pressure (DBP) rise after hand grip between cases and controls

The mean rise in DBP after hand grip in cases was 3.20 ± 1.54 and for controls was 10.13 ± 1.89. There was significant rise in DBP after hand grip in controls when compared to cases and the p value was < 0.0001 which is highly significant statistically.

3.7.2. Heart rate rise after hand grip between cases and controls

The mean rise in heart rate after hand grip in cases was 6.47 ± 2.27 and for controls was 11.00 ± 2.45. There was significant rise in heart rate after hand grip in controls than cases as the p value was < 0.0001.

3.7.3. Deep breathing difference in cases and controls

The mean deep breathing difference in cases was 1.099 ± 0.05 and for controls was 1.255 ± 0.11. There was significant difference in E/I ratio between cases and controls as the p value was < 0.0001.

3.7.4. Valsalva ratio between cases and controls

The mean Valsalva ratio in cases was 1.20 ± 0.12 and for controls was 1.40 ± 0.05. There was significant difference in Valsalva ratio between cases and controls as the p value was < 0.0001.

Table 1: Comparison of age between cases and controls

Parameter	Group	Mean ± SD	P Value
Age(yrs)	Cases	48.53 ± 5.12	0.2741*
	Controls	47.10 ± 3.59	

*Statistically not significant

Table 2: Comparison of time domain measures between cases and control

Parameter	Group	Mean ± SD	P Value
SDNN (ms)	Cases	27.84 ± 15.97	< 0.05*
	Controls	35.62 ± 16.64	
RMSSD	Cases	20.61 ± 16.81	< 0.05*
	Controls	28.65 ± 18.23	
	Controls	11.06 ± 17.28	

*Statistically significant

Table 3: Comparison of frequency domain measure between cases and controls

Parameter	Group	Mean ± SD	P Value
VLF power	Cases	86.71 ± 10.70	< 0.05*
	Controls	78.32 ± 18.54	
LF power	Cases	15.95 ± 13.07	<0.05*
	Controls	9.88 ± 8.51	
HF power	Cases	5.74 ± 6.95	< 0.05*
	Controls	4.82 ± 2.41	
LF/HF ratio	Cases	3.64 ± 1.6	<0.01**
	Controls	2.14 ± 0.95	

* Statistically significant.
**Statistically very significant

Table 4: Comparison of autonomic function tests between cases and controls

Parameter	Group	Mean ± SD	P Value
DBP rise After hand Grip	Cases	3.20 ± 1.54	< 0.0001*
	Controls	10.13 ± 1.89.	
Heart rate rise After hand grip	Cases	6.47 ± 2.27	< 0.0001*
	Controls	11.00 ± 2.45	
E/I ratio	Cases	1.099 ± 0.05	< 0.0001*
	Controls	1.255 ± 0.11	
Valsalva ratio	Cases	1.20 ± 0.12	< 0.0001*
	Controls	1.40 ± 0.05	

*Highly statistically significant

4. Discussion

Various epidemiological and pathological studies states diabetes is an independent risk factor for cardiac disorders both in men and women[5] In diabetes 65% of death is due to cardio vascular disorders. Myocardial infarction occurs without any preceding symptoms in diabetes[6]

Autonomic innervation is a primary control mechanism regulating HRV and cardiac performance. Chronic elevated

blood glucose promotes progressive autonomic neural dysfunction which parallels the development of peripheral neuropathy. Neuropathy is first seen in the long fibers, hence in diabetes the early feature of autonomic dysfunction is parasympathetic denervation because vagus is the longest nerve.

In normal persons the heart rate has a high degree of beat to beat variability and HRV changes with respiration, increases during inspiration and decreases during expiration[7].HRV denotes the individual's autonomic tone and frequency domain measures are considered as best quantitative method for sympathetic and parasympathetic activity.

A predominance of parasympathetic activity causes bradycardia and increase beat-to-beat variation, whereas increased sympathetic tone induces tachycardia and reduce beat-to-beat variations in HRV. High beat-to-beat variation is desirable and lower beat-to-beat variation is an established predictor of cardiac mortality and morbidity. Abnormal HRV predicts the cardiovascular etiology for mortality, coronary atherosclerotic development and cardiac arrhythmias.

Mean RR interval was less and mean HR was more in cases than controls which shows significant decreased parasympathetic activity in cases. SDNN and RMSSD were significantly lower in cases than controls. These findings show that high frequency variations in heart rate are less and vagal modulation of the autonomic nervous system is decreased.

In this study diabetic subjects were having both autonomic nervous system dysfunctions. It was found out that sympathetic as well as parasympathetic systems were altered in diabetes mellitus. Both autonomic function tests and heart rate variability showed significant changes compared to normal subjects.

The frequency domain measures like VLF power, LF power and LF/HF ratio were high in cases than controls. This shows that sympathetic activity is more in cases. The mean heart rate of the cases (81.16 ± 10.9) is higher than the controls (75.56 ± 8.9) which are due to increase in sympathetic tone associated with decrease in parasympathetic tone. This finding is well correlated with previous studies.[8,9]

Deep breathing test which is specific for parasympathetic activity was also done in this study. This study found that E/I ratio is less in cases than controls. Hence in diabetics the parasympathetic impairment is significant. This finding is similar t o study done by Sundkvist et al.[10]

Valsalva ratio test in this study showed decrease in cases than controls. Valsalva ratio is more sensitive test for both sympathetic and parasympathetic activity. This study showed impairment of autonomic system in which parasympathetic impairment was more than sympathetic impairment. Our finding correlated with other studies.[11].

This study gives a solid evidence of impairment of cardiac autonomic activity with dysfunction of both sympathetic and parasympathetic systems with slightly more impairment of parasympathetic system.

5. Conclusion

Time domain measures of HRV showed significant parasympathetic impairment in cases compared to controls. The frequency domain measures showed increased sympathetic activity and decreased parasympathetic activity. The diastolic blood pressure rise and heart rate rise after hand grip was very less in cases than controls. This finding showed the decreased sympathetic vasomotor efferent tone.

In deep breathing test E/I ratio and Valsalva ratio were less in cases compared to controls. These finding showed impairment of both sympathetic and parasympathetic systems in cases.

Compared with HRV, Classical Autonomic function tests showed very significant impairment ($P < 0.0001$) of autonomic functions in diabetics than impairment shown by HRV ($P < 0.05$). This study concludes classical autonomic function tests are superior in assessing autonomic functions than Heart rate variability (HRV).

6. Source of Funding

7. Conflict of Interest

None.

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Author biography

Rashmi Ramanathan Associate Professor

Mohan Jayabal Associate Professor

Manishankar Subramaniam Tutor

Vinothkumar Selvaraj Tutor