Original Article

A cross sectional study for the evaluation of autonomic nervous system functioning in type 2 diabetes mellitus patients

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ABSTRACT

AIM: Prevalence of Diabetes is increasing globally and India is no exception. One of the most important complication of diabetes is Cardiac Autonomic Neuropathy (CAN) which results from damage to the autonomic nerve fibers that innervate heart and blood vessels. The integrity of the autonomic system is studied with help of simple non-invasive cardiovascular reflex tests. Our aim was to study the pattern of autonomic neuropathy in newly detected diabetic patients.

MATERIALS AND METHOD: This study involved 100, newly diagnosed type 2 diabetic patients and 50 normal individuals. A pretested structured proforma was used & then they were subjected to cardiovascular reflex tests like. Resting Heart Rate, Valsalva Maneuver, Heart Rate response to standing, Heart Rate Response to Deep Breathing & Blood Pressure response to standing. Statistical analysis was performed by using 't' test. P < 0.05 was considered significant.

RESULTS: The resting heart rate was significantly higher and Valsalva ratio & Ratio of heart rate on standing (30:15) were decreased in diabetics as compared to normal. Significant decrease in diastolic blood pressure in standing position was also seen in diabetics as compared to controls.

CONCLUSION: In our study newly detected type 2 diabetic patients who did not have any symptoms of autonomic dysfunction, had abnormal cardiovascular reflex tests due to the impairment of parasympathetic and sympathetic systems. But no single test alone is useful for detection of CAN, & for screening diabetic patients.

1. 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. 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 include neuropathies which affect upto 50% of patients. Most common neuropathies are chronic sensorimotor distal symmetric polyneuropathy and autonomic neuropathy. Diabetic Autonomic Neuropathy (DAN) is a complication having significant negative impact on survival and quality of life in people with diabetes.

The duration of diabetes and degree of metabolic control are the two major predictors of the development of neuropathy and determination of its severity, other factors such as patients age, height, and presence of proliferative retinopathy, nephropathy, and cardiovascular diseases have been implicated. Degenerative changes are seen in autonomic ganglion cells together with demyelination and axonal loss in the white communicating rami, and in the vagus and splanchnic nerves. Although damage to autonomic nerves involves almost all parts of the body, the effects is most obvious clinically in the cardiovascular system. Autonomic nerve damage can be found in many diabetics often without any accompanying symptoms. It can involve the entire autonomic nervous system (ANS), vasomotor, visceromotor, and sensory fibers that innervate every organ. It is manifested by dysfunction of one or more organ systems like cardiovascular, gastrointestinal, genitourinary, or ocular. One of the most important complication of diabetes is Cardiac Autonomic Neuropathy (CAN) which results from damage to the autonomic nerve fibers that innervate heart and blood vessels and it causes abnormalities in the heart rate control as well as central and peripheral vascular dynamics, the clinical manifestations of which include
Resting tachycardia, Exercise intolerance
Intraoperative and preoperative cardiovascular instability
Orthostatic hypotension
Orthostatic tachycardia and bradycardia syndrome
Silent myocardial ischemia / cardiac denervation syndrome
Sudden death etc [8]

The integrity of the autonomic system is studied by measurement of changes in HR or Blood Pressure (BP) under various conditions. Ewing et al. proposed simple non-invasive cardiovascular reflex tests that have been applied successfully in many studies. [11,12,13] In fact many studies using these tests have provided information on the prevalence of DAN, its natural history, clinical prognosis and relationship with other chronic diabetic complications. Among the clinical reflex tests, the tests used most widely, validated and best known in their physiological basis are heart rate variation on deep breathing and lying-to-standing, the Valsalva manoeuvre and BP response to standing. Cardiovascular reflex abnormalities can be detected at the time or shortly after diabetes has been diagnosed and in diabetics of longer duration with any symptom of autonomic neuropathy [16]. Recently a new approach looking at changes in heart rate variation by measuring the sudden beat by beat changes that occur frequently throughout the day and night, but are markedly reduced in diabetic subjects with autonomic neuropathy. This technique is more sensitive than the conventional cardiovascular tests, but requires 24 hour ECG monitoring [17].

The present study was carried out to evaluate easy, non-invasive, bedside diagnostic tests of diabetic autonomic neuropathy in both symptomatic and asymptomatic diabetic patients and normal individuals. Our aim was to study the pattern of autonomic neuropathy in newly detected diabetic patients. And to assess the utility of bedside autonomic function tests as a tool, for diagnosing cardiac autonomic neuropathy in diabetic at the earliest.

METHODOLOGY

Inclusion Criteria:
- Age 35 to 50 years
- Both male and female having NIDDM were included in the study group.
- Patients who were not on any drugs that would interfere with the autonomic functions like anti hypertensives, vasodilators, phenothiazines, TCA's, and ß-Blockers.
- Patients on anti diabetic treatment for less than 3 Months
- Normal healthy control of both sexes between 35-50 years age.
- Exclusion Criteria:
  - Presence of hypertension
  - Smokers
  - Presence of ischemic heart disease.
  - Valvular heart disease.
  - Heart failure.
  - Chronic alcoholic and alcohol dependent.
  - Patients with acute complications of diabetes mellitus like diabetic ketoacidosis, non-ketotic hyperosmolar coma and hypoglycemia  

1. Resting Heart Rate: The patient was placed supine on an examination table and allowed to rest for 5 minutes, they were asked to breath regularly at 6 breaths per minute using Metronome and then they were connected to ECG machine. The ECG recording was done and resting heart rate is calculated from this.

2. Valsalva Maneuver: The patient was 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.

3. Heart Rate response to standing:
After completing the above procedure, the patient was 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 15th beat and the 30th 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 30th beat after starting to stand up to the shortest R-R interval around the 15th beat.

4. Heart Rate Responseto 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.

5. 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.

The results obtained were expressed as mean standard deviation. And the statistical analysis was performed for significance by using t test. P < 0.05 was considered significant.

RESULTS

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 (Table 1, Graph 1).

1 : Age wise distribution

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>Controls</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>40-49</td>
<td>16</td>
<td>44</td>
</tr>
<tr>
<td>50-59</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>60 +</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Mean age ± SD</td>
<td>39.3 ± 7.8</td>
<td>45.3 ± 8.3</td>
</tr>
</tbody>
</table>

Cardiovascular Reflex Tests:

Resting heart rate:

On comparison between controls and diabetic cases, the resting heart rate was significantly higher in diabetics than normal. (p < 0.01). (Table 2, Graph 2)

Valsalva ratio:

The Valsalva ratio was decreased in diabetics as compared to controls

( p < 0.01) (Table 2, Graph 2)

Heart rate response to standing (30:15):

Ratio of heart rate on standing (30:15) decreased in cases as compared to controls (p < 0.05). (Table 2, Graph 2)

E/I ratio

No significant difference was observed in E/I ratio between control and diabetics. (p < 0.94). (Table 2, Graph 2)

Blood pressure response to standing:

When the blood pressure response to supine to standing was evaluated there was a significant decrease in systolic blood pressure among controls and cases (p < 0.05). But there was no significant change in diastolic blood pressure in supine position between cases and controls. Significant decrease in diastolic blood pressure in standing position was also seen between controls and cases (p < 0.01). (Table 2, Graph 2)

Table 2 : Comparison of cardiovascular tests between controls and cases
DISCUSSION

Despite its significant negative impact on survival and quality of life in people with diabetes, Diabetic Autonomic Neuropathy (DAN) is among the least recognized and understood complications of diabetes. A subtype of peripheral polyneuropathies that accompany diabetes, DAN can involve the entire ANS.

Clinical symptoms of autonomic neuropathy generally do not occur until long after the onset of diabetes but symptoms suggestive of autonomic dysfunction may be common. These symptoms may be due to causes other than true autonomic neuropathy.

DAN is typically assessed by focusing on symptoms or dysfunction attributable to a specific organ system. CAN is a subtype of DAN, the most prominent focus because of the life threatening consequences of this complications and the availability of direct tests of cardiovascular autonomic function.

Following cardiovascular reflex tests were used in our study.

1) Resting heart rate,
2) Valsalva maneuver
3) Heart rate response to standing (30:15)
4) Heart rate response to deep breathing (E/I)
5) Recording of blood pressure from lying to standing.

Resting heart rate:

In our study the resting heart rate was increased in diabetics as compared to controls. These findings are in concurrence with many studies[19,20,12,9], which have suggested that increased resting heart rate in diabetics was mainly due to parasympathetic damage in early stage of cardiac autonomic involvement. Normally parasympathetic inhibits heart rate and damage results in increased heart rate.

Valsalva ratio:

On comparing the valsalva ratio among diabetic patients and controls, the ratio was decreased in diabetics. Sharpey-Schfer and Taylor[10] have also showed that Valsava maneuver was often abnormal in diabetics with neuropathy.

This test is performed by asking the subject to sit quietly and then blow into a mouthpiece attached to a manometer held at 40mm Hg pressure for 15 seconds while a continuous ECG is recorded. The ratio of the longest R-R interval during the maneuver (within about 20 beats) to the shortest R-R interval during the maneuver is then measured. The result is expressed as the valsalva ratio which is taken as the mean ratio from three valsalva maneuvers.[18]

American Diabetes Association[24] 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. Heart rate response to standing (30:15)

On comparing the heart rate response to standing the value decreased in diabetic patients.

E/I ratio:

When the E/I ratio is compared between two groups, the ratio was decreased in patients with diabetes.

Rathmann[21] suggested that during inspiration the heart rate increases and on expiration the heart rate decreases. The variation of heart rate with respiration often known as sinus arrhythmia is primarily mediated by the vagal innervation of the heart. The neuronal out put from the respiratory centre influences the gain of the afferent and efferent outputs at the nucleus tractus solitarius. Pulmonary stretch receptors as well as cardiac mechanoreceptors and possibly baroreceptors contribute to regulating the heart rate variation. But in diabetics due to the impairment of parasympathetic system (cholinergic and cardiovagal nerve fibres), the ratio decreases.
Blood pressure response to standing:

Our study shows that there is fall in systolic and diastolic blood pressure on standing. On comparing the blood pressure between the controls and diabetics there was a fall in blood pressure in diabetics.

Low PA[22] and Langer[23] have suggested that this may be because of damage to the efferent sympathetic vasomotor fibers particularly in the splanchnic vasculature. There is decrease in cutaneous, splanchnic, total vascular resistance and the baroreflex compensation is also impaired.

REFERENCES