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Original Research Article

Nonlinear Analysis (Poincare Method) of Heart Rate Variability in Type 2 Diabetes Mellitus Patients

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Abstract

Introduction: Diabetes Mellitus is a chronic metabolic disorder and poses a major medical health burden. The incidence of type 2 diabetes mellitus is increasing globally. Diabetes results in autonomic neuropathy associated with early vagal withdrawal, and increased sympathetic tone. The objective of the present study was to assess cardiac autonomic functions in type 2 diabetes mellitus (DM 2) patients using Nonlinear analysis (Poincare method) of Heart rate variability analysis.

Methods: The Present study was performed in Department of physiology including 50 patients of type 2 Diabetes Mellitus (Cases) and 50 Healthy Age, Sex and BMI matched subjects (age range 35-50 years) after obtaining approval from institutional ethics committee of SMS Medical College, Jaipur. SD1, SD2 and SD1/SD2 parameters were used as nonlinear analysis (Poincare analysis) of heart rate variability.

Results: Significant decrease of SD1/SD2 and non-significant decrease in SD1 and increase in SD2 was observed in diabetics as compared to healthy controls. No Significant changes were observed in heart rate and blood pressure between DM 2 patients and healthy subjects.

Statistical Analysis: Unpaired t test was applied for statistical analysis of data of both groups where P valve <0.05 considered as statistically significant.

Conclusions: Nonlinear analysis (Poincare plot method) can be used as an effective method for early diagnosis of cardiac autonomic neuropathy.

Keywords: Nonlinear Analysis, Poincare Plot Method, Heart Rate Variability, Type 2 Diabetes Mellitus (DM 2).

Introduction

Diabetes Mellitus is a chronic metabolic disorder and poses a major medical health burden. The incidence of type 2 diabetes mellitus is increasing globally [1]. Diabetes results in autonomic neuropathy and is associated with early vagal withdrawal, increased sympathetic tone and subsequently leading to sympathetic denervation and finally complete autonomic denervation [2-5]. The development of cardiac autonomic neuropathy in diabetes results in disruption of chief component of cardiovascular regulation, contributing to an elevated

incidence of cardiovascular diseases such as heart attack, unexpected cardiac death, and silent ischemia [6-9].

Heart rate is dynamically regulated by using intrinsic and extrinsic control systems, maintaining homeostasis. The most important extrinsic control is supplied through the autonomic nervous system. Heart rate variability (HRV) is a measure of the fluctuation within the interval between sequential sinus heartbeats, and reflects cardiac autonomic regulation [10-12].

Early diagnosis of autonomic diabetic neuropathy is difficult and the detection techniques available, e.g., the Ewing test Battery, are cumbersome and feature poor sensitivity and reproducibility. In contrast, HRV evaluation is noninvasive, more sensitive and the input records are received through conventional electrocardiography (ECG) [13-16]. However, because of the nonlinear dynamics of heart rate, conventional time and frequency domain parameters of HRV would not appropriately measure the nonstationary characteristics of ECG. [17-19] Non-linear method reflects interactions of central neural and autonomic nervous system [19].

Nonlinear techniques together with the Poincaré plot, detrended fluctuation analysis (DFA), tone/entropy analysis and HR complexity analysis are newly developed equipment used for identifying nonlinear patterns inside ECG data [19].The Poincaré plot is a scatter plot of RRn vs. RRn+1 in which RRnis the time among successive R peaks and RRn+1 is the time among the following two successive R peaks .Poincare plot reflects the non-linear dynamics of HRV[20] and entire RR time series in a single diagram [21]

In this study, we have used Poincare analysis to study the differences in HRV patterns between patients suffering from Type 2 diabetes mellitus and healthy controls. The motive of this study was to identify new parameters useful for detecting autonomic dysregulation in diabetes mellitus.

Method

The present study is a cross-sectional, comparative, observational study. The study was started after obtaining approval from institutional scientific and ethics committee. The study subjects include 50 patients of type 2 Diabetes Mellitus in the age range of 35-50 years with duration of disease of more than 2 years (Cases). 50 Healthy Age, Sex and BMI matched subjects were selected as controls. Individuals suffering from any acute or chronic illness other than diabetes mellitus were excluded from the study. Alcoholic, Smokers and persons taking drugs affecting cardiac autonomic functions were also excluded from the study.

Experimental protocol

The study subjects were asked to report to autonomic function laboratory of department of physiology for heart rate variability studies between 9AM to 12Noon. Informed written consent was taken from the subjects prior to performing heart rate variability. At test day, subjects were asked to come with light breakfast and were instructed to avoid caffeinated beverages, nicotine and vigorous physical activity 12 hours before the test. The temperature of the testing room was maintained at around 25°C throughout the procedure. Detailed clinical history and examination was done including recording of anthropometric parameters such as height and weight and body mass index (BMI) was calculated as per formulae-Weight (Kg)/Height(m2). The procedure of recording Heart rate variability was explained to subjects to alleviate anxiety. Resting heart rate and blood pressure was recorded using automated blood pressure monitor after taking rest for 10 minutes in sitting position. After 5 minutes of supine rest, lead II electrocardiography (ECG) was recorded for 5 minutes using RMS

Polyrite D (version 1.0). The analog signal is converted to digital signal at sampling frequency of 256 Hz and band pass filter of 2 Hz to 40 Hz. Guidelines of Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (19) were followed during recording of HRV. From the RR tachogram Poincare plot analysis was computed using Kubios 1.0 software (Bio-signal analysis Group, Finland) and the following parameters were noted.

1.SD1 - Standard deviation of short-term instantaneous beat-to- beat RR interval variability, represented by minor axis of the ellipse in the poincare plot diagram.

2.SD2 - Standard deviation of the long-term R-R interval variability represented by major axis of the ellipse in the poincare plot diagram.

3.SD1/SD2: Ratio of SD1/SD2. [22]

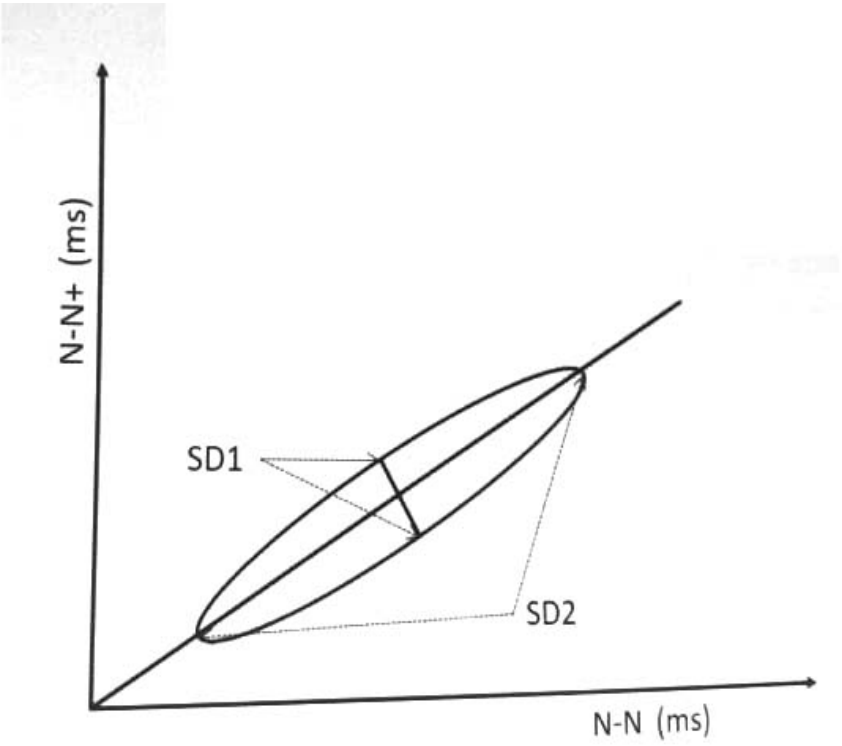

Fig.1 Poincare plot diagram

Statistical analysis

All parameters were expressed as mean ± standard deviation. The comparison between cases and control groups was performed by unpaired student t test by using primer software. All analyses were two-tailed and a significance level of $p<0.05$ was used in the study.

Results

The results of nonlinear analysis (Poincare analysis) of Heart rate variability were compared between the cases (Type 2 Diabetes Mellitus patients) and healthy age matched controls. Demographic profile of the patients and the controls were depicted in Table 1. There was no significant difference in values of the demographic parameters among cases and controls. The cardiovascular parameters of cases and controls were shown in Table 2. No significant changes in cardiovascular parameters were observed between both groups. Table 3 shows Poincare plot parameters of heart rate variability of study population. Significant decrease of SD1/SD2 and non-significant decrease in

SD1and increase in SD2 was observed in diabetics as compared to healthy controls.

Table 1: Demographic profile of study population

S.N.	Parameter	Diabetes mellitus patients (cases) Mean ± SD	Healthy controls Mean ± SD
1	Age (Years)	44.76 ± 5.09	44.90 ± 5.20
2	Gender (M/F Ratio)	4:1	3.7:1.3
3	Height(m)	1.63 ± 0.08	1.62 ± 0.09
4	Weight(kg)	72.88 ± 12.01	71.64 ± 13.08
5	BMI (Body mass index) (kg/m^2)	27.44 ± 4.77	27.47 ± 5.86

Table 2: Cardiovascular parameters of study population.

S.N.	Parameter	Diabetes mellitus patients (cases)Mean ± SD	Healthy controls Mean ± SD
1	Resting Systolic blood pressure (mmHg)	115.04 ± 9.04	114.56 ± 10.86
2	Resting Diastolic blood pressure (mmHg)	73.00 ± 7.35	73.24 ± 8.65
3	Resting Heart rate (Beats per minute)	77.52 ± 6.39	80.78 ± 9.85

Table 3: Poincare plot parameters of heart rate variability

S.N.	Parameter	Diabetes mellitus patients (cases)Mean ± SD	Healthy controls Mean ± SD
1	SD1(ms)	22.76 ± 24.78	31.29 ± 26.19
2	SD2(ms)	49.08 ± 51.45	46.82 ± 53.78
3	SD1/SD2	0.62 ± 0.77*	1.32 ± 1.87

*** Significant**

Discussion

Type 2 Diabetes mellitus is a chronic metabolic disorder with various complications. (1) One of the prominent complications is diabetic neuropathy and cardiac autonomic neuropathy (CAN) is a common manifestation of it (5). The fundamental pathology in CAN is hyperglycemia [5] and its activation of redox and/or multiple metabolic (Polyol aldose reductase) pathways because of hyperglycemia induced oxidative stress, alteration of Na +/K+-ATPase pump function, calcium disturbance and low grade inflammation. [5.23, 24] This, in conjunction with reduced blood flow to nerve fibers, contributes to CAN [2]. Involvement of parasympathetic nervous system occurs early due to long length of vagal fibres and involvement of sympathetic system is late phenomenon. [25]

Increased SD1values represent increased parasympathetic activity as there is a positive association of with RMSSD (time-domain analysis parameter of parasympathetic activity) (17). Similarly, SD2 can be used as a surrogate marker of sympathetic activity because of the positive relationship between SD2 and Low Frequency (LF) (Frequency domain parameter, which denotes sympathetic activity) [26]. Also Available evidences have reported the similarity of SD2/SD1 ratio with LF/HF ratio (marker of sympathovagal balance) [27, 28].

In present study, significant decrease in SD1/SD2 ratio was observed in patients of type 2 diabetes mellitus as compared to healthy controls suggesting a tilting of

sympathovagal balance towards increased sympathetic activity which can be due to either sympathetic over activity or vagal tone attenuation. Similar findings were also observed in a study by Roy.B et al, 2013[29] and Tarvainen PM et al,2014 [30] showing significant decrease in SD1/SD2 in diabetics as compared to healthy controls.

The cardiovascular parameters such as Heart rate and Blood pressure were not significantly different between both groups in our study. Previous studies showed conflicting reports of changes of diabetic cardiac autonomic neuropathy on heart rate [31,32,33]. Resting tachycardia and a fixed heart rate are characteristic late findings in diabetic patients with vagal impairment. [34]. Also, Significant alteration of blood pressure suggest impairment of sympathetic nervous system and sympathetic nervous system impairment is a late complication of diabetic neuropathy [2,4, 23].

The findings of our study suggest a parasympathetic attenuation of autonomic functions in diabetic patients (Decreased SD1/SD2 ratio) with no involvement of sympathetic nervous system (No significant change in resting heart rate and resting blood pressure). This may be due to the fact that early impairment of parasympathetic function occurs in diabetic neuropathy with sympathetic impairment being a late complication. [5]

Conclusion

Nonlinear analysis (Poincare plot method) can be used as an effective method for early diagnosis of cardiac autonomic neuropathy.

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