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Comparison of Heart Rate Variability in Newly Diagnosed Diabetic Patients with and without Autonomic Neuropathy

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Abstract

Background-Diabetic Autonomic Neuropathy is among the least recognized and understood complications of diabetes despite its significant negative impact on survival and quality of life in people with diabetes. **Objective**: to analyze short term frequency domain of Heart Rate Variability (HRV) in newly diagnosed diabetic patients with and without autonomic neuropathy and compare the results with controls. **Method-** The study was conducted in medical OPD of Bapuji Hospital and Chigateri General Hospital attached to J.J.M. Medical College, Davangere. 100 consecutive newly diagnosed type 2 diabetic patients age 35 to 50 years and 50 normal individuals formed the subjects of the study. **Results-** The age of subjects ranged from 30-60 years. The resting heart rate was significantly higher in diabetics than normal. When the blood pressure response to supine to standing was evaluated there was a significant decrease in systolic blood pressure among controls and cases. The Valsalva ratio was decreased in diabetics as compared to controls. No difference was observed in E/I ratio between control and diabetics. There was increase in systolic blood pressure during test as compared to rest. Ratio of heart rate on standing (30:15) decreased in cases as compared to controls.

Conclusion- Clinical observations should not be the sole basis for the diagnosis of cardiovascular autonomic dysfunction. Screening for abnormalities is infrequently done.

Keywords*: Resting heart rate, Valsalva ratio, Valsalva Maneuver, type-2 diabetic patients, E/I ratio, blood pressure*

Introduction

Prevalence of Diabetes is increasing globally and India is no exception. The concern is that India would be having the highest population of diabetes by 2025 and is all set to become the "Diabetic Capital" of world[1]. Though recognized as a major cause of death and disability, many who suffer from diabetes are unaware of that they are afflicted until they experience a debilitating side effect of this disease. Long term complications of diabetes includes neuropathies which affect upto 50% of patients[2-4]. Most common neuropathies are chronic sensorimotor distal symmetric polyneuropathy and autonomic neuropathy. Diabetic autonomic neuropathy can involve entire autonomic nervous system. It is manifested by involvement of one or more organ systems like Cardiovascular system, Gastro-intestinal tract, Genitourinary system, sudomotor and Ocular systems etc.

Clinical symptoms do not occur until long after the onset of diabetes. Sub clinical autonomic dysfunctions can however occur within a year of diagnosis of type II diabetic patients and within two years in type I diabetic patients.[5] Early recognition and treatment is important, as the autonomic complications of Diabetes are potentially treatable. It is possible that the patients develop subtle deficits in Heart Rate Variability much earlier and can be used as marker of cardiac autonomic neuropathy to

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study the benefits of therapeutic interventions.

The present study was taken up to analyze short term frequency domain of Heart Rate Variability in newly diagnosed diabetic patients with and without autonomic neuropathy and compare the results with controls.

Materials and Method

This cross sectional study was conducted in 100 consecutive newly diagnosed type 2 diabetic patients age 35 to 50 years and 50 normal individuals attending medical OPD of Bapuji Hospital and Chigateri General Hospital attached to J.J.M. Medical College.

Method of collection of data: A pre tested structured proforma were used to collect the relevant information regarding clinical findings, investigations and test results. These patients and normal individuals were subjected to 5 cardiovascular tests and heart rate variability after detail history regarding autonomic symptoms, peripheral neuritis and careful physical examinations.

The patients is placed supine on an examination table and allowed to rest for 5 minutes, they will be asked to breath regularly at 6 breaths per minute using Metronome and then they will be connected to ECG machine. The ECG recording is done and resting heart rate is calculated from this. Frequency Domain analysis is done by using NIVIQURE software.

Valsalva Maneuver: The patient is asked to perform the maneuver for a period of 15 seconds. With the patient still connected to the ECG machine, he is then asked to release the pressure and an ECG is recorded for a further period of 30 sec. The patient is then allowed to rest for one minute and the procedure is repeated once again. He will be then allowed to rest for a further period of 1 minute. The ratio of the longest R-R interval shortly after the maneuver (within about 20 beats) to the shorter R-R interval during the maneuver is measured and result is expressed as Valsalva ratio which will be taken as the mean.

Heart Rate response to standing: After completing the above procedure, the patient is allowed to rest for sometime, after which the ECG recording is done for about 30 second with patient still in the supine position. With ECG machine is running, patient is asked to stand up. After ECG baseline become normal, the 15^{th} beat and the 30^{th} beat after standing up is marked. The characteristic heart rate response can be expressed by the 30:15 ratio, which will be the ratio of the longest R-R interval around the 30^{th} beat after starting to stand up to the shortest R-R interval around the 15^{th} beat.

Heart Rate Response to Deep Breathing: At the end of one minute, with ECG running, the patient is asked to take deep breath at the rate of 6 breaths per minute and the E/I ratio is calculated.

Power spectral analysis of HRA: Analysis of HRV will also be assessed by spectral analysis of series of successive R-R interval on 5 min ECG Recordings. The heart rate power spectrum is typically divided into two frequency bands. Low and high frequency. The high frequency region will be generally considered a marker of vagal activity whereas the low frequency component influenced by both sympathetic and vagal activity.

Blood Pressure response to standing: Patient is again allowed to assume a supine position, and a recording of blood pressure is done in the supine position. Patient is then asked to stand up and blood pressure is recorded at 0 and 1 minute intervals.

Handgrip test: The baseline blood pressure is recorded in the subject. The subject is instructed about the test and demonstrated the procedure to use handgrip dynamometer. After the instruction the subject is asked to grip using maximum force with their dominant hand for a few seconds. The value is noted down and the procedure is repeated thrice. The maximum value of the three readings is considered as their Maximal Voluntary Contraction.

After the subject has started the contraction, the blood pressure is measured on the contra-lateral arm at 1^{st}, 2^{nd}, 4^{th}. One more reading is taken 2 minutes after the release of the grip.

Result

The age of subjects ranged from 30-60 years. Out of the 50 normal individuals, 29 subjects were in the age group of 30-39 years, 16 subjects were in the age group of 40-49 years, 3 subjects were in the age group of 50-59 years and 2 subjects were in the age group above 60 years.

Resting heart rate: the resting heart rate was significantly higher in diabetics than normal. ($p < 0.01$).

Blood pressure response to standing: When the BP response to supine to standing was evaluated there was a significant decrease in systolic blood pressure among controls and cases. But there was no significant change in diastolic blood pressure in supine position between cases and controls.

Valsalva ratio: The Valsalva ratio was decreased in diabetics as compared to controls ($p < 0.01$).

E/I ratio: No difference was observed in E/I ratio between control and diabetics.($p < 0.94$)

Blood pressure response to Hand grip test: In controls there was increase in SBP during test as compared to rest. There was increase in DBP during test when compared to rest. In cases there was increase in SBP during test as compared to rest. There was increase in DBP during test.

During hand grip test, when there was significant increase in the blood pressure during rest and the test ($p < 0.01$).

Heart rate response to standing (30:15): Ratio of heart rate on standing decreased in cases as compared to controls.

Table 1: Comparison of cardiovascular tests between controls and cases

Groups		Resting HR	Postural hypotension				Valsalva ratio	E/I ratio	Handgrip test				HR (30:15 ratio)
			SBP		DBP				SBP		DBP		
			Supine	Standing	Supine	Standing			Rest	Test	Rest	Test	
Controls (50)	Mean ± SD	76.5 ± 4.4	123.9 ± 7.2	114.4 ± 7.7	75.9 ± 4.8	80.5 ± 5.6	1.27 ± 0.02	1.24 ± 0.01	113.6 ± 7.1	134.8 ± 6.4	75.4 ± 4.6	94.2 ± 4.7	1.04 ± 0.06
Cases (100)	**Mean ± SD**	88.1 ± 4.3	120.6 ± 9.5	108.0 ± 11.1	75.1 ± 4.5	70.3 ± 5.1	1.24 ± 0.03	1.22 ± 0.02	111.9 ± 3.9	126.6 ± 5.8	74.6 ± 4.5	84.6 ± 4.5	1.06 ± 0.04
	P value	< 0.01	< 0.05	< 0.01	0.35	< 0.01		0.94	0.07	< 0.01			< 0.05

Heart rate variability: In relation to heart rate variability (LH, and LH/HF ratio), there was no significant change in the value among controls and cases.

Table 2: Comparison of HRV between cases and controls

Groups		LF	HF	LF/HF
Controls (50)	**Mean ± SD**	0.11 ± 0.09	0.28 ± 0.08	0.39 ± 0.30
Cases (100)	**Mean ± SD**	0.10 ± 0.07	0.27 ± 0.08	0.37 ± 0.23
	P-value	0.58	0.63	0.66

Resting heart rate (HR): The mean value of resting HR in group I, II and III was 76.5 ± 4.5, 86.8 ± 2.1 and 90.0 ± 5.7. there was a significant difference but in the normal range.

Blood pressure response to supine to standing: In comparison to in supine position in Group I, II & III the values ranged from 110-134, 116-132 and 100-120 respectively. The mean value was 123.9 ± 7.2, 127.5 ± 5.6 and 110.7 ± 5.9 in Group I, II and III respectively.

In standing position the SBP in Group I, II and III, the values ranged from 98-128, 106-124 and 90-108 respectively. The mean value was 114.4 ± 7.7, 116.3 ± 4.5 and 96.0 ± 4.9. There was slight fall in blood pressure, but in normal range.

The mean values were 75.9 ± 4.8, 73.7 ± 2.5 and 77.2 ± 5.7 in Group I, II and III respectively.

Similarly the DBP among Group I, II and III in standing position ranged from 72 to 92, 60 to 80, 60-84 and the mean values were 80.5 ± 5.6, 69.2 ± 5.2 and 72.0 ± 4.5 among Group I, II and III respectively. There was statistical significance. But in the normal range.

Valsalva ratio: The mean values among Group I, II and III were 1.27 ± 0.02, 1.25 ± 0.02 and 1.22 ± 0.01 respectively. The difference observed between the groups were statistically significant but in the normal range.

E.I. Ratio: The mean values among Group I, II and III were 1.24 ± 0.01, 1.25 ± 0.01 and 1.22 ± 0.01 respectively. The range was 1.22 to 1.26, 1.23 to 1.26 and 1.21 to 1.24 among Group I, II and III. ($P<0.05$)

Heart rate response to standing (30: 15): The values 30: 15 ratio ranged from 1.04 to 1.14, 1.00 to 1.13 and 1.04 to 1.07 among Group I, II and III respectively. The mean values were 1.06 ± 0.0, 1.05 ± 0.02 and 1.04 ± 0.02 respectively.

Handgrip test: The SBP at rest in Group I, II and III ranged from 100–124, 106–118 and 100–122 respectively. The mean values were 113.6 ± 7.1, 111 ± 2.3 and 112.1 ± 5.5 among Group I, II and III respectively.

The SBP during test in Group I, II and III ranged from 116 to 146, 110 to 138, 114–136 respectively.

At rest the DBP among Group I, II and III ranged from 70 to 84, 70 to 80 and 70 to 78 respectively. The mean values are 75.4 ± 4.6, 72.6 ± 2.4 and 77.5 ± 5.3 among Group I, II and III respectively. Table 3

During test the DBP among Group I, II and III ranged from 86–104, 70 to 80 and 80–98 respectively. The mean values were 94.2 ± 4.7, 81.6 ± 3.4 and 89.0 ± 5.3 among Group I, II and III. Table 3

Table 3: Comparison of cardiovascular test between Group I, II and III

Groups		Resting HR	Postural hypotension				Valsalva ratio	E/I ratio	Handgrip test				HR (30:15 Ratio)
			SBP		DBP				SBP		DBP		
			Supine	Standing	Supine	Standing			Rest	Test	Rest	Test	
Group I (50)	Mean ± SD	76.5 ± 4.4	123.9 ± 7.2	114.4 ± 7.7	75.9 ± 4.8	80.5 ± 5.6	1.27 ± 0.02	1.24 ± 0.01	113.6 ± 7.1	134.8 ± 6.4	75.4 ± 4.6	94.2 ± 4.7	1.06 ± 0.04
Group II (59)	Mean ± SD	86.8 ± 2.1	127.5 ± 3.6	116.3 ± 4.5	73.7 ± 2.5	69.2 ± 5.2	1.25 ± 0.02	1.25 ± 0.01	111.8 ± 2.3	127.6 ± 5.6	72.6 ± 2.4	81.6 ± 3.4	1.05 ± 0.02
Group III (41)	Mean ± SD	90.0 ± 5.7	110.7 ± 5.9	96.0 ± 4.9	77.2 ± 5.7	72.0 ± 4.5	1.22 ± 0.01	1.22 ± 0.01	112.1 ± 5.5	125.2 ± 5.8	77.5 ± 5.3	89.0 ± 5.3	1.04 ± 0.02

Discussion

In our study the resting heart rate was increased in Group II and III as compared to Group I. These findings are in concurrence with other studies. Many studies[6,7,8,] have suggested that increased resting heart rate in diabetics was mainly due to parasympathetic damage in early stage of cardiac autonomic involvement.

Blood pressure response to standing: Our study shows that there is fall in systolic and diastolic blood pressure on standing. there was a fall in blood pressure in Group II and III. Low PA[9] and Langer[10] have suggested that this may be because of damage to the efferent sympathetic vasomotor fibers particularly in the splanchnic vasculature.

Valsalva ratio: valsalva ratio decreased in Group II and III. American Diabetes Association[11] suggested that Valsalva maneuver is a much more complex reflex arc involving sympathetic and parasympathetic pathways to the heart, sympathetic pathways to the vascular tree, baroreceptors in the chest and lungs. The baroreflex system is impaired in diabetics. As a result the response is altered.

Handgrip test: There was decrease in diastolic blood pressure in Group II and III. Ewing DJ[12] suggested that when a normal person performs sustained isometric exercise, the heart rate and cardiac output increased to a modest degree while the blood pressure response is more marked. But in diabetics the blood pressure decreased due to decrease in the vascular resistance and impaired sympathetic activity.

E: I ratio: the E:I ratio was decreased in Group II and Group III. Rathmann[13] suggested that during inspiration the heart rate increases and on expiration the heart rate decreases. But in diabetics due to the impairment of parasympathetic system the ratio decreases.

HR response to standing (30:15): On comparing the HR response to standing the value decreased in Group II and III. Ewing DJ[14] observed that lying to standing test is mediated by sympathetic and parasympathetic reflex pathways.

Conclusion

Despite research evidence that clinical observations should not be the sole basis for the diagnosis of cardiovascular autonomic dysfunction. Screening for abnormalities is infrequently done. This is also despite the fact that office-based commercially available instrumentation for detection is readily available. Given the clinical and economical impact of this complication, testing of diabetic individuals for cardiovascular autonomic dysfunction should be part of their standard of care.

Conflict of Interest: None

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Ethical Clearance: Permission for the study was obtained from the College authorities prior to commencement.

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