Autonomic Neuropathy of Heart in Diabetes

Ashok Kumar Das, J. Balchandar, S. Chandrasekar

INTRODUCTION

Although the maximal incidence of coronary artery disease in diabetics is well recognized, the other forms of diabetic heart disease have received little attention. Among the latter, one of the major forms is diabetic autonomic cardiac dysfunction.

It was in the last century that Eichorst[1] thought persistent tachycardia to be due to vagal neuropathy and Rundles[2] proposed it as a possible feature of diabetic autonomic neuropathy. However, till quite sometime there were only sporadic references to the abnormal cardiovascular reflexes and cardiac denervation. Advent of newer investigative techniques of continuous heart rate monitoring by Wheeler and Watkins[3] has shown gross abnormalities of cardiac autonomic innervation. This might be responsible for painless myocardial infarction, altered responses to physiological and pathological stress and sudden cardiorespiratory arrest leading to death in a diabetic[4].

MATERIALS AND METHODS

The autonomic function tests were carried out in diabetics by subdividing them into patients with or without peripheral neuropathy. The clinical profile of the diabetics who underwent autonomic function tests is shown in table 1.

Table 1
Clinicial profile of diabetic patients who underwent autonomic function tests

Group	No. of Patients	Mean±SEM Age (yrs)	Mean±SEM duration of DM (yrs)	No.of patients with autonomic symptom
DM with peripheral neuropathy	22	34.7 ± 2.6	3.9 ± 0.4	15
DM without peripheral neuropathy	23	37.0 ± 2.4	3.8 ± 0.6	3

The mean age and the duration of DM in both the groups were identical. Out of the 22 patients with peripheral neuropathy, 15 (68%) patients showed autonomic symptoms while only 3 out of 23 DM patients (13%) without peripheral neuropathy exhibited the same. The details of the various autonomic symptoms are presented in table 2.

Table 2
Details of autonomic symptoms in both the groups of diabetics

Group	No.of patients	Postural giddiness	Impotency	Diarrhoea gastric fullness	Hypoglycemic unawareness	Gustatory sweating
DM with peripheral neuropathy	22	15	3	4	-	1
DM without peripheral neuropathy	23	3	1	-	-	-

Among the various symptoms, postural giddiness was predominant in 15 out of 22 DM patients with neuropathy (68%) and 3 out of 23 DM patients without neuropathy (13%). Other symptoms were minimal.

Cardiovascular Autonomic Function Tests[5]

Valsalva Manoeuvre

The reflex response to the valsalva manoeuvre includes tachycardia and peripheral vasoconstriction during strain, followed after release by an overshoot rise in blood pressure (BP) and bradycardia. Simple measurements of blood pressure and heart rate changes give a valuable and reliable guide to the associated haemodynamic events and have done away with invasive procedures like intra-arterial blood pressure recordings.

The resting values of blood pressure and heart rate were noted with the patient in the supine position. At the outset, the patient was trained to maintain the column of mercury in the standard sphygmomanometer at 40 mm by blowing. After the period of training, the test was performed with continuous heart rate monitoring before, during and after the period of strain. The BP was recorded at a minutes' interval before (3 readings), during (1 reading) and after the period of strain (3 readings). The entire process was repeated thrice.

From Departments of Medicine and Cardiology, JIPMER, Pondicherry – 605 006.

Calculation of valsalva ratio

The "valsalva ratio" was calculated from the ratio of the longest R-R interval after the manoeuvre (reflecting over-shoot bradycardia) to the shortest R-R interval during the strain (reflecting tachycardia during the manoeuvre).

Beat-to-beat (R-R interval) variation

Out of several methods currently available to measure beat-to beat variation, the simplest one namely heart rate variation, during forced deep breathing was adopted here. The subject lies quietly in a supine posture and Lead II of the ECG machine is connected for record the heart rate. After obtaining a stable heart rate record, the patient is instructed to breath deeply at 6-8 breaths/min (for one respiratory cycle, time taken is 10 secs; 5 secs inspiration and 5 secs expiration). This produces the maximum variation in heart rate which is calculated by measuring the differences between minimum heart rate on inspiration and maximum on expiration. Two recent modifications of this technique have been adopted in this study. The first was the measurement of expiration/inspiration ratio - the mean of longest R-R interval during expiration to the mean of shortest R-R interval during inspiration. The second modification is to measure successive maximum and minimum heart rates from an ECG during a period of deep breathing and record the difference.

According to Watkins et al, all normal subjects have a score greater than 9 and the presence of autonomic neuropathy is ruled out if the score is greater than 12.

Postural reflexes

a) Heart rate changes on standing

Change from horizontal to vertical position produces an integrated cardiovascular response including alteration in the heart rate. There is a characteristic and rapid increase in heart rate maximal at about the 15th beat after standing, with a subsequent relative bradycardia, maximal at about 30th beat in normal persons. This reflex is mediated through the vagus nerve. The HR was recorded by the transistorized bedside ECG machine (Siemens) and R-R intervals at beats 15-30 after standing was noted to give the 30/15 rates.

b) BP changes on standing

On standing, there is an immediate fall in BP due to pooling of blood in the legs. In presence of normal baroreflex functions, this is rapidly corrected by peripheral vasoconstriction and tachycardia.

The BP was recorded at 1 minute intervals in the recumbent, sitting and standing position. Three recordings were obtained and the mean value was calculated.

The Atropine Test

This test was done on a different occasion separately on all the patients. Continuous ECG recordings were obtained in the resting state and 3 mins after administration of 1.2 mg of atropine intravenously. HR was again recorded at the 6th and the 10th min. The R-R intervals before and after 3,6 and 10 mins were obtained.

The Nitroglycerine Test

The resting HR and BP was measured initially. Then the patient was administered sublingual tablets of 0.5 mg of nitroglycerine and following complete dissolution, the postural reflexes were repeated as stated above.

Resting Tachycardia

The resting tachycardia was made out by palpatory method while the patient was lying comfortably in a supine postural with complete mental rest. Simultaneous ECG monitoring confirmed the presence of resting tachycardia.

The details of the several autonomic function tests carried out in diabetics (both the groups) are presented in table 3.

Table 3
Autonomic function in diabetic patients with and with out peripheral neuropathy (PN)

Para Meters	Non-diabetic controls (20)	DM with out PN (23)	DM with PN (22)
Beat-to-Beat varia Tion score (no./min.)	19.6±1.9	15.9±1.6	9.4±1.3**
Postural mean arte-rial pressure change (mm Hg)	+6.7±0.6	+2.5±0.4**	-5.2±1.0**
Postural Heart rate change	16.0±1.1	12.2±1.8	7.4±1.2**
Valsalva ratio	1.5±0.06	1.3 ±0.4	1.2±0.05***
Atropine Test(rise in heart rate	25.2±1.2	24.4±1.8	10.1±2.6***

Values are mean ± SEM
Numbers in parentheses indicate the number of patients **P<0.01, ***P<0.001 compared to control

The beat-to-beat variation, HR changes and the valsalva ratio were significantly reduced in diabetics with peripheral neuropathy as compared to non-diabetics (control group), while these parameters were not significantly altered in diabetics without peripheral neuropathy. Seventeen out of 22 patients of DM with peripheral neuropathy (78%) had beat-to-beat variation in HR below 10, whereas only 3 out of 23 patients of DM without peripheral neuropathy (13%) had similar variation. When patients were tested for mean arterial pressure change, there was a significant fall in diabetics with peripheral neuropathy in contrast to the rise observed in non-diabetics. However, in diabetics without peripheral neuropathy, there was a significant reduction in the mean arterial pressure (MAP) rise as compared to non-diabetics.

The atropine test in the diabetics with peripheral neuropathy produced a significantly less rise in heart rate compared to that of non-diabetics and diabetics without neuropathy.

In trinitroglycerine (TNG) test, the vasodilatory action o the drug results in a fall in mean arterial pressure to which compensatory tachycardia occurs. The TNG test revealed that the diabetics without peripheral neuropathy showed a corresponding fall in MAP with a concomitant reflex increase in HR similar to that observed in the non-diabetic control group. On the contrary, diabetic patients with peripheral neuropathy failed to show an increase in the heart rate even though the fall in MAP was much greater. On repeating the postural reflexes on standing after TNG in the control group, the mean arterial pressure fell and was fallowed by an appropriate rise in HR. In this group without peripheral neuropathy(PN), there was a fall in MAP with an attendant increase in HR. In contrast, in the group of DM with PN the fall in MAP was significantly greater than either of the previous groups and the heart rate increase was much lower showing loss of the baroreceptor reflex.

SUMMARY AND CONCLUSION

These investigations denote that autonomic cardiac dysfunction is one of the most important facets in the genesis of diabetic heart disease. Absence of several cardiovascular reflexes in a diabetic is bound to have repercussions in times of stress during which normal cardiac reserve will not come into play. As discussed, by using the simple, reproducible above mentioned tests, it is possible to detect and quantify autonomic dysfunction. Hence, it is recommended that each diabetic clinic should carry out such initial evaluation procedures to identify these groups of DM patients who warrant special attention.

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.

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