Assessment of Peripheral and Autonomic Neuropathy among Patients with Impaired Glucose Tolerance: A Clinical Study

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ABSTRACT

Introduction: One of the major diseases of worldwide concern is the Diabetes mellitus. 2.8 percent is the current global prevalence of DM in all the age groups and is estimated to be more than 4 percent by the end of 2030. Treatment and prevention of the risk factors to minimize the morbidity of the disease is the present need of thee hour for reducing the prevalence of the disease. Peripheral neuropathy often accompanies DM and also is an important cause of foot ulceration, and amputation. Hence; we investigated the influence of the IGT on peripheral or autonomic nervous system.

Material and Methods: The present study was conducted in the department of physiology of the medical institution and included a total of 50 patients with age group of 37 to 62 years who were diagnosed with IGT on testing the 2hPG (second-hour plasma glucose) in oral glucose tolerance testing. 50 normal healthy controls were also included in the present study with comparable age and other demographic parameters. The difference between the longest and the shortest R-R intervals was named 'a'. The median of all R-R intervals was named 'b'. The ratio of 'a' to 'b' was multiplied by 100. The result gives the heart rate variation variability. Increase in pressure above or equal to 16 mmHg was accepted as normal response, increase in pressure between 11 and 15 mmHg was accepted as borderline response, and increase in pressure lower than 11 mmHg was accepted as abnormal response. All the results were analyzed by SPSS software.

Results: The mean heart rate variation in the patients group and control group was 21.45 and 23.41 respectively. The mean E:I rate in the patients group and the control group was 1.42 and 1.28 respectively. Non-significant results were obtained while comparing the heart rate variation, E:I rate and valsalva rate in between the two study groups. Non-significant results were obtained while comparing the blood pressure response in between the patients of the two study groups.

Conclusion: The degeneration of small-fibers was reached as a conclusion of the evaluation of queries about the complaints, neurological examination, and electrophysiological tests.

Keywords: Autonomic, Diabetes mellitus, Peripheral

INTRODUCTION

One of the major diseases of worldwide concern is the Diabetes mellitus (DM). 2.8 percent is the current global prevalence of DM in all the age groups and is estimated to be more than 4 percent by the end of 2030.[1] Treatment and prevention of the risk factors to minimize the morbidity of the disease is the present need of thee hour for reducing the prevalence of the disease. Peripheral neuropathy (PN) often accompanies DM and also is an important cause of foot ulceration, and amputation. Early diabetic neuropathy is the current topic of research and is the centre of focus. Recent data has shown that with the improvement in the glycemic control, a slowing of progression of neuropathy is seen.[2] It has been suggested in the recent studies that some amount of association exists in between impaired glucose tolerance (IGT) and neuropathy.[3,4] Hence; we investigated the influence of the IGT on peripheral or autonomic nervous system.

MATERIAL AND METHODS

The present study was conducted in the department of physiology of the medical institution and included a total of 50 patients with age group of 37 to 62 years who were diagnosed with IGT on testing the 2hPG (second-hour plasma glucose) in oral glucose tolerance testing. 50 normal healthy controls were also included in the present study with comparable age and other demographic parameters. Individuals who have diseases with potential risk of peripheral and/or autonomic neuropathy were excluded on the basis of complete blood count, renal function tests, liver function tests, thyroid function tests, vitamin- B12 level, folic acid level, sedimentation rate, rheumatoid factor, anti-nuclear antibody, and protein electrophoresis.

Autonomic tests

Two consecutive QRS complexes were observed on the monitor. The first QRS complex was triggered and stabilized at a steady level after the stimulation artifact and variability in the latency of the second QRS complex was evaluated. Recordings were obtained after a grounded electrode on the forearm and two stainless steel 6-mm in diameter disc electrodes on the dorsum of the hands were positioned The difference between the longest and the shortest R-R intervals was named 'a'. The median of all R-R intervals was named 'b'. The ratio of 'a' to 'b' was multiplied by 100. The result gives the heart rate variation variability (HRR).

Blood pressure response to isometric exercise

Patients were asked to grip the sphygmomonometer with their right hands (using 30% of their maximum power for 5 min or 60 mmHg of pressure for 3 min). Systolic and diastolic blood pressures were recorded before and during each 3 consecutive min of the exercise. Increase in pressure above or equal to 16 mmHg was accepted as normal response, increase in pressure between 11 and 15 mmHg was accepted as borderline response, and increase in pressure lower than 11 mmHg was accepted as abnormal response. All the results were analyzed by SPSS

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software. Chi-square test was used for the assessment of level of significance.

RESULTS

Figure 1 shows the heart rate variation (HRR), expirium: inspiration rate and valsalva rate in the patients of the two study groups. The mean heart rate variation in the patients group and control group was 21.45 and 23.41 respectively. The mean E:I rate in the patients group and the control group was 1.42 and 1.28 respectively. Table 1 shows the p-value for the comparison of the heart rate variation (HRR), expirium: inspiration rate and valsalva rate in the patients of the two study groups. Non-significant results were obtained while comparing the heart rate variation, E:I rate and valsalva rate in between the two study groups. Figure 1 shows the blood pressure response to standing in the patients of the two study groups. Non-significant results were obtained while comparing the blood pressure response in between the patients of the two study groups.

DISCUSSION

Diabetic Autonomic Neuropathy belongs to the group of diffuse Diabetic Neuropathies, it is included in peripheral secondary Autonomic Neuropathies and carries a risk of vascular complications and sudden death, it is considered the most common AN in industrialized countries.[5,6] Characterized by Sudomotor Autonomic Dysfunction and Cardiovascular autonomic dysfunction, DAN is the most frequent Autonomic Dysfunction with the greatest morbidity and mortality. A latency period of four to approximately seven years has been observed in patients with type 2 diabetes. It is the time period in which reversible damage occurs on the nerve fibers due to the gluco-lipotoxicity.[7,8] As the time progresses and the diseases increases in severity, the damage becomes irreversible passing through various substages and acquiring a more higher staging. Hence; we investigated the influence of the IGT on peripheral or autonomic nervous system.[9,10]

In the present study, we observed that since the metabolic basis of the two processes is different, prevalence of IGT differs from prevalence of FPG. The two conditions do not frequently co-exist. We also observed that in the patient group, median FPG was statistically higher than the controls ($p < 0, 005$). This data made us think that subjects in the IGT group have more risk of morbidity than controls. Detecting no significant differences of smoking, polycystic ovarian disease and diabetes among first-degree relatives, made us think that both IGT group and controls have been exposed to the same kind of genetic and environmental influence. On the basis of the absence of responses between patients and controls, no statistical difference was observed. Isak et al investigated the presence of peripheral and autonomic neuropathy in individuals who had been diagnosed with IGT. The diagnosis of IGT in that individual was primarily made on the basis of results of oral glucose tolerance test. Comparison was made with the patients of comparable age and other demographic details and in whom values of oral glucose tolerance test were in physiologic limits. No statistical significant difference was observed while comparing the cardiac autonomic neuropathy in between the subjects of patients group and healthy control group. From the results, they concluded that in conventional electroneurography,

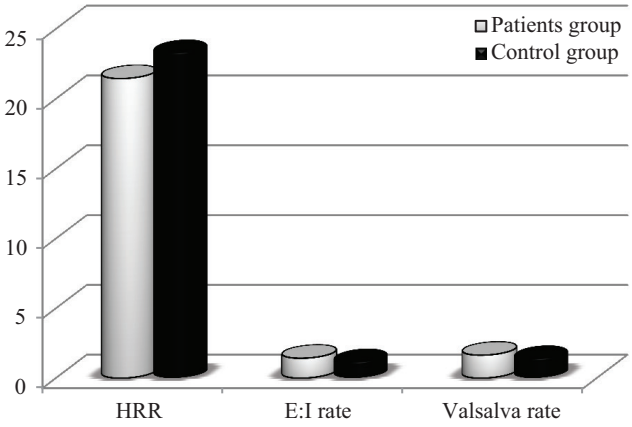

Figure-1: Shows the heart rate variation (HRR), expirium: inspiration rate and valsalva rate in the patients of the two study groups

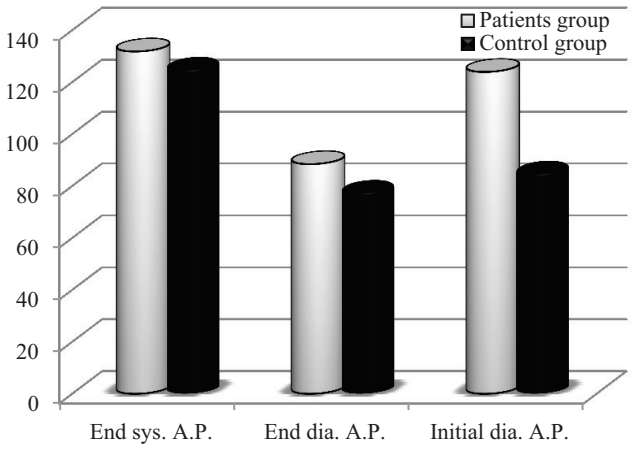

Figure-2: Blood pressure response to standing

Parameter	Patients group	Control group	p-value
HRR	21.45	23.41	0.845
E:I rate	1.42	1.28	0.651
Valsalva rate	1.64	1.51	0.715

Table-1: p-value for the comparison of the heart rate variation (HRR), expirium: inspiration rate and valsalva rate in the patients of the two study groups

Parameter	Patients group	Control group	p-value
End sys. A.P.	131.78	125.52	0.210
End dia. A.P.	88.42	78.12	0.112
Initial dia. A.P.	123.91	85.52	0.162

Table-2: p-value for the blood pressure response to standing in the patients of the two study groups

no neuropathic findings are detected which further indicate that sufficient time is required for the settling down of large-fiber neuropathy.[11] Rezende et al evaluated the association between the autonomic neuropathy and IGT by analyzing 44 patients that were reported with impaired glucose intolerance test. From the results, they concluded that in patients with IGT, autonomic nervous system is involved more frequently in comparison with the control groups.[12] Singleton et al examined records of 121 patients coded as idiopathic polyneuropathy, extracting neuropathy symptoms, electromyographic data, and diagnostic blood work. Of 89 patients screened for glucose handling, 28 demonstrated frank diabetes mellitus. From the results, they

concluded that an association between IGT and painful sensory polyneuropathy exists.[13] Popović-Pejicić et al determined the neuropathy associated with autonomic nervous system in patients with diabetes mellitus and assessed their correlation with cardiovascular risk factors and risk of development of other coronary diseases. They assessed a total of 90 patients and divided them into three main groups with thirty patients in each group. The first group comprised of 30 patients which were suffering from type 1 diabetes mellitus. Group 2 included patients with type 2 diabetes while the third group comprised of 30 patients in which diabetes was absent and were taken as control group. They observed that cardiovascular autonomic neuropathy was more frequent in type 2 diabetes, manifesting as autonomic neuropathy. From the results, they concluded that cardiovascular autonomic neuropathy is a common complication of diabetes that significantly correlates with coronary disease.[14] Tiftikcioglu et al investigated the association of the plasma markers of the endothelial dysfunction and autonomic neuropathy in diabetic patients. They analyzed 25 patients each with IGT and Type 2 diabetes and 30 control subjects and compared their demographic details. They also assessed and compared the E-selectin (sE-selectin) levels and observed that no correlation exist in between biomarkers of endothelial damage and SSR.[15] Ziegler et al evaluated the frequency of occurrence of risk factors associated with Cardiac autonomic nervous dysfunction (CAND) in glucose intolerance and diabetes. They observed that normal glucose tolerance (NGT) in 565 individuals and in 336 individuals, presence of isolated impaired fasting glucose. From the results, they concluded that in diabetic individuals, prevalence if CAND increases in comparison with the general population.[16] Rasic-Milutinovic et al assessed the existence of autonomic dysfunction in patients with metabolic syndrome (MetS). They evaluated 32 patients out of which 15 were suffering from MetS and 17 were from type 2 diabetes mellitus. They observed that in type 2 diabtetic patients, significant lowering of the Mean total power (TP) log-transformed (ln), very low frequency (VLF) ln power, and high frequency (HF) was observed in comparison with the control group patients. From the results, they concluded that before the development of Type 2 diabetes, patients with MetS represent with disturbed HRV indices.[17,18]

CONCLUSION

From the above results, they conclude that the degeneration of small-fibers was reached as a conclusion of the evaluation of queries about the complaints, neurological examination, and electrophysiological tests. Therefore, newly diagnosed patients of IGT should get priority in treatment.

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