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Autonomic dysfunction in type 2 diabetes mellitus by using spectral analysis of heart rate variability

KEYWORDS

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ABSTRACT *Diabetes mellitus (DM) is the most common endocrine and metabolic disease of humans.*

DM is classified generally in to 2 types

1. Type 1 diabetes also called insulin dependent DM (IDDM) is caused by lack of insulin secretion.

2. Type 2 diabetes also called non insulin dependent DM (NIDDM) is caused by decreased sensitivity of tissues to the metabolic effects of insulin. This is called as insulin resistance2.

. DM occurs throughout the world, which is a major burden for health care facilities in all countries4. To study the autonomic dysfunction in type 2 diabetes mellitus by spectral analysis of heart rate variability. Compare HRV analysis between type 2 diabetes and normal volunteers. In this study the important finding is from comparing autonomic dysfunction with different HbAIc levels . Hence from this study we found that, if a person develops diabetes irrespective of the glycemic control he continues to have autonomic impairment

Introduction

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

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 representation.

HRV analysis has become an important tool to depict autonomic nervous system (ANS), because of its regulation based on functions of sympathetic and parasympathetic nervous system. The first clinical application of HRV was brought about by Hon and Lee in 1965. They observed that there is alteration in inter beat intervals before occurrence of any alteration in heart rate itself.

Reduced HRV is associated with aging and impaired autonomic activity. Different types of autonomic neuropathy also increased the risk of sudden cardiac death.

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 DM[8]. 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 DM[9]. Persons with postprandial elevated blood glucose have been shown to have lower HRV even before the onset of DM.

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

MATERIALS AND METHODS

50 cases and 50 controls were included.

The duration of the study was one year.

Heart rate variability analysis:

The resting autonomic activity was assessed by HRV. Two types of parameters are determined by HRV analysis which includes,

Time Domain parameters

- Frequency Domain parameters

- The Time Domain parameters:

Mean RR (NN) This is the average of all NN intervals. It is inversely proportional to mean heart rate at a given physiological state and indicates sympatho-vagal imbalance.

SDNN

It is the standard deviation of all NN intervals. This is a measure of total variability. When considered for a short period of time, it reflects HRV in low and high frequency ranges.

NN50

It is the number of pairs of adjacent NN intervals differing more than 50 ms.

PNN50

It is the proportions of NN50 divided by total number of NNs. This is an estimate of high frequency variation in heart rate.

RMSSD

The square root of the mean of the sum of the squares of differences between adjacent NN intervals. This is an estimate of high frequency variations in heart rate and hence a measure of vagal response.

Frequency Domain Parameters:

Low frequency power (LF)

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LF spectrum is presented in the range from 0.04 to 0.15 Hz This band can reflect both sympathetic and parasympathetic tone.

High frequency power (HF)
HF power spectrum is presented in the range from 0.15 to 0.4 Hz. This band reflects vagal tone.

LF norm (nu)
Low frequency power in normalized units. LF/(Total power – VLF) X100

HF norm(nu)
High frequency power in normalized units. HF/(Total power – VLF)X100

LF/HF power ratio:
The LF/HF ratio is used to study the coordinated functioning between sympathetic and parasympathetic tone. A decrease in the score indicates either decrease in sympathetic tone or increase in parasympathetic tone.

Values were expressed as Mean ± SD.
$p < 0.05$ was considered to be statistically significant.

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.

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.

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

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.

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[9]. HRV denotes the individual's autonomic tone and frequency domain measures are considered as best quantita-

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tive 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.

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. 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.

In this study the important finding is from comparing autonomic dysfunction with different HbAIc levels . Hence from this study we found that, if a person develops diabetes irrespective of the glycemic control he continues to have autonomic impairment.

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