Research Paper

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The Autonomic Dysfunction in Type 2 Diabetes Mellitus by Spectral Analysis of Heart Rate Variability and its Clinical Significance

Medicine

KEYWORDS : autonomic dysfunction diabetes mellitus heart rate variability

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ABSTRACT

Diabetes mellitus(DM) is the most common endocrine and metabolic disorder found in the humans. DM occurs throughout the world, which is a major burden for health care facilities in all countries. This study is to find out the autonomic dysfunction in type 2 diabetes mellitus by spectral analysis of heart rate variability and compare HRV between type 2 diabetes and normal volunteers.

Time domain measures of HRV showed significant parasympathetic impairment in cases as compared to controls. Parasympathetic modulation is decreased in cases.

These patients are prone to develop cardiovascular complications like arrhythmias and atrial fibrillations. This finding is significant in risk prevention

INTRODUCTION

The ANS controls functions of the involuntary organs of the body that includes heart, blood vessels, exocrine glands, endocrine glands and visceral organs.1

Heart Rate Variability (HRV)

Heart rate variability is a common procedure to assess the autonomic variations in humans for clinical studies. Autonomic nervous system is evaluated by using HRV in the form of time-frequency representation2.

HRV analysis is based on the measurement of the interval between R-R waves. Many research articles have been published pertaining to HRV. Fast Fourier Transformation (FFT) is the most commonly used spectral analysis method3.

HRV and Diabetes Mellitus

Clinical manifestations of autonomic impairment in diabetes will appear long after the onset of DM, but subclinical cardiac autonomic neuropathy manifested as changes in HRV is detected early in type 2 DM8. Reduced HRV is associated with inflammation and is an early sign of macrovascular disease which includes carotid artery atherosclerosis. CAN are associated with adipose tissue inflammation in persons with type 2 DM4. Persons with postprandial elevated blood glucose have been shown to have lower HRV even before the onset of DM5.

Parasympathetic tone may decline further with autonomic imbalance, moving towards sympathetic drive during progression of pre-diabetic state to type 2 DM6

MATERIALS AND METHODS

30 cases and 30 controls were included.

The duration of the study was one year.

Heart rate variability analysis:

It was done by recording electrocardiogram. It is a non-invasive procedure. Electrocardiograph was done for 5 minutes in a computerized physiograph (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

The Time Domain parameters:

- Mean RR (NN)
- SDNN
- RMSSD

Frequency Domain Parameters:

- Low frequency power (LF)
- High frequency power (HF)
- LF norm (nu)
- HF norm(nu)
- LF/HF power ratio

RESULTS

The HRV parameters (Time domain measures and the frequency domain measures) were compared between the cases and controls.

p value of < 0.05 was considered as significant.

1. Comparison of time domain measures between cases and controls

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.

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.

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

MSSD:

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.

NN50:

The mean NN50 of cases was 22.03 ± 42.21 and for controls was 32.13 ± 45.44. There was no significance in NN50 between cases and controls as the p value was 0.38.

pNN50: The mean pNN50 of cases was 6.74 ± 14.40 and for controls was 11.06 ± 17.28. There was no significance in pNN50 between cases and controls as the p value was 0.29.

Comparison of frequency domain measure between cases and controls:

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.

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.

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.

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.

Parameter	Group	Mean ± SD	P Value
VLF power Controls	Cases	86.71 ± 10.70	< 0.05*
	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	

Table - 1 Comparison of frequency domain measure between cases and controls:
*** Statistically significant.**
****Statistically very significant**

DISCUSSION

Diabetes mellitus is a group of metabolic diseases with high blood glucose due to lack of insulin or insulin resistance which leads to classical features of polyuria, polydipsia, and polyphagia.

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.

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. 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.

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.

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. A significant number of cases showed NN50 and pNN50 equals 0. These finding emphasizes that adjacent NN intervals differing by more than 50 ms is zero. Hence the high frequency variations in heart rate in these patients were zero. So the vagal activity is very less. These patients are high risk persons for cardiovascular complications like arrhythmias and atrial fibrillation. This finding is significant in risk prevention.

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. In diabetes parasympathetic dysfunction is more compared to sympathetic dysfunction. Hence sympathetic to parasympathetic ratio is increased.

In most of the controls the LF/HF ratio is more than 1, showing sympathetic dominance, which could be stress related but when it is compared to diabetics it is not significant because LF/HF ratio is much more than controls. The primary cause for high LF/HF ratio in diabetics is parasympathetic dysfunction than sympathetic dominance.

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[10, 51]. Hence from the above finding, it is evident that both good and poor glycemic control had no significant difference in autonomic dysfunction. Even good glycemic control patients had similar autonomic impairment as that of poor glycemic control patients. With the help of HRV analysis and autonomic function tests, subjects who are at risk of cardiac complications are found out and early intervention can be done to prevent morbidity and mortality due to diabetes.

CONCLUSION

Time domain measures of HRV showed significant parasympathetic impairment in cases compared to controls. Parasympathetic modulation is decreased in cases. These patients are prone to develop cardiovascular complications like arrhythmias and atrial fibrillation. This finding is significant in risk prevention.

The frequency domain measures showed increased sympathetic activity and decreased parasympathetic activity. This is evident in LF/HF ratio. The high LF/HF ratio is due to reduced parasympathetic activity and increased or impaired sympathetic activity.

Clinical significance

Orthostatic Hypotension:

In diabetes mellitus, orthostatic hypotension develops because of damage to sympathetic vasomotor outflow fibers, mainly splanchnic vascular bed. Symptoms include faintness, weakness, giddiness, visual dysfunction and even syncope.

Silent Myocardial Infarction:

In diabetes the subject cannot appreciate the ischemic pain

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which can impair early recognition of myocardial infarction, hence delaying appropriate treatment. The possible mechanisms for painless myocardial ischemia are impaired pain thresholds, sub -threshold ischemia not sufficient to induce pain and dysfunction of the afferent cardiac autonomic nerve fibers. So it is essential to test cardiovascular autonomic function during assessment of diabetics with coronary artery disease

Cardiac autonomic neuropathy

Cardiac autonomic neuropathy results from injury to the autonomic nerve fibers which innervate the heart and blood vessels which results in altered heart rate control and vascular dynamics. Decreased heart rate variability is the initial indicator of cardiac autonomic neuropathy. HRV has become widely accepted method for diagnosis of cardiac autonomic neuropathy in DM.

Advanced assessments like cardiac sympathetic imaging, microneurography, occlusion plethysmography and baroreflex sensitivity are used nowadays in research but may be used in clinical assessment near future.

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