

Original Article

Prevalence of Autonomic Neuropathy in poorly controlled Diabetics

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Abstract

Objective: To determine the prevalence of diabetic autonomic neuropathy (DAN) in patients with diabetes for five or more years duration.

Methods: Two hundred (200) diagnosed diabetics with five or more years duration seen in Diabetic clinic at Benazir Bhutto Hospital, Rawalpindi between 1st June 2006 to 31st May 2007 were included in the study. Standard cardiovascular function tests were applied on the patients. Clinical history included queries about nocturnal diarrhea, constipation, early satiety, impotence and erectile dysfunction.

Results: Among the two hundred patients included in the study, diabetes was more than five years duration. The mean duration of illness was 9.6 years (SD 3.8). There were ninety three [93] males and one hundred seven [107] females. 177 patients [88.5%] in our study were with type -II Diabetes Mellitus and 23 (11.5%) with type -I diabetes mellitus. In our study 2/3rd of the patients showed evidence of autonomic neuropathy.

Out of two hundred patients, 133 (66%) patients had evidence of autonomic neuropathy, of these 18(11.5%) had type I and 115 (88.5%) had type II diabetes mellitus.

Gastro-intestinal system was the most commonly involved system accounting for 93 (46.5%) patients. The next commonly involved system was cardiovascular system 89(43%) followed by genitourinary system in 15 (7.5%) of the patients. When Pearson Chi square test was applied at 5% level of significance, p value was 0.204. Thus there was no statistically significant association between type of diabetes mellitus and autonomic neuropathy.

Conclusion: Complications of diabetic autonomic neuropathy contribute significantly to morbidity, mortality and reduced quality of life in a person with diabetes. The treatment of diabetic autonomic neuropathy is unsatisfactory. It is desirable to prevent this complication and if once established, to slow its progression. We recommended that tests for autonomic functions should be included in the annual checkups of all diabetic patients particularly in those with disease of more than five years.

Introduction

Diabetic patients are susceptible to long term complications that cause morbidity and premature mortality. Diabetic neuropathy is a heterogeneous disorder that encompasses a wide range of abnormalities affecting sensory, motor nerves as well as autonomic nervous system. Diabetic autonomic neuropathy (DAN) is the most common and troublesome complication of diabetes mellitus. Symptoms may be confined to a single target organ or system.^{1,2} Diabetic autonomic neuropathy can result in silent heart attacks; kidney dis

ease, gastrointestinal disturbances; unawareness of hypoglycemia; and genitourinary dysfunctions.^{1,2,3} Despite its relationship to an increased risk of cardiovascular mortality and its association with multi system involvement, the significance of DAN has not been fully appreciated.

Quantitative bedside tests documenting DAN have been used for nearly two decades⁴. Apart from their diagnostic value, they have enabled clinicians to follow the course of disease and assess the effects of treatment. These tests are called "Cardiovascular autonomic tests" (CATs). These are based on measuring cardiovascular reflex changes in response to standardized stimuli. CATs are abnormal in patients with

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long standing and poorly controlled diabetes with absence of symptoms in majority of these patients. The present study was aimed to document autonomic neuropathy in diabetics of more than five years duration. Studies have been done to detect DAN, however little attention has been given for its prevention.

Patients and methods

Two hundred diagnosed diabetics with disease duration of five or more years were recruited from diabetic clinic of Benazir Bhutto Hospital Rawalpindi, between 1st June 2006 to 30th May 2007. Convenience {non-probability} sampling was used. Patients with comorbid states like ischemic heart disease, malignancy, strokes and those on vasodilator and sympatholytics agents were excluded from the study.

Standard five cardiovascular function tests were performed. The tests were performed and evaluated according to the procedures described by Ewing et al¹⁵. DAN was established by presence of one or more abnormal tests. After obtaining the base line characteristics of patients, tests for para-sympathetic integrity were performed.

History of symptoms like nausea, vomiting, epigastric discomfort early satiety was taken. This was followed by examination of resting heart rate, postural hypotension, heart rate response to respiration and response to Valsalva maneuver. Resting heart rate of 100/min or more was taken as evidence of autonomic neuropathy.

Heart rate response to respiration was assessed by asking the patient to take six deep breaths while being monitored electrocardiographically. Minimum and maximum R-R were measured and expressed in beats/ min. Variation of less than 10 beats/min was taken as evidence of autonomic neuropathy.

Valsalva maneuver was performed. Patient blew against an aneroid or mercury manometer to 40mm. for 15 seconds while being monitored electrocardiographically. Valsalva ratio was calculated against longest R-R interval to shortest R-R interval. Values less or equal to one were taken as evidence of cardiac autonomic involvement.

To test for sympathetic integrity, blood pressure response to standing from sitting or lying position was measured. A fall in blood pressure more than 15 mmHg at five minutes was considered abnormal.

The statistical package for social sciences (SPSS, version 11.0) was used to enter and analyze the data. The means, SD, were measured for the continuous numerical variables like, age. Mean value with standard deviation was calculated for duration of illness. Fre-

quencies with proportion were calculated for categorical variables like gender, symptoms and signs.

Chi-square test was used on categorical variables looking for any association among defined study groups. The significance level was assumed by P value < 0.05. Presence or absence of clinical features and laboratory results of all the participants of study were calculated.

Results

Two hundred patients were enrolled in this study, consisting of ninety three [93] males and one hundred and seven [107] females.

The mean age of the study population was 50.7 years (SD 9.2) Youngest patient was 20 years old and the oldest patient 60 years of age. The maximum duration of illness was 24 years. Control of blood sugar was assessed by measuring fasting blood sugar [FBS] and postprandial blood sugar level on more than one occasion. It was found that 95 [47.5%] had FBS > 150 mg/ dl and 105 [52.5%] had FBS > than 150 mg/dl. Post prandial recordings was between 150 to 250 mg/dl in 107 [53.5%] and 250 to 350 mg/dl in 66 [33%]. Twenty seven [13.5%] had values more than 350 mg/dl. HbA1C could not be measured due to financial constraints.

In our study 133 (66%) patients showed evidence of autonomic neuropathy, of these 18 (11.5%) had type 1 and 115 (88.5%) had type 2 diabetes mellitus.

Gastrointestinal system was the most frequently involved system seen in 93 (46.5) followed by cardiovascular system 89 (43%). Genitourinary system involvement was seen in 15 (7.5%) patients.

GIT involvement was seen in 12 patients with type- 1 diabetes mellitus and 81 with type 11 diabetes mellitus. Genitourinary involvement was seen in 14 patients of type- 2 diabetes and only one (1) patient with type- 1 diabetes mellitus.

Nausea and vomiting was the complaint in 87 (43.5%) patients whereas constipation and bloating occurred in about half of the patients with GIT involvement. Nocturnal diarrhea was the least common presentation seen in 31 (15.5%) patients.

Early satiety was the most frequent GIT symptom among the affected group seen in 121 (60.5%) patients. This was followed by epigastric discomfort, seen in 116 (58%) patients.

When Pearson chi square test was applied at 5% level of significance, P value was 0.204. There was no statistically significant association between the type of diabetes mellitus and autonomic neuropathy.

CVS involvement was seen in 86 (43%) patients. On clinical reflex testing sinus arrhythmia was seen 118(59%) patients; abnormal response to valsalvama-neuver was found in 94 (47%) patients. Dizziness was present in more than half of total patients in 58(29%).

Resting tachycardia was seen in 52 (26%) of patients with evidence of CVS autonomic neuropathy. Least frequently positive abnormal reflex test was postural hypotension found in 32 (16%) patients .

Genitourinary system was the least frequently system involved in our study seen only in 15 (7.5%) patients. Urinary hesitancy was the main presenting symptoms see in 58 (29%) patients followed by impotence in 19 (9.2%).

Table 1: Frequency of Cardiovascular manifestationsn=200

CVS symptoms	Frequency	Percentage %
Dizziness	58	29
Resting tachycardia	52	26
Sinus Arrhythmia	118	59
Valsalva maneuver Abnormality	94	47
Postural hypotension	32	16

Table 2: Frequency of Gastrointestinal System manifestations n=200

	Early satiety	Nausea/vomiting	Epigastric discomfort	Bloating	Nocturnal diarrhea	Constipation
Frequency	121	87	116	56	31	56
Percent %	60.5	43.5	58	28	15.5	28

Discussion

In our study of two hundred diabetic patients the overall prevalence of diabetic autonomic neuropathy was 66 % in our study population. Diagnosis of autonomic neuropathy was based on two or more abnormal cardiovascular reflex tests and symptomatic in-

volvement of gastrointestinal and genitourinary systems. .

In our study, majority of patients were with type 2 diabetes mellitus (88.5%).There were only twenty three (11.5%) patients with type 1 diabetes mellitus. There was no significant association between type of diabetes and autonomic neuropathy. In our study, patients with disease duration of morethan five years were included. Clinically disabling autonomic neuropathy was seen in those with long standing disease.

Estimates of the prevalence of diabetic neuropathy is dependent on the criteria used for diagnosis and specific population under study.⁷ The prevalence of symptoms of autonomic dysfunction and abnormal tests of autonomic nervous system function in diabetic clinic and tertiary referral centers is high. In one population based study of diabetic patients in Rochester, Minnesota, symptomatic visceral autonomic neuropathy had prevalence of 5.5%¹

Poor glycaemic control was evident in our study. This is due to poor diabetic care, lack of education, non-compliance and slack dietary control. In patients with adequate control of blood sugar level evidence of DAN was negligible. Patients with long duration of diabetes had diabetic autonomic neuropathy irrespective of blood sugar control. There is evidence that early intervention by optimum glycaemic control may limit progression of DAN at early stage¹⁶Early detection by simple autonomic reflex tests even in long standing diabetes can affect the further progression of DAN at least if not its reversal^{1,2,3,8}. The treatment for autonomic disorders should include improvement of symptoms and enhanced glycaemic control to prevent continued deterioration. The cardiovascular system is mostly affected by DAN. This may be responsible for certain serious consequences and life threatening complications like painless myocardial infarction, and sudden death.^{1, 2,9,10,, 11.}

In our study 86 (43%) patients showed involvement of cardiovascular system .Most common abnormality was sinus arrhythmia seen in one hundred and eighteen 118 (59%) patients followed by abnormal response to valsalva maneuver seen in ninety four (47 %). One Pakistani ⁸ study on hundred diabetic patients showed DAN 32(32%) and abnormal CATS in thirteen (40 %) .

Most of our patients with two or more abnormal cardiovascular reflex tests had parasympathetic involvement. This shows that progression of autonomic neuropathy is similar as reported in other studies (from normal to parasympathetic and eventually sympathetic damage ^{1 ,10 ,11} Once autonomic abnormalities are present they persist . In another study on six hun-

dred and seventy four patients, significant relationship was observed between cardiac autonomic neuropathy, duration of disease, control of blood sugar and other complications of diabetes¹². It was found that 83% patients had cardiac autonomic symptoms, sometimes showing progressive deterioration but rarely if ever improving¹³. In our study gastrointestinal autonomic dysfunction was seen in ninety three (46.5%) patients. The most frequent abnormality was early satiety seen in one hundred and twenty one (60.5%), epigastric discomfort in one hundred and eighteen (58%) indicating significant association between glycaemic control and disease duration.

The overall prevalence of symptoms caused by autonomic dysfunction was 76%.¹ gastro-paresis is reported in five to 12% of patients with diabetes.¹

The studies of diabetic gastro-paresis are limited by relatively small number of patients and referral bias, or short follow up periods. This difference might be because in our set up, patients do not have good diabetic control, lack of education about the disease and are neither evaluated nor treated for autonomic dysfunction. Genitourinary autonomic dysfunction was seen in only fifteen (7.5%) patients in our study. Genitourinary involvement is common in diabetes mellitus. Erectile dysfunction is commonly observed in such patients with researchers reporting figures from 35 to 75%.¹ In one study, impotence was common seen in 9 (27%) out of 33 patients.²⁸

It seems that erectile dysfunction is common but less reported due to embarrassment of patients and the reluctance of doctors to discuss sexual problems.

Optimal blood glucose control may influence autonomic neuropathy in long term, but once it develops symptomatic treatment is the only choice. Mortality rate is high in patients with symptomatic autonomic neuropathy than those without symptoms.

Conclusion

All diabetic patients with disease duration of more than five years and poor glycaemic control should be evaluated for autonomic dysfunction. This can be done by detailed clinical history, examination and simple clinical tests in outpatients and inpatients department.

Patients should also be educated about the importance of life style modification, dietary habits and regular exercise. Finally more research is needed to identify the problem early and search for means to control and treat autonomic dysfunction more effectively.

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