ORIGINAL RESEARCH PAPER
Volume-6 | Issue-11 | November-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HEART RATE VARIBILITY AS AN INDICATOR OF CARDIAC AUTONOMIC NEUROPATHY IN TYPE 2 DIABETES MELLITUS

Physiology

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ABSTRACT

Diabetes is gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease (1). It is estimated that almost one in six people are currently at risk of developing diabetes related complications(2). This study intends to detect the change in heart rate variability (HRV) in diabetic patients as well as its relationship with cardiac autonomic neuropathy. The present study was conducted on 40 type 2 diabetic patients 20 males and 20 females and 40 age and sex matched controls. ECG was recorded and analysed for HRV. The findings showed significant decrease in LF, HF and total power of the study as compared to controls. There was no significant difference seen in LF/HF ratio.

KEYWORDS

HRV, CVD, DM

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients of type 2 diabetes mellitus (DM). Cardiac autonomic neuropathy (CAN) is a very common and often overlooked diabetes related complication that has a major impact on mortality and morbidity in patients with DM. Improving understanding of the pathogenesis of CAN and its role in CVD, offers the potential of new treatment targets that might reduce the burden of CVD in patients with DM[3]. The assessment of autonomic function is an important part of evaluation of peripheral and central nervous system. CAN has been traditionally diagnosed by cardiovascular autonomic function tests like standing lying ratio (S/L ratio), valsalva ratio, sinus arrhythmia, hand grip test. The diagnosis of autonomic neuropathy is indirect, based on measurement of physiological variables which are controlled by ANS[4, 5]. The present study aims to evaluate CAN using new methods that are non invasive and independent of patient cooperation i.e. HRV.

MATERIAL AND METHODS

The study was carried out in department of physiology IGGMC Nagpur. The study was approved by institutional ethics committee The study sample size was calculated to 40 per group considering the mean ± S.D. of the parameters with α Error 5% and power 80% .

A total of 40 patients (20 males and 20 females) with type 2 DM of more than 5 years duration were recruited from diabetic OPD of IGGMC, Nagpur. Age and gender matched controls (40) who were non diabetic were recruited from in and around the medical college, after obtaining written informed consent from each subject.

Subjects with heart disease, hypertension, pregnant women, chronic renal failure, endocrine disorder, alcoholics, smokers, athletes, sport persons, subjects on hypolipidemic drugs, yoga practitioners and those consuming drugs affecting ANS were excluded from the study.

All The subjects were asked to refrain from ingesting beverages containing caffeine and alcohol for 24 hrs before starting the study work. All investigations were carried out between 10 am to 1 pm under optimum environmental conditions in quiet surrounding with room temperature between 22^0c – 24^0c. Baseline ECG, resting heart rate (RHR), systolic and diastolic blood pressure (SBP & DBP) of all the participants were recorded.

After five minutes mandatory rest continuous ECG was recorded in lead II in supine position with the help of computerised polygraph, a computerised 16 channel bio potential box (PHYSIOPAC pp-4, Medicaid system, Chandigarh, India) . Then the recording was manually checked for artifacts and only artifact free section of five minutes was included in the analysis and transferred in kubios software installed in the computerised polygraph. The frequency domain parameters i.e. high frequency (HF), low frequency (LF) in ms^2 and normalised units (n.u.) and total power (TP) of HRV were recorded.

The data was analysed using statistical software STATA version 13.1. Variables were presented as mean ± SD. Continuous variables (Age, Height, Weight, W/H ratio, SBP, DBP, FBG, PMBG, GHb) were compared between diabetic patients and control subjects by performing unpaired t- test for normalized data. Wilcoxon Rank Sum test was performed to compare non-normalized variables (LF, LF(n.u.), HF, HF (n.u.), LF/HF and Total power) between diabetic patients and control subjects. $p<0.05$ was considered as statistically significant.

OBSERVATIONS AND RESULTS

Table 1: Comparison of anthropometric parameters in cases & controls

Variables	Control group (n=40) Mean ± SD	Cases group (n=40) Mean ± SD
Age (yrs)	48.12 ± 6.03	50.02 ± 6.78
Height (cm)	157.27±7.78	155±7.98
Weight (Kg)	58.22 ± 7.08	69.45 ± 10.81***
BMI (Kg/m2)	23.53 ± 2.31	28.65 ± 4.34***
W/H Ratio	0.86 ± 0.05	0.92 ± 0.07***

*** p< 0.001 very highly significant.

There was no significant difference in age and height of the control and cases group. (p- > 0.05). The weight, BMI and W/H ratio was significantly increased in cases group than control group. (p< 0.001) (Table 1)

- **Table 2 : Comparison of glycemic status and cardiac parameters in cases and controls**

Variable	Control Group (n=40) Mean ± SD	Cases Group (n=40) Mean ± SD
FBG (mg/dl)	86.07 ± 9.43	178.25 ± 29.64***
PMBG (mg/dl)	122.2 ± 11.74	272.6 ± 27.92***
GHb (%)	4.94 ± 0.94	8.02 ± 0.7***
RHR	78.57 ± 13.48	84.05 ± 13.09
SBP	120.75 ± 6.89	129.6 ± 6.69***
DBP	80.1 ± 3.89	83 ± 3.97**

** p <0.01 highly significant, *** p< 0.001 very highly significant.

There is significant increase in values of fasting blood glucose (FBG), post meal blood glucose (PMBG) and glycated haemoglobin (GHb) in cases group than control group also the systolic (SBP) and diastolic blood pressure (DBP) is more in cases group than in control group (p < 0.001) (Table 2).

- **Table 3 : Comparison of frequency domain parameters of HRV in cases and controls.**

Parameter (ms)	Control Group (n=40) Mean ± SD	Cases Group (n=40) Mean ± SD	Z value
LF (ms2)	681.05 ± 626.82	206.35 ± 214.19	4.499***
LF (n.u.)	85.01 ± 3.31	83.32 ± 5.38	1.569
HF (ms2)	104.57 ± 83.42	39.07 ± 37.67	4.504***
HF (n.u.)	14.98 ± 3.31	16.68 ± 5.38	1.569
LF/HF	5.90 ± 1.32	5.39 ± 1.58	1.564
Total power (ms2)	2519.42 ± 1597.78	1123.1 ± 836.33	4.686***

*** p< 0.001 very highly significant.

The values of LF, HF (frequency domain parameters) and total power was significantly less in cases group as compared with control group (p<0.001) (Table 3).

The values of LF (n.u.), HF (n.u.) and LF/HF ratio were not statistically significant (p >0.05) (Table3).

DISCUSSION

Data of our study shows significant increase in weight, body mass index and W/H ratio this is due to increase in weight gain and obesity which is typically central type due to gradual impairment in glucose metabolism[6].

Long standing older patients with diabetes have considerable autonomic dysfunction when assessed by recently developed methods i.e. heart rate variability[7]. The heart rate variability data suggest that there was a reduction in frequency domain parameters high-frequency (conventionally suggestive of cardiac parasympathetic) and low-frequency (conventionally suggestive of cardiac sympathetic) power spectra of heart rate variability suggesting autonomic modulation of the heart is affected in long standing diabetes[7].

LF/HF ratio reflects sympatho vagal balance or sympathetic modulations. The total power of RR interval variability is the total variance and corresponds to the sum of spectral bands LF, HF, VLF.[8] cardiac automaticity is intrinsic to various pacemaker tissues, heart rate and rhythm are largely under the control of the autonomic nervous system. Under resting conditions, vagal tone prevails and variations in heart period are largely dependent on vagal modulation. The vagal and sympathetic activity constantly interact [8].

As a complication of diabetes mellitus, autonomic neuropathy is characterized by early and widespread neuronal degeneration of small nerve fibers of both sympathetic and parasympathetic tracts. A reduction in time domain parameters of HRV seems not only to carry negative prognostic value but also to precede the clinical expression of autonomic neuropathy. In diabetic patients without evidence of autonomic neuropathy, reduction of the absolute power of LF and HF during controlled conditions was also reported however when LF/HF ratio was considered or when LF and HF were analysed in normalized units no significant difference in comparison to normal subjects was present. Thus, the initial manifestation of this neuropathy is likely to involve both efferent limbs of the autonomic nervous system.[8]

In conclusion, data from the current study demonstrated that diabetics had cardiac sympathetic and cardiac parasympathetic nervous system involvement suggesting that autonomic dysfunction has been present in these diabetics[7].

ABBREVIATION'S USED:

CAN- cardiac autonomic neuropathy,
ECG- electrocardiogram,
LF- low frequency,
HF- high frequency,
TP-total power,
CVD- Cardiovascular diseases,
DM- diabetes mellitus,
S/L ratio- standing / lying ratio.

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