ORIGINAL ARTICLE

A SIMPLE TEST OF ONE MINUTE HEART RATE VARIABILITY DURING DEEP BREATHING FOR EVALUATION OF SYMPATHOVAGAL IMBALANCE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Heart rate variability (HRV) refers to the magnitude of the fluctuation in the number of heart beats per minute in conjunction with respiration. HRV with deep breathing (HRVdb) has recently become a popular non-invasive research tool in cardiology. This study was carried out to determine and compare the HRV in patients with Type 2 DM with those of Non diabetic controls. **Methods:** Sixty diabetic patients attending out patient department in Karnataka Institute of Diabetology, Bangalore and 60 age-matched controls were enrolled. HRV was performed on all the subjects and the results obtained were compared between the groups. The One minute HRV was analysed during deep breathing and defined as the difference in beats/minute between the shortest and the longest heart rate interval measured by lead II electrocardiographic recording during six cycles of deep breathing. **Results:** Statistically significant decrease in mean minimal heart rate and 1 minute HRV (16.30±6.42 vs 29.33±8.39) was observed during deep breathing among Type 2 Diabetic patients on comparison with that of healthy controls. There was no significant difference in mean maximal heart rate between the groups. **Conclusion:** Significant decrease in HRV in Type 2 DM patients is suggestive of reduced parasympathetic activity or an imbalance between sympathetic and parasympathetic neural activity in them. Hence HRVdb provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders.

Keywords: HRVdb, Sympathetic and Parasympathetic function

INTRODUCTION

The cardiovascular system is influenced by the autonomic nervous system (ANS). The two neural mechanisms for controlling heart rate are the sympathetic nervous system, which has positive chronotropic, ionotropic, dromotropic and bathmotropic effect where as the parasympathetic nervous system have negative effect of the same. The ANS plays an important role not only in physiological situations but also in various pathological settings such as diabetic neuropathy, myocardial infarction (MI) and congestive heart failure (CHF). Autonomic imbalance associating increased sympathetic activity and reduced vagal tone has been strongly implicated in the pathophysiology of arrhythmogenesis and sudden cardiac death. ANS abnormalities may increase cardiovascular morbidity and mortality.[1] The integrity of the autonomic control of the cardiovascular system in diabetics can be studied by observing the heart rate variability and the effects of standing on heart rate and arterial blood pressure.[2]

Among the different available noninvasive techniques for assessing the autonomic status, heart rate variability (HRV) has emerged as a simple, noninvasive method to evaluate the sympathovagal balance at the sinoatrial level. HRV with deep breathing (HRVdb) is a highly sensitive measure of cardiovagal or parasympathetic cardiac function. This sensitivity makes HRVdb an important part of the battery of cardiovascular autonomic function tests used in clinical autonomic laboratories. HRVdb is a reliable and sensitive clinical test for early detection of cardiovagal dysfunction in a wide range of autonomic disorders.[3]

The first report linking HRV to respiration has been credited to Karl Ludwig, who in 1847 noted that heart rate increased with inspiration and decreased with expiration.[4,5] Reduced HRV has been established as a powerful predictor of mortality and arrhythmic complications following acute myocardial infarction.[1] The methods developed for clinical tests of cardiovagal function typically involve measuring HRVdb over short intervals (one minute). Deep breathing magnifies HRV with respiration, allowing for methods to assess HRV with respiratory cycles.[3]

Clinical interest in HRV was sparked by the 1973 report of Wheeler and Watkins, who first drew attention to cardiac vagal innervation as the mediator of HRV and its potential value as a clinical test of cardiovagal function.[6] These investigators studied HRV with deep breathing (HRVdb) in normal subjects and diabetic subjects, some with and some without evidence of autonomic neuropathy. They noted that HRVdb was reduced or abolished in diabetic subjects with autonomic neuropathy and thus concluded that HRVdb was a clinically useful test for autonomic neuropathy in diabetic patients.

HRV reflects the balance between the sympathetic and the parasympathetic tone: when the sympathetic tone is dominant the HRV is low and *vice versa*.[7] Decreased HRV has been demonstrated to be a marker of poor outcome in patients with diabetic

autonomic neuropathy[8] and in patients with coronary artery disease.[9]

Many studies have been done using frequency domain HRV analysis in diabetic patients, which is more sensitive and specific. However the clinical usefulness of HRVdb measurement from short term ECG recording is well established. Hence the present work was undertaken to assess the autonomic imbalance in Type 2 Diabetes Mellitus patients by a simple bedside evaluation of one minute HRV during deep breathing.

MATERIAL AND METHODS

This study was conducted in Karnataka Institute of Diabetology, Bangalore. Prior to the commencement of the study, permission from the Director and Institute Ethics committee were obtained.

The study included 60 patients and 60 controls (Table-1). Sixty previously diagnosed Type 2 Diabetes mellitus patients, who were on treatment (age 35–80 years) including 16 females and 44 males, attending outpatient department were recruited for the study from Karnataka Institute of Diabetology. Age and gender-matched non-diabetic healthy controls were recruited from staff of JSS Medical Collage, Mysore.

Heart rate variability was measured using a simple bedside test of 1 minute HRV during forced deep breathing.[10,11] The test was performed using CARDIART 6108-T electrocardiograph. The subjects laid down quietly in a supine posture and Lead II of the ECG machine was connected to record the heart rate. After obtaining a stable heart rate record, the patients were instructed to breath deeply at 6–8 breaths/min (for one respiratory cycle, time taken was 10 sec, 5 sec inspiration and 5 sec expiration). The maximum variation in heart rate produced was calculated by measuring the differences between minimum heart rate on inspiration and maximum on expiration. Lead II was then recorded continuously at paper speed of 25 mm/sec for one minute. The HRV interval (R-R intervals between adjacent QRS complexes resulting from sinus node depolarisation) was measured manually with a scaled caliper. R-R intervals surrounding premature ventricular contractions were excluded.

The results are presented as Mean±SD. Independent sample *t*-test was employed for statistical comparison of HRV between the diabetes mellitus patients and control group, using SPSS-16 for windows. The $p<0.05$ was considered statistically significant.

Table-1: The characteristic of patients and controls

Parameters	Patients	Controls
Number	60	60
Male	44	44
Female	16	16
Age (yr)	57±12.3	55±12.2
Smokers	18	10
Alcoholics	10	Nil
Hypertensives	30	15
Ischemic heart disease patients	6	Nil
Hyperlipidemia	20	Nil

RESULTS

The average age of the study and control groups was similar (57±12.3 vs 55±12.2 respectively).

Statistically significant decrease in mean Minimal heart rate and One minute HRV was observed during deep breathing among Type 2 Diabetic patients on comparison with that of healthy controls (Table-2). There was no significant difference in mean maximal heart rate between the groups.

Table-2: Comparison of maximum, and minimum HR, and HRV in diabetics and controls

Parameter	Diabetic (Mean±SD)	Control (Mean±SD)	*t*-value	*p*-value
Maximum HR	88.52±13.57	92.67±12.82	-1.722	0.088
Minimum HR	72.97±11.73	62.80±10.63	4.976	0.000*
HRV	16.30±6.42	29.33±8.39	-9.558	0.000*

HR=Heart Rate, HRV=Heart Rate Variability, *highly significant

The change in heart rate was calculated as the difference in beats per minutes between the shortest and the longest R-R interval (Figure-1, 2): HRV= short R-R interval (calculated as beats/min), long R-R interval (calculated as beats/min).[12]

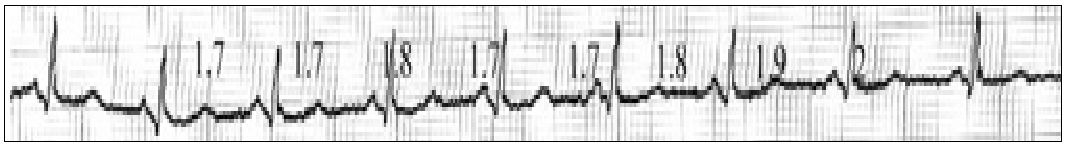

Figure-1: Sample ECG recording of a patient with a low HRV

ECG was measured at paper speed of 25 mm/sec and deflection of 1 mV=10 mm. The shortest and longest beat-to-beat interval was 1.7 and 2.0 sec respectively. HR: 150/1.7=88, 150/2.0=75. The difference is 13 beats/min, hence the HRV=13.

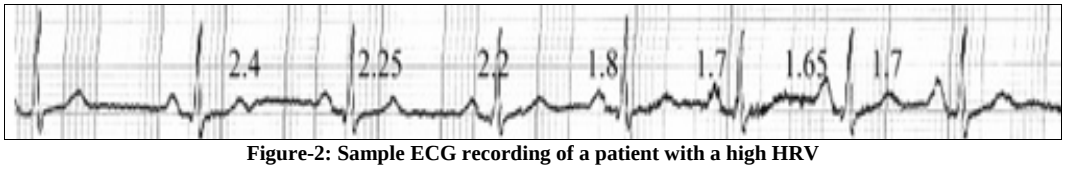

Figure-2: Sample ECG recording of a patient with a high HRV

Paper speed=25 mm/sec, 1 mV=10 mm. The shortest and longest beat-to-beat interval was 1.65 and 2.4 sec. respectively. HR: 150/1.65=90, 150/2.4=62. The difference is 28 beats/min, hence the HRV of 28.

DISCUSSION

Consistent with previous studies and hypothesis, we found a significant decrease in mean HRV in Type 2 DM patients on comparison with the control in our study. This indicates that cardiac autonomic function had been negatively affected in DM patients.

HRV with deep breathing is the simplest and most widely performed measure of autonomic control of the heart. This test produces a sensitive, specific, and reproducible indirect measure of vagal cardiac function. The decreased beat-to-beat variability during deep breathing in diabetic neuropathy similar to our study was first reported by Wheeler and Watkins.[6] In studies comparing cardiac autonomic function tests and HRV indices, based on both short (5-min) and 24-h ECG recordings, show that in diabetic patients without abnormal autonomic function tests HRV was lowered.[13]

A study reported that beat-to-beat variation, HR changes, and the valsalva ratio were significantly reduced in diabetics with peripheral neuropathy as compared to non-diabetic control group, while these parameters were not significantly altered in diabetics without peripheral neuropathy.[10]

It has been observed that cardiovascular autonomic diabetic neuropathy is associated with the loss of heart rate variability. In diabetes mellitus-associated neuropathy, characterised by the alteration of the small nerve fibres, a reduction in time domain parameters of the HRV seems not only to carry a negative prognostic value, but also to precede the clinical expression of autonomic neuropathy.[14,15]

A study by Girach *et al* showed that people with diabetes have lower HRV than control subjects that is expressed with a near flat appearance.[16] Another similar study by Rand *et al* proved that HRV is lower in people with diabetes showing a very small variation in heart rate that is nearly flat in appearance.[17]

HRVdb represents a very sensitive measure of cardiovagal or parasympathetic cardiac function and thus is an important component of the battery of cardiovascular autonomic function tests used in clinical autonomic laboratories. In most autonomic disorders, parasympathetic function is affected before sympathetic function, so HRVdb provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders. HRVdb has proven to be a sensitive and reliable clinical test for the early detection of cardiovagal dysfunction in a wide spectrum of autonomic disorders, including diabetic autonomic neuropathy,[18] uremic neuropathy,[19] familial autonomic neuropathies,[18] and various small fiber neuropathies.[20,21] HRVdb has also been valuable in assessing patients with pure autonomic failure,[22] multisystem atrophy,[23] and other central neuro-degenerative disorders.[24]

Autonomic cardiac denervation is an important companion of diabetic peripheral neuropathy and every diabetic clinic should have group of such patients identified by using simple, non-invasive, reproducible tests so as to fallow its natural evolution and exercise caution in the management of such patients.

Limitations of standard HRV measurements:

Because HRV deals with RR interval variations, its measurement is limited to patients in sinus rhythm and to those with a low number of ectopic beats. In this sense, approximately 20 to 30% of high risk post-MI patients are excluded from any HRV analysis due to frequent ectopy or episodes of atrial arrhythmias, particularly atrial fibrillation. The latter one may be observed in up to 15 to 30% of patients with CHF, excluding these patients from any HRV analysis.

CONCLUSION

To conclude our results confirm the previous findings: a significant decrease in HRV in Type 2 DM patients by using the simple, non-invasive bedside test of evaluating one minute HRV during deep breathing. It is possible to detect and quantify autonomic dysfunction with this simple test.

It is recommended that each diabetic clinic should carry out such simple, non-invasive initial evaluation procedures to identify these groups of DM patients who warrant special attention.

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