Research Article

Impact Of Autonomic Function Test On Nasal Mucociliary Function In Diabetic Patients

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ABSTRACT

Background: Autonomic neuropathy is a complication of diabetes having higher mortality rate often diagnosed too late, autonomic function test are the screening test to diagnose autonomic neuropathy in early stage and delay the progress of autonomic dysfunction. This autonomic dysfunction which can affect the nasal mucociliary function in diabetes patients can lead to nasal mucosal dysfunction.

Objectives: 1. To study the effect of diabetes on autonomic function tests and to compare with healthy controls, 2. To evaluate the nasal mucociliary function in patients with diabetes and to compare with healthy controls.

Materials and methods: This comparative case control study done in physiology lab, the test subjects are diabetic patients, and control groups are staffs, they underwent autonomic function test includes deep breathing test, valsalva manoeuver, cold pressor test, heart rate response to standing and hand grip test. Nasal mucociliary function was evaluated by saccharin test.

Result: Total 60 subjects available and values correlated between control and diabetic patients, for valsalva ratio (<0.01), deep breathing test(0.0008), DBP during cold pressor test (0.159), heart rate response to standing (0.013), DBP response to hand grip (0.016).

Conclusion: From this study it is concluded that detection of autonomic neuropathy among Diabetes patients.
INTRODUCTION:
Diabetes mellitus is an endocrine disorder in which high blood glucose either due to deficiency of insulin or its resistance which is the leading causes of mortality and morbidity. According to international Diabetic Federation, the current capital of world, our India will be having 101.2 million diabetic patients by 2030. The number of patients with diabetes mellitus is increasing constantly world-wide, with the increase in the cases of diabetes, complications associated with it are also likely to increase. Diabetes mellitus is characterised by hyperglycaemia, polyuria, polydipsia and polyphagia. The nervous system is so frequently involved in diabetes mellitus that neuropathy has been included in the triad of pathological conditions characteristics of this disease retinopathy, nephropathy and neuropathy. It is known that CAN significantly increases the risk of life threatening arrhythmias and sudden death with the contribution from other risk factors such as hypoglycaemia, adverse effects of drugs, hypokalaemia, hypotension, ischemia, etc. Diabetes is leading cause of autonomic neuropathy. It’s prevalence ranges from 1% to 90%, depending on the diagnostic method, on characteristics of patient cohort and the type of diabetes studied. Although autonomic neuropathy is often subclinical, it is associated with an increased risk for other diabetes complications and mortality. One of the matters of concern is impaired mucociliary clearance that plays an important role in persistence of respiratory infections. Many studies have also shown that Cardiac parasympathetic involvement precedes sympathetic damage. In keeping with the recommendations of the American Diabetes Association (1992), five standard cardiovascular reflex tests are used to assess cardiovascular autonomic function. These include changes in heart rate during deep timed breathing, Valsalva manoeuvre and standing up to assess cardiac parasympathetic activity and blood pressure responses to standing up and sustained handgrip to evaluate sympathetic activity. In addition we also evaluated nasal mucociliary function which also gets affected by the autonomic neuropathy that is seen in diabetes patients. The present study was done with the following objectives.

Aim & Objectives:
1. To study the effect of diabetes on autonomic function tests and to compare with healthy controls
2. To evaluate the nasal mucociliary function in patients with diabetes and to compare with healthy controls

Materials and methods:
Thirty cases of controlled type II diabetes mellitus and thirty non-diabetic age matched controls, including both males and females, were assessed for cardiovascular autonomic status after obtaining written and informed consent.

Inclusion criteria for cases:
1. The individuals of controlled (i.e. fasting blood sugar level ≤126 mg/dl and post prandial blood sugar level ≤180 mg/dl) type II diabetes mellitus attending medicine O.P.D. for regular check up.
2. Age between 30-50 years.
3. Not suffering from any other disease or complications.

All the healthy subjects (controls) and patients (cases) were subjected to general and physical examination. Cardiovascular autonomic function tests and nasal mucociliary function test were carried out in the morning, after familiarising the subjects with the testing procedures.

Laboratory setting
All experiments were performed at the cardiac autonomic function research laboratory in Dept of Physiology, Narayana Medical College.
(NMC), Nellore. The patients were asked to refrain from heavy physical activity for 24 hours and from consumption of alcohol and caffeinated beverages for 12 hours prior to the measurements. The temperature of the laboratory was kept between 25o C - 28o C and lights subdued. The patients were asked to void urine before testing and made to sit in the lab comfortably to accustom to the new environment. First heart rate and auscultatory blood pressure was measured after subject had been sitting quietly for 10mins. The mean of three consecutive measurements with a maximum variation of 4mm Hg of both systolic and diastolic blood pressures was accepted.

**Tests for assessment of cardiovascular autonomic status**

The test for the assessment of CAN was done as per standard protocols published in literature (10,11,12,13).

**Deep breathing test**

The recording of heart rate was done from the ECG recordings on the ECG machine (Cardiowin system, PC based 12 channel simultaneous digital ECG, Genesis Media System Pvt. Ltd, India). A baseline recording of ECG was taken for 30 seconds. The subject was asked to take slow and deep inspiration followed by slow and deep expiration such that each breathing cycle lasted for 10 seconds. Calculation was done from the tracing of ECG. The changes in the heart rate between inspiration and expiration were averaged over 6 cycles.

**Valsalva manoeuver**

It was done in sitting position. The patient was instructed to blow into a mouth piece attached to sphygmomanometer. The expiratory pressure was kept at 40 mmHg for 15 seconds. At the end of15 seconds the subject was asked to release the pressure. Valsalva Ratio was calculated from the longest RR interval during phase IV and shortest RR interval during phase II.

**Handgrip test**

The baseline blood pressure was recorded. The subject was asked to press a handgrip dynamometer at 30% of maximum voluntary contraction for 4 minutes. The blood pressure was recorded at 1st, 2nd and 4th minute of contraction. The rise in the diastolic pressure above the baseline was noted.

**Cold pressor test**

The baseline blood pressure was recorded. The subject was instructed to immerse the right hand in the cold water (8 degree Celsius) for 1 minute up to the wrist. The blood pressure was measured at the end of one minute. The rise in the diastolic pressure over baseline was noted.

**Heart rate response to standing:** Lying to standing test: This test was conducted after 10 min of supine rest. Then the patient was told to stand within 3 s and BP and heart rate were recorded at baseline and at 2nd min. 30:15 ratios were calculated as the ratio between longest R-R at or around the 30th beat and shortest R-R at or around the 15th beat.

**Nasal mucociliary function by Saccharin test:**

**Saccharin test:**

Patient was made to sit erect with 10 degree flexion of the neck. A small piece of saccharin of size 1 mm was placed under direct vision on the inferior turbinate 1 cm away from the anterior end. The patients were instructed not to spit, sneeze or cough during the test duration. After placing the saccharin particle, the time taken for the patient to perceive the sweet taste of saccharin the throat was recorded in minutes.

**RESULT:**

In our study, we have enrolled 30 cases and 30 age- and sex-matched controls. There is no much difference in, Baseline characteristics of the control group and patients with type 2 diabetes and the results of autonomic function results for the control compared with diabetics for delta.
Heart rate in deep breathing test, valsalva ratio, rise in diastolic pressure during handgrip test and cold pressor test and heart rate response to standing are, $P=0.0008$, $P<0.01$, $P=0.2166$, $P=0.159$, $P=0.013$ respectively.

**Table 1: Baseline characteristics of the control group and patients with type 2 diabetes**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameter</th>
<th>Controls</th>
<th>Diabetics</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age*</td>
<td>52.766±5.998</td>
<td>52.8±4.302</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Gender</td>
<td>20:10</td>
<td>21:9</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Weight*</td>
<td>65.46±11.95</td>
<td>67.533±10.081</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>SBP*</td>
<td>127.533±8.315</td>
<td>129.06±8.59</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>DBP*</td>
<td>89.73±11.3</td>
<td>86.066±11.03</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Duration*</td>
<td>NA</td>
<td>4.933±1.25</td>
<td></td>
</tr>
</tbody>
</table>

*Values expressed in Mean ± SD

**Table 2: Autonomic function tests of control group and diabetes patients**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Test</th>
<th>Parameter</th>
<th>Control</th>
<th>Diabetics</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Deep breathing test</td>
<td>Delta heart rate</td>
<td>1.154±0.0638</td>
<td>1.076±1.099</td>
<td>0.0008</td>
</tr>
<tr>
<td>2</td>
<td>Valsalva Manoeuver</td>
<td>Valsalva ratio</td>
<td>1.241±0.112</td>
<td>1.263±0.091</td>
<td>0.091</td>
</tr>
<tr>
<td>3</td>
<td>Response to standing</td>
<td>Heart rate</td>
<td>3.733±3.687</td>
<td>1.00±4.404</td>
<td>0.013</td>
</tr>
<tr>
<td>4</td>
<td>Handgrip test</td>
<td>Rise in diastolic pressure</td>
<td>9.133±3.626</td>
<td>7.933±3.805</td>
<td>0.216</td>
</tr>
<tr>
<td>5</td>
<td>Cold pressor test</td>
<td></td>
<td>13.8±3.907</td>
<td>12.166±4.913</td>
<td>0.159</td>
</tr>
<tr>
<td>6</td>
<td>Saccharin test</td>
<td>Time taken</td>
<td>17.972±3.368</td>
<td>25.417±6.429</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values expressed in mean±standard deviation

**DISCUSSION:**

P value of 0.0008 has been observed in heart rate response to deep breathing, when healthy volunteers are compared with diabetics. This value is statistically significant, which shows that there is a parasympathetic involvement in Diabetic group, because this test is predominantly parasympathetic in nature. In diabetic patients vagal tone is decreased this leads to decreased heart rate variability in respiration which is reflected as decreased E:I ratio values in diabetes our deep breathing test results are in accordance with previous study conducted by Valensi et al\(^{15}\) who conducted a study on diabetics with large sample. In valsalva manoeuver comparison between healthy volunteer and diabetic is 0.001 which is significant, reason for this study in patients with autonomic damage from diabetes, the reflex pathways are damaged resulting in a slow and
steady decline in blood pressure during strain, followed by gradual return to normal after release. Heart rate responses are often unchanged in this, This is reflected in our Study as decreased valsalva ratio our study is in accordance with Levitt et al\textsuperscript{16}, the rate of deterioration of the Valsalva ratio was 0.015 per year for Individuals with type 1 diabetes which was more than twice that expected from Cross-sectional studies of the aging effect in normal individuals of a similar age range. Our study matches with Hathaway et al\textsuperscript{16} he found that end stage renal failure and diabetes mellitus are known to cause autonomic dysfunction. Variation in his study is they used power spectral analysis as well as cardio vagal reflex test (deep breathing and valsalva) and they compared between 4 groups 1,IDDM patients, Type2 DM patients, 3.without DM and4.CRF patients awaiting kidney transplant. His study matches in the aspect that both type 1 and type 2 diabetic had poorer values in deep breathing and valsalva In heart rate response to standing result obtained for control Vs diabetics is \(p=0.013\) (significant). The nasal mucociliary function was less in diabetes patients when healthy controls this reflects the autonomic dysfunction. In diastolic pressure change in cold pressor test and handgrip had \(p\) value of 0.159 and 0.216. these values are not significant.our result in autonomic function test using 5 battery of we found that all the parasympathetic tests are abnormal for diabetic patients.our test results are correlated with following studies Ewing et al\textsuperscript{18} reported parasympathetic dysfunction in 55.73% patients and sympathetic dysfunction was seen in 26.33% patients. Gupta and Pandit found an incidence of 66.3% studied in 47 patients with proven diabetes.\textsuperscript{12} The findings of the present study correlated well with the studies of Ewing et al and Gupta and Pandit.\textsuperscript{12,21} Patnaik et al reported a very high incidence of abnormality (80%).\textsuperscript{16} Many workers have reported a lower incidence. John L et al observed an incidence of 40% in patients with diabetes mellitus, whereas Kudrimoti et al reported 34.28% incidence.\textsuperscript{14,20} Thus the study confirms that the parasympathetic neuropathy is much more common than sympathetic neuropathy in diabetes patients.

**CONCLUSION:**

The autonomic function test can be used to assess the status of autonomic nervous system in diabetics as these tests are simple, non-invasive and inexpensive. As the population of diabetes is rapidly increasing. It has been proved by many studies that, Diabetic Patients were found to have parasympathetic abnormality. From this test it is concluded that detection autonomic neuropathy among patients with diabetes in earlier stages may provide a mean to follow diabetes complications and prevent further progression of disease.

**REFERENCES:**

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