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Cardiovascular sympathetic functional status of controlled type II diabetes mellitus

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Abstract: *Objective:* The blood pressure responses to standing and sustained handgrip were studied in cases and controls. *Background*: The cardiovascular sympathetic functional status can be assessed by using simple tests; effective for diagnosis of early cardiovascular autonomic dysfunction. *Material and Method:* The cardiovascular sympathetic function tests have been conducted in 40 cases of controlled type II diabetes mellitus and 40 controls, aged between 30-50 years, including both sexes. *Result and Discussion:* Cases showed significantly decreased response of systolic and diastolic blood pressure to standing and to sustained handgrip. The responses in cases were significantly correlated to age and duration of DM, but not to BMI; signifying that autonomic dysfunction occurs in Diabetes Mellitus and progresses with the duration of the disease and the age.

Keywords: Diabetes mellitus, Cardiovascular autonomic neuropathy, Sympathetic function tests

Introduction

Diabetes mellitus is most common among endocrine and metabolic disorders. It is ranked fifth as a leading cause of death worldwide, and is responsible for almost 3 million deaths annually [1]. The worldwide prevalence of diabetes mellitus is rising rapidly because of increasing obesity and reduced physical activity levels; as countries become more industrialized. Although, the most common neurological disturbance in diabetes is the involvement of peripheral nerves; the concomitant involvement of autonomic nervous system has long been known**.** When autonomic nervous system is affected, it can lead to variety of symptoms such as tachycardia, orthostatic hypotension, gastro-paresis, fecal incontinence, bladder dysfunction; thus significantly affecting the quality of life of a diabetic patient. Furthermore, the presence of autonomic neuropathy carries a significantly increased risk of cardiovascular mortality, i.e. sudden cardiac arrest**.** Clinical symptoms of autonomic neuropathy generally do not occur until long after the onset of diabetes**.** Sub-clinical autonomic dysfunction, can however, occur within a year of diagnosis in type II diabetic patients [2-3].

Cardiovascular autonomic neuropathy (CAN) is clinically important form of diabetic autonomic neuropathy (DAN) which is associated with an increased risk of silent myocardial ischemia and mortality**.** The determination of presence of CAN is usually based on a battery of autonomic function tests [4].

In this study, we tried to assess cardiovascular sympathetic function in cases of controlled type II diabetes mellitus by measuring the blood pressure response to standing from the supine position and blood pressure response to sustained handgrip. These blood pressure responses in cases were compared with age matched healthy non diabetic controls. The results in cases were, also analyzed for correlation with age, body mass index and duration of diabetes mellitus.

Material and Methods

Forty cases of controlled type II diabetes mellitus and forty non-diabetic age matched controls, including both males and females, were assessed for cardiovascular sympathetic functional status after obtaining written and informed consent. The study was approved by institutional ethics committee.

The following criteria were followed while selecting the patients as 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 sympathetic function tests were carried out in the morning, after familiarizing the subjects with the testing procedures.

The following tests were performed to assess the cardiovascular sympathetic functional status:

1. Blood pressure response to standing from the supine position.
2. Blood pressure response to sustained handgrip.

The maneuver and recording of responses was carried out as follows:

1. Blood pressure response to standing from the supine position [2, 5]: The subject was asked to lie supine on the examination table. The blood pressure was recorded after the 5 minutes of rest from the right arm with the help of sphygmomanometer (cuff size 12.5cm×40.0cm) by Auscultatory method. The cuff was deflated and the subject was asked to stand up. The systolic and diastolic blood pressure was measured again at the end of 1 minute after standing from the supine position from the same arm. The difference in the blood pressure was noted.

2. Blood pressure response to sustained handgrip [2, 5]: The subject was asked to sit comfortably on the chair. The systolic and diastolic blood pressure was measured from the right arm with the help of sphygmomanometer by auscultatory method. The subject was, then, asked to grip the dynamometer with the left hand to determine the maximum voluntary contraction. The handgrip was then maintained steadily at 30% of that maximum voluntary contraction for 1 minute. Again blood pressure was measured with the cuff of the sphygmomanometer on the right arm (non exercising arm) by auscultatary method, at the end of 1 minute after the onset of handgrip. The difference in the blood pressure was noted.

Statistical analysis: Statistical analysis was done by using a test of standard error of difference between two means (z-test) [6].

Results

The results of the above tests were compared between the cases (controlled type II diabetes mellitus) and healthy age matched controls. Values are expressed as mean ± SEM in the tables. The comparison of results was, also, done between two groups of cases made according to the duration of diabetes mellitus as under-

Group 1: Cases with the duration of DM < 5 yrs (n = 23).
Group 2: Cases with the duration of DM ≥ 5 yrs (n = 17).

Table-1: Change in systolic blood pressure in response to standing from the supine position and to sustained handgrip. (Values are expressed as mean ± SEM.)

parameter	Cases (n=40)	Controls (n=40)	Z value	P value
dSBP with supine to standing test (After 1 min.)	(-)7.0±1.22	(-)2.9±0.41	3.20	<0.01
dSBP with sustained handgrip (After 1 min.)	(+)14.85±1.20	(+)19.55±0.86	3.48	<0.01

dSBP: change in systolic blood pressure (-) indicates fall (+) indicates rise

Table-2: Change in diastolic blood pressure in response to standing from the supine position and to sustained handgrip. (Values are expressed as mean ± SEM.)

parameter	Cases (n=40)	Controls (n=40)	Z value	P value
dDBP with supine to standing test (After 1 min.)	(-)5.43±0.66	(-)2.20±0.43	4.08	<0.01
dDBP with sustained handgrip (After 1 min.)	(+)11.5±0.96	(+)15.9±0.83	3.49	<0.01

dDBP: change in diastolic blood pressure (-) indicates fall (+) indicates rise

As shown in Table-1, the fall of the systolic blood pressure in response to the standing from the supine position was highly significantly ($p<0.01$) more in cases as compared to controls. Similarly, increase in the systolic blood pressure in response to sustained handgrip was highly significantly ($p<0.01$) more in controls as compared to cases. According to Table-2, the fall of the diastolic blood pressure in response to the standing from the supine position was highly significantly ($p<0.01$) more in cases as compared to controls. Similarly, increase in the diastolic blood pressure in response to sustained handgrip was highly significantly ($p<0.01$) more in controls as compared to cases.

Table-3: Change in systolic and diastolic blood pressure in response to sympathetic function tests between two groups of cases made according to the duration of diabetes mellitus. (Values are expressed as mean ± SEM.).

parameter	Change in the blood pressure after standing from the supine position		Change in the blood pressure after sustained handgrip	
	SBP (mmHg)	DBP (mmHg)	SBP(mmHg)	DBP (mmHg)
Group1[Duration of DM < 5 yrs (n = 23)]	4.08 ± 0.84	2.78 ± 0.53	18.00 ± 1.43	14.95 ± 1.67
Group2[Duration of DM ≥ 5 yrs (n = 17)]	11.36 ± 1.38	9.29 ± 0.87	10.58 ± 1.17	8.70 ± 1.36
Z value	3.25	6.44	4.01	3.04
P value	<0.01	<0.01	<0.01	<0.01

SBP: systolic blood pressure DBP: diastolic blood pressure

Table-4: Correlation of BMI, age and duration of diabetes mellitus with blood pressure responses to standing from the supine position and to sustained handgrip in cases

Correlation coefficient(r)	Change in blood pressure after standing from supine		Change in blood pressure after sustained handgrip	
	SBP(mmHg)	DBP(mmHg)	SBP(mmHg)	DBP(mmHg)
BMI	r = 0.06 (p>0.1)	r = 0.19 (p>0.1)	r = 0.05 (p>0.1)	r = 0.02 (p>0.1)
Age	r = 0.42 (p<0.05)	r = 0.38 (p<0.05)	r = 0.43 (p<0.01)	r = 0.35 (p<0.05)
Duration of diabetes mellitus	r = 0.53 (p<0.001)	r = 0.78 (p<0.001)	r = 0.59 (p<0.001)	r = 0.04 (p<0.05)

SBP: systolic blood pressure DBP: diastolic blood pressure

Table-3 shows highly significant ($p<0.01$) difference in blood pressure response to standing from the supine position and to sustained handgrip between two groups of cases. Table-4 shows no significant ($p>0.05$) correlation of the BMI with the cardiovascular sympathetic function tests in cases. The age of the patient and duration of diabetes mellitus shows significant ($p<0.05$) correlation with the cardiovascular sympathetic function tests.

Discussion

Cardiovascular sympathetic function tests which were carried out in this study have been extensively used in the past. They are standard, non invasive, safe and easily reproducible [2, 5]. In our study, the cases of controlled type II diabetes mellitus showed more fall of systolic as well as diastolic blood pressure, 1 minute after standing from the supine position, as compared to controls. When these differences of fall of blood pressure were tested by applying Z test, it was found to be highly significant (Table 1 & 2). Similar findings are published earlier [2, 7-8]. On standing from the supine position, there is pooling of blood in circulation of dependent parts i.e. lower part of the body. This causes decreased venous return to the heart. This decreases cardiac output subsequently, resulting in fall of the blood pressure [5, 9]. In healthy subjects, fall of blood pressure after standing from the supine position initiates peripheral vasoconstriction and tachycardia mediated through sympathetic efferent vasomotor fibers via baroreflex mechanism to correct the fall in blood pressure. Usually systolic blood pressure does not fall below 10 mmHg within 30 seconds after standing in normal adults [2].

In cases (of controlled type II diabetes mellitus), we have observed more fall in the systolic as well as diastolic blood pressure on standing from the supine position as compared to controls. This might be because of autonomic dysfunction in cases, causing damage to the efferent sympathetic vasomotor fibers. This may have resulted in the impairment of the baroreflex mediated vasoconstriction and tachycardia [2, 7]. Similarly, the increase in the systolic and diastolic blood pressure in response to sustained handgrip was significantly less in cases as compared to controls (Table-1 & 2). Our findings match with those published earlier [2, 8, 10]. The transition from the rest to the muscular exercise is followed by rapid adjustments of circulatory and respiratory parameters. The onset of cardiac acceleration almost instantaneously follows the start of muscular activity. The initial phase of acceleration is induced through inhibition of cardiac vagal tone, followed by increased activity of sympathetic accelerator nerves. This causes rise in heart rate and blood pressure [11-12]. In normal healthy subjects, the diastolic blood pressure increases by 16 mmHg or more at 1 minute after sustained handgrip, maintained at 1/3rd of maximum voluntary contraction. This rise is caused by a reflex arc from the exercising muscle to a central command and back along the efferent sympathetic fibers. These efferent sympathetic fibers innervate the heart & blood vessels, resulting in vasoconstriction and increased heart rate, cardiac output, and finally altogether causing increased blood pressure [2, 5, 13]. In cases, we have observed a lesser increase in the systolic as well as diastolic blood pressure than controls. This may be attributed to the autonomic dysfunction [11]. Damage to the sympathetic nerve fibers innervating the heart & blood vessels may be responsible for the above mentioned findings. In the present study, the cases were divided into two groups depending on duration of diabetes mellitus (Table-3). Cases with the duration of DM $<$ 5 yrs (n = 23) and those with the duration of DM $\geq$ 5 yrs (n = 17). Both the groups were tested for cardiovascular sympathetic function tests. The fall in the systolic as well as diastolic blood pressure 1 minute after standing from the supine position was found to be more in cases with the duration of DM $\geq$ 5 years than those with the duration of DM $<$ 5 years. Similarly, when tested for the blood pressure response to sustained handgrip, the increase in the systolic as well as diastolic blood pressure was more in the cases with the duration of DM $<$ 5 years than those with the duration of $\geq$ 5 years. These findings suggest that the frequency of autonomic neuropathy in type II DM patients increases with the duration of diabetes. Poor glycemic control with increasing duration of diabetes may be an important determinant of the progression of autonomic nervous dysfunction [2, 8, 14].

We have observed a statistically significant correlation between the age of the patient and blood pressure responses to standing from the supine position and to sustained handgrip (Table-4). This suggests that with increasing age, impairment of circulatory reflexes occurs resulting in abnormal response of blood pressure to cardiovascular sympathetic function tests. Whereas a non significant correlation was observed between the BMI of the cases and the blood pressure responses to cardiovascular sympathetic function tests. It can be concluded that cardiovascular sympathetic autonomic neuropathy occurs in the diabetes, resulting in the decreased response of the blood pressure to standing from the supine position and to sustained handgrip. Similarly the sympathetic autonomic dysfunction progresses with the duration of the diabetes mellitus and with the age of the patient. Thus the cardiovascular sympathetic functional status of controlled type II diabetes mellitus patients can be assessed by using these tests, which are very simple, easy and can detect autonomic neuropathy even before appearance of its clinical manifestations.

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