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Research Paper

Correlation of Duration of Diabetes With Cardiac Autonomic Function Tests in Type Ii Diabetes Mellitus Patients

Medical Science

KEYWORDS : autonomic neuropathy, type II DM, Disease duration.

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ABSTRACT

Background and objectives: There are very few asian studies that have shown the correlation between duration of diabetes and cardiac autonomic neuropathy (CAN) in type II Diabetes Mellitus (DM) patients ,as in type II Diabetes Mellitus (DM) autonomic abnormalities are almost the rule. So we undertook this study.

Research Design and Methodology: This study is a cross sectional comparative study, which involved 60 randomly selected patients with type II DM (Group I- 30, short duration of 0-5 years and group II- 30, long duration of >5 years) and 30 healthy controls. The results obtained by performing cardiac autonomic function tests to which score where given. Then, for each patient, Average score was obtained. Pearson's correlation analysis was performed, by taking all test parameters, score as depended variable & duration as independent variable

Results and conclusion: The study showed that as the duration of diabetes mellitus increases, susceptibility to CAN also increase accordingly.

INTRODUCTION

Autonomic neuropathy is the most common complication of Diabetes, which mainly affects the cardiovascular system, gastrointestinal system and urogenital system. Cardiovascular autonomic neuropathy is the earliest form of autonomic dysfunction, which causes abnormalities in heart rate control as well as defects in central and peripheral vascular dynamics.

Type II DM is constituting about 90% of the diabetic population in the Asians. With advancement in the age and duration of diabetes, there is a gradual tendency for the level of blood sugar to rise. It has been observed that mortality of diabetic patients with autonomic neuropathy is greater than those without it. [1] It has been claimed that diabetic patients are more prone to painless myocardial infarction. [2]This could be due to cardiac autonomic neuropathy [CAN].

In view of the immense clinical significance of CAN, it is essential to detect this disorder as early as possible by simplest diagnostic tests. So the present study was designed with the objectives of evaluating and comparing cardiac autonomic functions and in patients of type II DM with age and gender matched healthy controls, with special reference to association of CAN with duration of DM.

MATERIAL AND METHODS

The study was conducted in the Department of Physiology and Department of Medicine from August 2009 to 2011. The study was accepted by the ethical committee of our institution. Inclusion criteria were the following: Type II DM patients between 40 and 60 years, non smokers, non alcoholics and non tobacco chewers with Body Mass Index < 30 kg/m2, controlled diabetic subjects. Exclusion criteria were the following: history of cardiovascular diseases including hypertension, subjects with history of thyroid or other endocrine disorders, patient having drug history which affect autonomic functions (β blockers, antipsychotics, anticholinergics), patient with Diabetic ketoacidosis and any other acute complication of DM.

Based upon these criteria, subjects were thoroughly interviewed and clinically examined. Thus a total of 90 subjects were selected for the present study and were divided into three groups as follows –

Group	Selected subjects / patients	
Control	30 subjects, non diabetic, age and gender matched	
Study	Group I (30 patients)	0- 5 yrs of type II DM
	Group II (30 patients)	> 5 yrs of type II DM

A] Tests based on heart rate for assessment of cardiovascular autonomic status.-

1] Heart-rate response to deep breathing test: -

The subject was in supine position with all ECG leads attached. After breathing normally for 2 minutes, the patient was asked to perform 6 maximum deep breathings in one minute. Continuous ECG record was obtained. E: I ratio was obtained by following formula. [1,3,4]

$$\text{E: I ratio} = \frac{\text{Mean value of longest RR interval during expiration}}{\text{Mean value of shortest RR interval during deep inspiration}}$$

2] Heart-rate response to Valsalva maneuver: -

The subject was in sitting position with all ECG leads attached. Each subject performed the valsalva maneuver for 15 seconds by blowing against a closed glottis through a mouthpiece attached to a sphygmomanometer and maintain a pressure of 40 mm Hg for 15 sec. Three trials were performed at intervals of 5 minutes. A continuous ECG was recorded 1 min before the maneuver (resting period), during the maneuver (strain period, 15 sec.) and 1 min subsequent to the strain period. The valsalva ratio was calculated as follows. [1,3,4]

$$\text{Valsalva ratio} = \frac{\text{Longest RR interval after the maneuver}}{\text{Shortest RR interval during the maneuver}}$$

3] Immediate Heart-rate response to standing :-

Each subject was asked to lie quietly for 3 minutes. He was then asked to stand up and remain motionless. A continuous ECG was recorded and a point was marked on ECG paper to identify the point of standing. The 30:15 ratio was calculated by taking the ratio of the R-R interval at 30^{th} beat and at 15^{th} beat after standing. [1,3,4]

B] Tests based on blood pressure for assessment of cardiovascular autonomic status

4] Hand Grip Test (HGT): -

It is Blood Pressure Response to Static Exercise. The subject was asked to apply pressure on a handgrip dynamometer [Inco-Ambala] for 1 minute at 30% of maximal voluntary contraction and simultaneously the blood pressure, by using automatic digital machine-[Omron] changes were observed. The difference between the diastolic blood pressure (DBP) just before the release of contraction and before handgrip began, was taken as a measure of the response. [1,3,4]

5] Cold Pressor Test (CPT) :-

Resting BP was recorded with the subject sitting comfortably, following which his hand was immersed in cold water and the temperature was maintained at 4-60C throughout the procedure. BP measurement was made from the other arm at 30-second intervals for a period of 2 minutes. After 2 minutes, the subject was asked to remove his hand. The maximum rise in the diastolic pressure was recorded. [1,3,4]

6] Orthostatic test:

The BP was recorded in upper limb in supine position and immediately after standing. Three such readings were taken and a mean fall in systolic BP was recorded. [1,5]

Table I- Normal, borderline, and abnormal values in above tests

Tests	Normal (score 0)	Borderline (score1)	Abnormal (score2)
Heart-rate (R-R interval) variation during deep breathing. (E:I ratio)	≥ 1.21	1.11-1.20	≤ 1.10
Heart-rate response to Valsalva maneuver (Valsalva ratio)	≥ 1.21	1.11-1.20	≤ 1.10
Immediate heart-rate response to standing (30:15 ratio)	≥ 1.04	1.01-1.03	≤ 1.00
Blood-pressure response to sustained handgrip (increase in diastolic blood pressure)	≥16 mmHg	11-15 mmHg	<10 mmHg
Blood-pressure response to cold pressor test(increase in diastolic blood pressure)	≥16 mmHg	11-15 mmHg	<10 mmHg
Blood-pressure response to standing (fall in systolic blood pressure)	≤10 mmHg	11-29 mmHg	≥30 mmHg

OBSERVATIONS AND RESULTS

Table II -Demographic profile of the subjects.

PARAMETERS	CONTROL (n=30)	GROUP-I	GROUP-II	P value
Age (in years)	51.23 ± 6.68	48.43 ± 5.75	52.33 ± 5.28	p>0.05
Sex (M:F)	23:7	21:9	23:7	p>0.05
Systolic BP (mmHg)	125.0 ± 3.51	132.93 ± 4.86	131.80 ± 6.33	p<0.05*
Diastolic BP (mmHg)	71.46 ± 3.27	82.06 ± 6.54	78.60 ± 7.65	p<0.05*
Fasting BSL (mg/dl)	80.77 ± 16.39	85.90 ± 5.49	91.06 ± 10.40	p<0.05*
Postprandial BSL (mg/dl)	127.76 ± 5.72	128.53 ± 4.92	140.0 ± 27.01	p<0.05*
Duration of DM (in years)	-	3.20 ± 1.16	7.83 ± 1.96	-
BMI (kg / m^2)	23.39 ± 1.05	22.93 ± 1.17	22.77 ± 1.24	p>0.05

***p<0.05- Statistically significant**

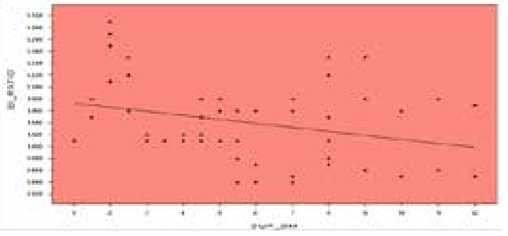
To understand relationship between autonomic deficit & duration of disease Pearson's correlation analysis was performed. By taking all test parameters,average score(total score divided by number of tests that were performed by each patient) as depended variable & duration as independent variable.

Table III - Correlation of all parameters with duration of illness by Pearson's correlation coefficient.

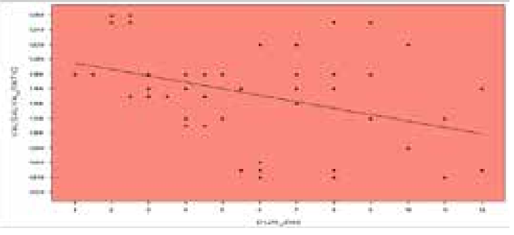
Independent variable	Dependent variable	Pearson's Correlation Coefficient "r"	P-value and Statistical Significance
Duration of DM	Resting HR	0.2596	0.0451*
	E:I Ratio	-0.2862	0.0266*
	Valsalva Ratio	-0.3861	< 0.001**
	30:15 Ratio	-0.2869	0.0262*
	Hand Grip Test	-0.1805	0.1675
	Cold Pressor Test	-0.2636	0.0418*
	Orthostatic Test	0.3219	0.0121*
	Average score	0.4540	< 0.001**

*** < 0.05:- statistically significant and ** < 0.001:- statistically highly significant.**

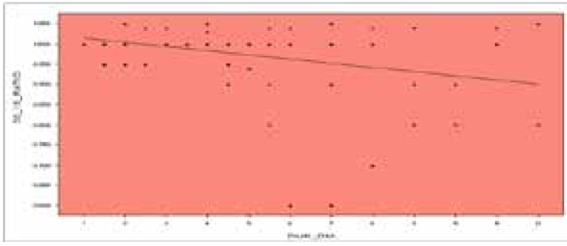
Simple Linear Regression : Dependent Variable – E:I-Ratio, Independent Variable – Duration of DM



Simple Linear Regression: Dependent Variable - Valsalva-Ratio, Independent Variable – Duration Of DM

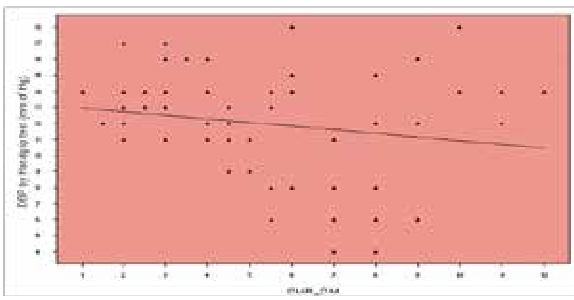


Simple Linear Regression: Dependent Variable – 30:15-Ratio, Independent Variable – Duration of DM

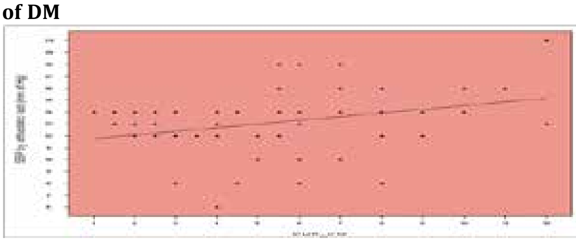


Simple Linear Regression : Dependent Variable – Rise In DBP By Hand Grip Test , Independent Variable – Duration Of DM

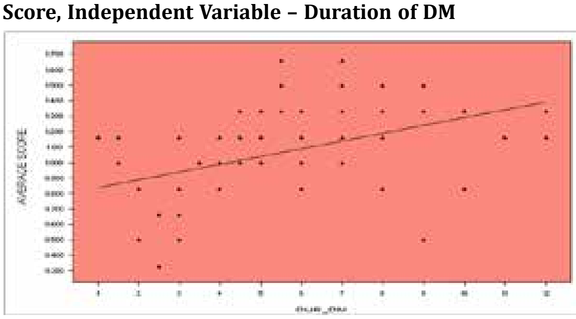
Simple Linear Regression : Dependent Variable –Rise In DBP By Cold Pressor Test Independent Variable – Duration of DM



Simple Linear Regression : Dependent Variable – Fall In SBP By Orthostatic Test, Independent Variable – Duration of DM



Simple Linear Regression : Dependent Variable – Average Score, Independent Variable – Duration of DM



DISCUSSION

A number of simple objective tests of autonomic function based on cardiovascular reflexes have been developed and these tests are now widely accepted as simple bedside assessment of CAN.

As shown in table -III it was observed that Resting HR progressively increases with duration of DM (p=0.0451). Similarly E: I ratio, Valsalva ratio and 30:15 ratio progressively decrease with duration of disease (p=0.0266, p= <0.001, p=0.0262 respectively). Also, rise in DBP by cold pressor test progressively decreases with duration of DM (p=0.0418). Fall in SBP by orthostatic test progressively increases with duration of DM (p=0.0121). Average score showed significant correlation with duration of disease (p=<0.001) i.e. average score increases progressively with duration of disease. As far as rise in DBP by hand grip is concerned, we did not get any significant correlation with duration of diabetes mellitus.

Findings indicate that, as the duration of diabetes mellitus increases, susceptibility to CAN also increase accordingly. Similarly Gunderson et al studied the correlation of beat to beat variation with duration of diabetes. They found that all three types of variations which indicate vagal damage, reduced in long term diabetics and the reduction was in all cases correlated with the duration of diabetes. [6] Page Watkins found a similar correlation of heart rate response to deep breathing with duration of diabetes. [7] In the study observed by Alexandra, he states that autonomic impairment is an early and frequent finding in type II diabetes. It correlated well with age, disease duration, BMI, HbA1c and systolic BP. [8] When pattern and prevalence of cardiovascular autonomic neuropathy in DM visiting a tertiary care referral center was observed at AIIMS (New Delhi), it was noted that there is a direct correlation between the presence of CAN and duration of DM. [9]

Correlation of all above mentioned parameters and average score with duration of illness showed that, there is a linear relation between these parameters with duration of diabetes mellitus. Because of this CAN should be actively diagnosed beginning from its subclinical phase long before clinical signs of autonomic dysfunction become obvious in type II diabetes to prevent further complications.

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