Original Research Paper

Volume : 5 | Issue : 11 | November 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Assessment of Cardiac Autonomic Neuropathy among type 1 & 2 diabetic patients in North India.

Medicine

KEYWORDS: Cardiovascular Autonomic Neuropathy (CAN); Cardiac Autonomic function tests; Ewing's criteria ; Diabetes Mellitus

Dr. Nitin Gupta — Senior Resident, Medicine Department, M.M. Institute of Medical Sciences and Research, Mullana, Ambala.

Dr. Vijay Kumar — Assistant Professor, Cardiology Department, M.M. Institute of Medical Sciences and Research, Mullana, Ambala.

Dr. Sunita Gupta — Gupta, Professor, Medicine Department, M.M. Institute of Medical Sciences and Research, Mullana, Ambala.

ABSTRACT

Introduction: CAN (Cardiovascular Autonomic Neuropathy) is a least understood complication of diabetes which is often under diagnosed. It causes resting tachycardia, orthostatic hypotension, exercise intolerence and is associated with higher cardiovascular mortality in diabetic patients. This stresses the need of early diagnosis of CAN to prevent higher mortality rates.

Aim: To study prevalence of cardiac autonomic neuropathy in diabetic patients.

Methods: Fifty cases of diabetes mellitus (type 1&2) with no clinical evidence of cardiac disease were subjected to cardiac autonomic function tests according to Ewing's criteria which were heart rate variability during deep breathing, Valsalva maneuver ratio, heart rate response on standing and BP response to standing and BP response to sustained handgrip to find the prevalence of CAN. Patients were categorized as with no CAN, early, definite and severe type of CAN depending upon abnormality of one or more tests.

Results: In this study prevalence of CAN was 54% out of which early, definite and severe involvement was found in 16%,14% and 24% respectively. Cardiac autonomic function tests of heart rate variability during deep breathing, Valsalva maneuver ratio, heart rate response on standing and BP response to standing and BP response to sustained handgrip found abnormal response in 38%,22%,34%,14% and 20% respectively. Diabetic retinopathy and nephropathy were significantly associated with CAN.

Conclusion: Prevalence of CAN among diabetics was 54% and parasympathetic cardiac autonomic function tests are more sensitive for the detection of CAN than sympathetic cardiac autonomic function tests. Development of CAN in diabetic patients lead to poor prognosis, increased silent myocardial infarction and sudden cardiac death hence all diabetic patients should be routinely evaluated for CAN using these feasible bedside tests.

INTRODUCTION

Diabetes mellitus (DM) is a constellation of common metabolic disorders that share the phenotype of hyperglycaemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. Diabetes mellitus is a major concern in India. According to WHO, the burden of diabetes mellitus in India is 31.7 million and projected figure for 2030 is 79.44 million[1,2].

Diabetic macro- and micro-vascular neuropathies, including CAN (Cardiovascular Autonomic Neuropathy), are a common chronic complication of type 1 and type 2 diabetes and confer high morbidity and mortality to diabetic patients.CAN is a serious chronic complication of diabetes and an independent predictor of cardiovascular disease mortality. CAN is associated with a poor prognosis and poor quality of life.CAN is a common form of diabetic autonomic neuropathy and causes abnormalities in heart rate control as well as central and peripheral vascular dynamics, the clinical manifestations of which include exercise intolerance, intraoperative cardiovascular lability, orthostatic hypotension and painless (silent) myocardial ischemia.

Very little data is available regarding cardiac autonomic neuropathy in literature concerning this part of the world. People in the present study area enjoy all the amenities and are increasingly prone to lifestyle diseases such as hypertension and diabetes. As cardiac autonomic neuropathy is often over looked both in diagnosis and treatment of diabetes, it becomes imperative to study the prevalence of this life threatening complication. So the present study aims to assess the prevalence of cardiac dysautonomia.

Materials and Methods

The study was conducted at M.M Institute of Medical Sciences and Research Mullana, Ambala, Haryana. Fifty Diabetic (Both Type I & type II) patients from OPD and indoor wards of the Department of Medicine. American Diabetes Association Guidelines were followed to diagnose diabetes. All patients were subjected to detailed history and systemic examination. Patients were selected irrespective of the duration of disease and therapeutic status. Study was conducted from June 2014 to December 2014.Patients who gave history of chronic alcoholism,asthma,chronic obstructive pulmonary disease, recent use of sympatholytic or parasympatholytic drugs and those patients who were unable to perform valsalva manoeuvre were excluded from the study.

Written informed consent was obtained from each patientprior to inclusion in the study. Approval from the Institutional Ethics Committee was taken before commencing the study.

Study protocol

Each subject was given rest for at least 20 minutes before carrying out the actual tests. Standard 12- lead electrocardiogram was taken and heart rate was measured by continuous electrocardiographic recording using lead –II. Before every test, the heart rate was allowed to come down to normal. All patients underwent following tests for CAN[3] (cardiac autonomic neuropathy):

A. Tests reflecting cardiac parasympathetic action:

I. By the patient blowing into a mouth piececonnected to a sphygmomanometer and holding it at a pressure of 40 mmHg for 15 seconds while a continuous ECG was recorded. The manoeuvre was performed 3 times with an interval of one minute in between.The result was expressed as theValsalva ratio. The mean of three Valsalva ratios was taken as the final value (normal Valsalva ratio 1.21; borderline between 1.11and 1.20; abnormal < 1.10).

II. Heart rate variation during deep breathing:The patient sat quietly and breathed deeplyat 6 breaths a minute (5 seconds in, and 5seconds out) for one minute. An ECG wasrecorded throughout the

period of deepbreathing with a mark used to indicate theonset of each inspiration and expiration. Themaximum and minimum R-R intervalsduring each breathing cycle were measuredand converted to beats/minute. The resultwas then expressed as the mean of thedifference between maximum andminimum heart rates for the 6 measuredcycles in beats/minute; (normal response >15 beats/minute, borderline 11 - 14 beats/minute; abnormal response < 10 beats/minute).

III. Immediate heart rate response to standing:The test was performed with the patientlying quietly on a couch while heart rate wasrecorded continuously on the ECG machine.The patient was asked to stand up unaidedand the point at starting to stand wasmarked on the ECG. The shortest R-R intervalat or around the 15th beat and largest R-Rinterval at or around the 30th beat afterstarting to stand was measured with a ruler.The characteristic heart rate response wasexpressed by 30 - 15 ratio (which is normalif > 1.04; borderline between 1.01 and 1.03;and abnormal if < 1.00).

B. Tests reflecting cardiac sympathetic action:
I. BP response to standing: The test wasperformed by measuring the patient's BPwhile he was lying down quietly and againwhen he stood up. The postural fall after 2minutes in BP was taken as the differencebetween systolic BP lying and the systolic BPstanding (normal response < 10 mmHg;borderline 11 - 29 mmHg; abnormal response> 30 mmHg).

II. BP response to sustained handgrip: Afterinstructions in using hand grip of an inflatedBP cuff, the subject gripped maximally withhis dominant arm for a few seconds; this wasrepeated thrice. Highest of the 3 readings iscalled maximum voluntary contraction(MVC). Now the subject was instructed tomaintain hand grip. The result was expressed as the difference between the highest DBP during hand grip exercise and mean of 3 DBP readings before hand grip began(normal response > 16 mmHg; borderline 11- 15 mmHg; abnormal < 10 mmHg).

Results obtained from above said tests were interpreted according to Ewing's criteria for CAN.

Test	Normal	Borderline	Abnormal
Heart rate variations during deep breathing (in beats per minute)	>15	11-14	<10
Valsalva ratio (R-R interval ratio)	>1.21	1.11-1.20	<1.10
Tachycardia response to standing 30:15 ratio	> 1.04	1.01-1.03	< 1.00
blood pressure response to standing: fall in systolic BP (in mmHg)	<10	10-20	>20
blood pressure response to sustained handgrip: rise in diastolic BP (in mmHg)	>16	11- 15	<10

Normal = all tests normal or 1 test borderline.
Early = one of the three heart rate tests abnormal or two borderline.
Definite = two heart tests abnormal.
Severe = two heart tests abnormal + one or both BP tests abnormal.

Further correlation between presence and severity of CAN with presence of microalbuminuria(diabetic nephropathy) or diabetic retinopathy was done.

Statistical analysis was done using appropriate statistical tests with help of SPSS version 20.0. Statistical significance was considered when p value was <0.05. Data was presented as simple mean and standard deviation for quantitative data and as proportions for qualitative data.

Results

A total of 50 cases out of which type 2 diabetes patients were 86% while type 1 diabetes patient were 14% , were included in the study group after using proper exclusion criteria.

There was male (52%) predominating over females(48%).Maximum number of patients(36%) were in the agegroup 41 - 50 years, followed by age group 51 - 60 (24%).Older patients (71 - 80 years age group) constituted in insignificant portion (4%) of total patients in the studygroup.

54% of the patients had positive CAN whereas 46% had no CAN. Early and definite type of CAN was 16% and 14% respectively whereas severe CAN was present in 24% of subjects. Subjects with no CAN and severe CAN had mean duration of 6.78±1.73 and 10.87±3.90 years respectively whereas early and definite CAN had mean duration of diabetes as 8.25±3.61 and 10.07±4.41 years respectively(Table 1).

Table 1: Type of CAN among patients and mean duration of years.

Type of Cardiac autonomic	No of patients (percentage)	Mean Duration in years
No	23 (46%)	6.78±1.73
Early	8 (16%)	8.25±3.61
Definite	7 (14%)	10.07±4.41
Severe	12 (24%)	10.87±3.90

Giddiness was the most common neuropathic symptom constituting 38% of studied subjects. Other common symptoms were bladder symptoms (36%), sweating (22%) and bowel symptoms (20%).

Table 2: Ewing's criteria variables for CAN among patients.

Ewing's Variable	Normal	Borderline	Abnormal
Heart rate variability	25 (50%)	6 (12%)	19 (38%)
Valsalva ratio	24 (48%)	15 (30%)	11 (22%)
Tachycardia response to standing 30:15 ratio	29 (58%)	4 (8%)	17 (34%)
Postural hypotension	31 (62%)	12(24%)	7 (14%)
BP response to sustained handgrip	22 (44%)	18 (36%)	10 (20%)

Heart rate variability and Tachycardia response to standing were abnormal in 38% and 34% of patients respectively whereas Blood Pressure response to sustained handgrip and Valsalva ratio were termed as abnormal in 20% and 22% patient respectively (Table 2).

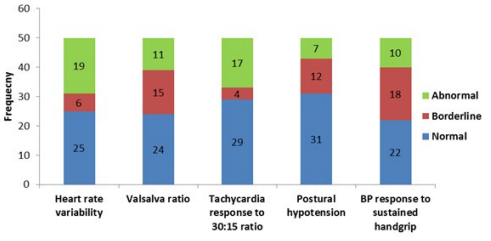

Figure 9: distribution of Ewing's variables among partients

Table 3: Retinopathy and nephropathy among diabetic patients.

Type of CAN	Retinopathy present	Nephropathy present
No CAN	0	6 (12%)
Early CAN	0	5 (10%)
Definite CAN	2 (4%)	4 (8%)
Severe CAN	5 (10%)	7 (14%)
Total	7 (14%)	22 (44%)

A total of 7 (14%) patients were found to have diabetic retinopathy and all of them had either definite or severe CAN whereas 22 (44%) out of 50 patients had diabetic nephropathy out of which 16 (72%) patients had CAN (Table 3).

Volume : 5 | Issue : 11 | November 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Discussion

Diabetic cardiac autonomic neuropathy (CAN) is a common, chronic and serious complication found in both type 1 & 2 diabetic patients.

In our study CAN was present in 27 patients (54%) out of 50 patients. Barthwalet al[4] reported prevalence of cardiac dysautonomia as 36.2% in Indian diabetic patients whereas Mathur et al[5] reported prevalence of definite CAN as 58%. Kumar et al[6] and Veglio et al[7] reported prevalence of cardiac dysautonomia as 60% and 63.7% respectively. Most of the studies done among diabetic patients had a CAN prevalence of 50-60% which correspondsto the results of our study. This shows that more than half of the diabetic subjects had one or more signs of CAN as per Ewing's criteria.

In present study out of 27 (54%) patients having CAN, 8 (16%) had early CAN, 7 (14%) had definite CAN and 12 (24%) had severe CAN. Mathur et al[5] (2006) reported 58% CAN among diabetics including 20% having early CAN, 30% having definite CAN and 8% having severe CAN . Another study by Ahireet al[8] reported severe CAN as 20%. Early and definite cardiac dysautonomia was present in 33.3% and 23.3% respectively. Prevalence of severe CAN was comparatively higher in current study which may be due to late reporting of diabetic subjects where the CAN had already set in.

In the present study, duration of diabetes correlated with the severity of CAN. The mean duration of diabetes was found to be 8.25±3.61, 10.07±4.41 and 10.87±3.90 in patients with early CAN, definite CAN and severe CAN respectively while patients with no cardiac autonomic involvement had 6.78±1.73 mean duration of diabetes. Kumar et al[6] reported that mean duration of diabetes with CAN was 8.52 ± 6.26 years whereas among patients without CAN it was 3.19 ± 2.81 years. In a similar study by Barthwalet al[4], duration of diabetes among patients with CAN was 7.11 ± 3.49 years and in patients without CAN was 3.51 ± 2.81 years.

Postural dizziness was observed in 19 (38%) out of 50 subjects. It was however less than as reported by other studies, but it was the most common presenting complaint of the studied patients. Basu et al[9]. also reported postural dizziness as most common symptom. Sweating abnormalities were noted in 22% of our patients. Basu et al[9] reported that 16% of patients had hyperhidrosis whereas Lakhotia et al[10] reported that 26% of patients had sweating abnormalities. The findings of our study are similar to results reported by Basu et al[9] and Lakhotia et al[10]. Similarly impotence was observed in 23% of males in the current study whereas 54% and 30% impotency was found by Lakhotia et al[10] and Shetty et al[11]. In the current study impotence was reported by male subjects only which may account for low proportion of impotence among our study population.

Heart rate variability on deep breathing, valsalva ratio, tachycardia response to standing(30:15 ratio), BP response to sustained handgrip and postural hypotension found abnormal results in 19(38%), 11(22%), 17(34%), 10(20%) and 7(14%) respectively. The results of the present study support the findings of Mathur et al[5] and Basu et al[9]as deep breath test was the most sensitive test, found abnormal in 38% patients in this study. Also, Mathur et al[5] and Basu et al[9] had also reported deep breath test as the most sensitive test with sensitivity as 48% and 32% respectively. Postural hypotension was the least sensitive test for cardiac autonomic dysfunction in the present study (14%), similar findings were shared by Basu et al[9].

In the present study 22(44%) subjects had nephropathy (micro-albuminuria) out of which CAN was present in 16 (72.7%) subjects. Study from western India by Shethet al[12] reported higher incidence of micro-albuminuria as 42%. Mehta et al[13] also reported similar incidence of micro-albuminuria (35%).

In the current study, diabetic retinopathy was present in 14% of studied subjects of which all had CAN.Domuschiev I et al[14] (2005) in their 42 type 2 patients reported that 10 had proliferative retinopathy and all these patients had cardiac dysautonomia also. Similar results were given by Ziegler et al.[15] which showed significant relationship between autonomic neuropathy and diabetic retinopathy.

Conclusion

Cardiac autonomic reflex tests (CARTs) as described by Ewing's criteria involving five bedside simple tests are important feasible and reproducible diagnostic tool for evaluation cardiac autonomic neuropathy in diabetic patients.All diabetic patients whether symptomatic or asymptomatic should be routinely evaluated for presence of CAN using CARTs at the time of diagnosis and every five years thereafter. Also, development of CAN is strongly associated with other chronic micro-vascular complications of diabetes like diabetic retinopathy and diabetic nephropathy (albuminuria) and is a predictor of sudden cardiac catastrophic events.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(3):1047–53.
2. Whiting D, Guariguata L, Weil C, Shawj. IDF Diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res ClinPract. 2011;94:311–21.
3. Spallone V, Menzinger G. Diagnosis of cardiovascularautonomic neuropathy in diabetes. Diabetes. 1997; 46(Suppl 2):S67-76.
4. Barthwal SP,Agarwal R, Khanna D,Kumar P. QTc prolongation in diabetes mellitus- an indicator of cardiac autonomic neuroapathy. JAPI 1997; 45:15-17.
5. Mathur CP, Gupta D. QTC prolongation in diabetes mellitus – an indicator of cardiac autonomic neuropathy. J Indian academy of clinical medicine. 2006; 7(2):130-32.
6. KumarMR, Agarwal TD, Singh VB, Kochar DK, Chadda VS. Cardiacautonomicneuropathyanditscorrelationwith QTC dispersion in type 2 diabetes. IHJ. 2000; 52(4),421-26.
7. VeglioMetal.PrevalenceofQTprolongationinatype1diabeticpopulation and its association with autonomic neuropathy. DiabeticMed. 1993;10:920-24.
8. Ahire C, Sarode V, Jadhav K, Shreeram V, Gaidhani N. Prevalence of cardiac autonomic neuropathy in short and long standing type 2 diabetics in western Maharashtra. International Journal of basic and applied medical research. 2014; 3(4):252-59.
9. Basu AK, Bandyopadhyay R, Chakrabarti S, Paul R and Santra S. A Study on the Prevalence of Cardiac Autonomic Neuropathy in Type-2 Diabetes in Eastern India. Journal Indian Academy of Clinical Medicine. 2010; 11(3):190-4.
10. Lakhotia M, Shah PKD, Vyas R, Jain SS, Yadav A. Clinical dysautonomia in diabetes mellitus – a study with seven autonomic reflex function tests. JAPI. 1997; 45:15-17.
11. ShettyKJ,MohanchandR.AstudyofautonomicdysfunctionindiabetesmellitusJDiabAssocIndia. 1987: 27:53-57.
12. Sheth J, Trivedi B, Shah L, Sheth VS. Prevalence of micro-albuminuria in diabetic subjects. J Assoc Physicians India. 1993; 41 (9): 562-4.
13. Mehta S, Mathur D, Chaturvedi M, Verma K. Incidence of cardiac autonomic neuropathy and its correlation with retinopathy, micro-albuminuria and glycatedhaemoglobin in non-insulin dependent diabetes mellitus. JIMA. 2002; 100:141-3.
14. Domuschiev I. Cardiac autonomic neuropathy and its correlation with retinopathy in type 2 diabetics. Biotechnol&Biuotechnol. 2005;19(3):180-3.
15. Ziegler D, Gries FA, Muhlen H. Prevalence and clinical correlates of cardiovascular autonomic and peripheral diabetic neuropathy in patients attending diabetes centres. The Diacan Multicenter Study Group. Diabetes Metab. 1993; 19:143–51.