

Conventional Method to Evaluate Autonomic Functions in Obese Type-II Diabetics

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Abstract

Introduction: The efficiency and functional status of autonomic activity can be assessed by using the simple noninvasive tests for effective diagnosis of autonomic imbalance in various diseases. The obesity and diabetes mellitus are the leading clinical conditions which deviates the autonomic tone and affects homeostasis. This study had objective of investigating alterations in sympatho vagal balance in obese type II diabetes mellitus.

Method: The autonomic function tests were done in thirty obese diabetic adults and 30 non obese adults aged between 30-50 years. All the procedures were performed in the morning after their light breakfast in a less noise and illuminated room.

Results: The results showed all autonomic function tests are statistically significant except valsalva manoeuvre. Trend in decrease in these variables in obese diabetes were suggestive of decreased efficiency of autonomic balance.

Conclusion: Therefore, early detection of functional impairment of autonomic changes and its appropriate management is the only means by which the morbidity and mortality can be reduced.

Keywords: Obesity, Autonomic nervous system, Diabetes mellitus, Body Mass Index.

Introduction

According to WHO, the term Diabetes Mellitus (DM) describes a metabolic disorder of multiple etiology, characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion or insulin action or both¹. Diabetes mellitus (DM) is increasingly common worldwide. Estimates indicate that the total number of people with DM will more than double from 171 million in 2000 to 366 million in 2030. By 2030, more than 75% of people with DM will live in developing

countries². The greatest relative increase is expected to occur in countries in the Middle East, and India. DM in these countries is associated with higher mortality rates because of acute and chronic complications that occur early in the course of the disease³. It is accepted that hyperglycemia among persons with diabetes causes degradation of the microvasculature that results in Peripheral and autonomic diabetic neuropathy which are common chronic complications of DM that occur in diabetic patients⁴. DAN in diabetes is an irreversible complication, but early detection is important, because although the condition cannot be reversed, intensive diabetes care may delay its further development. DAN may affect both the parasympathetic and sympathetic nervous system⁵.

In India Nutritional problem is gradually shifting from undernourishment to obesity. This shift is because of the advent of civilization, sedentary lifestyle and high-calorie diet. Autonomic neuropathy is a common

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and serious complication of Type-II Diabetes mellitus associated with obesity⁶. It is generally accepted that the increasing prevalence of diabetes is associated with increased rates of obesity and it has been estimated that 90% of type 2 diabetes is attributable to excess weight⁷.

Ewing et al. suggested utilizing a standard battery of autonomic functions tests, including heart rate (HR) variation in response to deep breathing, HR response to standing, postural changes in BP, the Valsalva manoeuvre, and sustained handgrip. Thus, genetic and environmentally caused variations in autonomic nervous regulation may exist; hence, studying responses to autonomic function tests in DM patients is highly warranted. Recent studies show the past two decades have correlated sympathetic nervous system activity in normal-weight and obese individuals⁸. These studies include hypertension, myocardial infarction, congestive heart failure, and vascular thrombosis. It is mainly because of Autonomic dysfunction where the sympathetic activity is decreased and parasympathetic activity is increased. The aim of the study was to establish reference values for a battery of five easy-to-use, non-invasive cardiovascular autonomic function tests for clinical use. The study was undertaken to assess the AFT in obese Type-II Diabetics and the results were compared with non-obese Type-II Diabetic controls.

Materials and Method

This is a cross-sectional study undertaken in the Department of Physiology, Narayana Medical College, and Nellore. Institutional Ethical clearance was obtained for this study. Entire AFT procedure was explained to the each subject and informed written consent was taken as per the declaration of Helsinki. All the subjects were instructed to maintain their normal sleep pattern, not to ingest beverages with caffeine or alcohol, and not to perform physical exercise before the evaluations. This test was conducted in morning after 2 hours of light breakfast. Subjects were encouraged to void urine before commence of recording. In all the procedures were done in a less illuminated and noise free room. The test group subjects were Obese Type 2 Diabetes Mellitus patients, who were otherwise normal attending the outpatient department, and central laboratory of Narayana Medical College and Hospital. The control group subjects were teaching and non-teaching staff of Narayana Medical College. All subjects underwent autonomic function tests which included 1) Deep Breathing Test 2) Valsalva Manoeuvre 3) Cold Pressor test (Cold pressure test) 4) Heart rate response to standing 5) Hand grip test.

Anthropometric measurements: Anthropometric measurements such as height by stadiometer, weight by the electronic weighing machine were assessed. BMI was calculated by dividing body weight (in kg) by height (in meters) squared. The BMI less than 25 kg/m² considered as normal weight, 25-30 kg/m² as overweight and more than 30kg/m² as obese.

Deep breathing test: Heart rate increases during inspiration due to decreased cardiac vagal activity and decreases during expiration due to increased vagal activity. This is detected by recording the heart rate while the subject is breathing deeply. The subject was instructed to maintain deep breathing at a rate of six breaths per minute. The subject was made to lie down in supine position. ECG electrodes were connected for recording Lead II ECG. While the subject was breathing deeply maximum and minimum heart rates were recorded with each respiratory cycle.

Valsalva manoeuvre: The Valsalva ratio is a measure of parasympathetic and sympathetic functions. For the response to occur in Valsalva manoeuvre parasympathetic acts as afferent and efferent and sympathetic acts as a part of the efferent pathway. Therefore the Valsalva ratio assesses more of parasympathetic function. The Valsalva ratio is a measure of the change of heart rate that takes place during a brief period of forced expiration against closed glottis or mouthpiece (Valsalva manoeuvre). During and after the Valsalva manoeuvre there will be the change in cardiac vagal efferent and sympathetic vasomotor activity, resulting from stimulation of carotid sinus, aortic arch baroreceptors, and other intra-thoracic stretch receptors.

Blood pressure response to cold pressor test: The subject was asked to sit on the chair and instructed regarding the test, blood pressure was measured from the right arm by the auscultatory method. The subject was asked to submerge one of his limbs in cold water for 60 seconds. BP was recorded at the end of 60 seconds of submersion of the limb.

Heart rate response to standing: On changing the posture from supine to standing heart rate increases immediately by 10-20 beats per minute. This is detected by recording ECG in supine and standing postures. The subject was made to lie down in the supine posture. Electrodes were connected from the subject to the cardio win system. The subject was asked to relax completely for a minimum period of 10 minutes. Basal heart rate

was recorded by using cardio win system. The subject was asked to stand up immediately and change in heart rate was noted from the cardio win. Heart rate response to standing was determined by using the formula heart rate in standing position–heart rate in supine position.

Blood pressure response to sustained handgrip:

The subject was then asked to 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 by auscultatory 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 carried out using graph pad prism & data was represented as mean and SD. Normality of data was tested using Kolmogorov-Smirnov test. A *p* value of > 0.05 indicated normal Gaussian distribution. As the data sets were skewed, Mann-Whitney test was performed and Spearman correlation were done to find out associations.

Results

Table 1 shows Age distribution and BMI in Obese and Non-obese diabetic patients.

Status of Obese diabetes	Mean age	BMI
Obese DM	38.640.27	32.4±2.37
Non-obese DM	36.92±0.23	25.02±4.23
P value	0.73	<0.01

Table 2 shows different parameters of AFT in Obese and Non-obese diabetic patients.

Test	Mean Obese DM	Mean Non obese DM	P value
E: I ratio	1.47± 0.22	1.22± 0.27	<0.05
Valsalva maneuver	1.18± 0.16	1.33± 0.23	0.07
Cold pressor (SBP)	19.60±2.99	9.44±2.53	<0.01
Cold pressor (DBP)	10.66±3.6	7.06±3.8	0.02
HR response to standing	19.9±2.01	11.8±3.40	<0.01
Handgrip (SBP)	5.33±2.3	8.33±3.56	<0.01
Handgrip (DBP)	6.1±2.8	4.1±3.1	0.05

Discussion

The autonomic nervous system consists of sympathetic and parasympathetic divisions. Intact cardiac autonomic innervations are essential for normal

heart rate. The sympathetic nervous system has control of the myocardial contractility and heart rate whereas the parasympathetic effect is essential on the heart rate. The resting heart rate measurement signifies the autonomic tone at rest while, the cardiovascular response to stimuli which is essentially reflexive in nature.

Under resting conditions, the cardiovascular system is under the control of both the division of the autonomic nervous system. The fact that variability of the heart rate occurs because of the autonomic innervations of the SA node has been utilized to develop the following tests that stimulate the autonomic supply and produce variability in heart rate. The extent of the control by these two autonomic limbs varies from individual to individual. The autonomic reactivity was assessed in the study group by viewing the reflex of the cardiovascular system to lab stressors like standing from the supine position, undergoing handgrip exercise and by giving a painful stimulus by immersing the hand in cold water. The parasympathetic reactivity and sympathetic reactivity were separately tested by these stressors.

Heart rate response to standing: When a subject assumes an erect posture from supine posture, gravity causes pooling of blood in the lower limbs. As a result venous return, cardiac output and arterial BP decreases. This leads to decrease stretch of baroreceptors and activation of the vasomotor center. This, in turn, leads to increased sympathetic discharge, decreased vagal tone and an instantaneous increase in HR. In our study Heart rate is increased in all the subjects but this heart rate was significantly increased in the hypertensive group when compared to the normotensive group. This finding indicates the possible dysfunction of the sympathetic and parasympathetic component of the autonomic nervous system. The findings in our study correlated with the study conducted by WW McCrory, AA Klein et. al ¹¹. This is reflected in our study as increased Heart rate response to standing.

It is difficult to show the BP response to standing because according to WHO, for recording Arterial BP by sphygmomanometer three minutes duration is required. But, within 15-30 seconds Baroreceptor mechanism corrects the change in BP in response to standing. The results of all the above-mentioned tests are statistically significant.

Cold pressor test: Under conditions of stress either physical or psychological origin there is activation of the sensory nervous system. The cold pressor response

consists of placing the hands in cold water acts as a painful stimulus, which has been used to study the autonomic response. In cold pressor test, an increase in the SBP by 10-20 mm of Hg and DBP by 10 mm of Hg is considered as a normal response. The afferent fibers for this response are the somatic fibers carrying the pain sensation which are stimulated by placing the hand in cold water and efferent fibers are the sympathetic fibers. In our study there is a significant rise in systolic blood pressure was found in the hypertensive group, whereas diastolic blood pressure also rises significantly in the hypertensive group over the normotensive group by cold pressor test. The pattern of the rising of blood pressure was within 30 seconds reaching its peak at around 60 seconds and the basal blood pressure was achieved within 2 minutes in normotensive subjects and the prolonged pressor response was found in hypertensive patients.

Generally, Cold pressor test is largely related to great sympathetic efferent discharge causing arterial vasoconstriction. Hypertensive subjects respond to cold pressor stimulus with a predominant rise in total peripheral resistance and also there were higher levels of plasma norepinephrine. The findings in our study correlated with the study conducted by Benetos A.¹² and Douglas L. et. al¹³. The result of the above-mentioned tests is statistically significant.

Hand grip test: Isometric exercise produces a significant increase in blood pressure and heart rate, a response which can easily be elicited by using sustained hand grip. In this test, increase in blood pressure is due to increased sympathetic activity mediated by the alpha-adrenergic receptors. An increase in heart rate in response to handgrip is due to impulses from the limbic cortex, motor cortex, and the proprioceptors as afferent inputs into the cardiac centers cause inhibition vagal tone and increases in heart rate. Impaired sympathetic noradrenergic function of SA node, myocardial activity and peripheral resistance in patients is responsible for decreased SBP and DBP values, increased heart rate in the handgrip. The results for the above-mentioned tests are statistically significant similar findings were reported by Vijayalakshmi et. al¹⁴.

Deep breathing test: In healthy young individuals breathing at a normal rate, the heart rate varies with the phases of respiration i. e; heart rate accelerates during inspiration and decelerates during expiration, Sinus arrhythmia is a normal phenomenon and is due

to fluctuation in parasympathetic output to the heart. Baroreceptors are solely responsible for resting heart tone in the normal breathing individuals. During inspiration, neuronal activity of inspiration neurons in the medulla besides initiating inspiration also discharge to nucleus tractus solitarius (NTS), nucleus accumbens and inhibit both the relay centers of the baroreceptors, NTS-NA pathway. This leads to inhibition of vagal tone which in turn increases heart rate during inspiration and a decreases during expiration. An altered sympathovagal balance and reduced influence of parasympathetic nervous system on heart rate lead to impaired heart rate variability in respiration which is reflected in our study as increased E: I ratio values. The results of the above test are not statistically significant.

Valsalva manoeuver: The Valsalva ratio is a measure of vagal and sympathetic activity on the heart. For the response to occur in Valsalva manoeuver, parasympathetic acts as afferent and efferent. Sympathetic acts as a part of the efferent pathway. Therefore, Valsalva manoeuver assesses more of parasympathetic activity. The result of the above-mentioned test was statistically not significant. Similar findings have been reported by Sujatha gautam et. al¹⁵.

Limitations: The present study has some limitations, the conventional AFT are cumbersome to perform the procedures and analyze the data results. It is tedious to determine the autonomic derangement. There are so many advanced noninvasive techniques to determine neuropathy in the autonomic nervous system like HRV and dynamic pupillometry^{9, 10}.

Conclusion: The autonomic derangement can be evaluated by traditional autonomic function tests. The improper management of glycemic index and lipid profile leads to long nerve neuropathy in diabetic patients which is augmented by obesity.

Conflict of Interest: None declared

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