A Study of Qtc Changes and Its Association with Cardiac Autonomic Neuropathy in Diabetes Mellitus

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ABSTRACT: Cardiac autonomic neuropathy (CAN) is the one of the most complication in Diabetes Mellitus (DM). Ventricular arrhythmias are more common with prolonged corrected QT (QTc) interval and it causes sudden cardiac death. This is a cross sectional study detects the prevalence of CAN in patients with DM by doing cardiac autonomic function tests and to correlate the CAN with QTc interval. This study was conducted on 100 diabetic patients. CAN was assessed by non-invasive tests: Valsalva ratio, Deep breathing test, immediate heart rate response to standing 30:15 ratio, BP rise with sustained hand grip and postural hypotension. Grading and scoring were done for CAN. QTc interval was determined. Out of 100 diabetic patients, 44 were males and 56 were females. 52 patients had grade I CAN with no prolongation of QTc interval and 48 patients had prolonged QTc interval associated with grade II, III and IV CAN. The QTc prolongation correlated positively with degree of CAN in Diabetes.

KEY WORDS: Diabetes, cardiac autonomic neuropathy, QTc interval, ventricular arrhythmias.

I. INTRODUCTION

Cardiac autonomic neuropathy (CAN) is a silent killer in diabetes, because only few patients realize that they suffer from it. QTc prolongation as marker of CAN was first described by Flugelman et al., 1980 [1]. Early sub clinical detection of CAN and its intervention are important for risk stratification in preventing sudden death due to silent myocardial infarction [2]. Similar studies have observed and substantiated the role of prolonged QTc in sudden cardiac death [3,4]. Diabetes mellitus (DM) is associated with increased incidence of sudden cardiac death [5]. And prolonged QTc interval has been found to be an independent risk factor for strokes [6].

In type 1 and type 2 DM patients with prolongation of QTc interval has been shown to predict sudden cardiac death [7]. Diabetic patients having both QTc prolongation and CAN could be utilized for risk of cardio vascular and cerebrovascular morbidity and mortality. So the main objective of this study is to make effect on the existing knowledge that QTc prolongation in DM detects CAN.

AIMS AND OBJECTIVES

1. To determine the prevalence of CAN in patients with DM by doing cardiac autonomic function tests.
2. To correlate the CAN in DM with QTc interval changes.

II. MATERIALS AND METHODS:

The present study was conducted on 100 diabetic patients (both male and female) admitted in medical ward, department of Medicine, Tirunelveli Medical College, from July 2015 to December 2015. Type 1 and type 2 DM patients with symptoms of autonomic neuropathy like postural dizziness, hyperesthesia, tingling sensation and numbness were included as subjects. Cases with evidences of heart diseases, having abnormal resting ECGs and taking drugs known to interfere with autonomic function tests were excluded.

After getting institutional ethical committee clearance and written informed consent, study subjects underwent a battery of noninvasive autonomic function tests, and those with score 2 or more were defined to have Cardiac dysautonomia as recommended by Ewing's et al. [8]. These include: valsalva ratio, deep breath test, 30:15 ratio (immediate heart rate response to standing), postural hypotension (BP response to standing) and SHGT (BP response to sustained handgrip). Scoring was done as per criteria advocated by Bellavere et a[9].,(1983). Autonomic neuropathy was also graded by Lakhotia et al[10].,(1997) from grade 0-IV, grade I onwards had definite CAN. These patients were subjected to resting ECG and QT interval; R-R interval calculated and the QTc were determined. QTc was calculated based on Bazett's formula; $QTc = QT/\sqrt{R-R}$ and a value exceeding 440msec was considered prolonged.

III. RESULTS: TABLE1: CARDIAC AUTONOMIC TESTS IN DM

Valsalva Ratio					
Sr. no	Fall in diastolic BP(mmHg)	score	T 2 DM	T 1 DM	No of cases	%
1	>1.21	0	26	10	36	36
2	1.11-1.20	1	32	4	36	36
3	<1.10	2	24	4	28	28

Deep breath test					
Sr. no	E:I ratio (beat/min)	score	T2 DM	T 1 DM	No of cases	%
1	>15	0	18	8	26	26
2	11-15	1	26	2	28	28
3	<10	2	38	8	46	46

30:15 beat ratio					
Sr. no	30:15 ratio	score	T 2 DM	T 1 DM	No of cases	%
1	>1.04	0	20	10	30	30
2	1.01-1.03	1	34	2	36	36
3	<1.0	2	28	6	34	34

Postural hypotension					
Sr no	Fall in diastolic BP(mmHg)	score	T2DM	T1 DM	No of cases	%
1	<10	0	62	12	74	74
2	11-29	1	14	4	18	18
3	>30	2	6	2	8	8

SHGT					
Sr. no	Fallin diastolic BP(mmHg	score	T2 DM	T1 DM	No of cases	%
1	>16	0	60	8	68	68

2	11-15	1	14	6	20	20
3	<10	2	8	4	12	12

TABLE 2: AGE WISE DISTRIBUTION OF DIABETIC PATIENTS

Age group	No of cases	Percentage
10 -20	8	8
21-30	6	6
31-40	20	20
41-50	42	42
51-60	24	24
Total	100	100

Hundred cases of DM were subjected to autonomic function tests to find the incidence of cardiac autonomic neuropathy. From table 2, most of the patients (42%) belonged to age group between 41-50 years

GRAPH 1: SEX WISE DISTRIBUTION OF CASES

In this study , 44 cases were males and 56 cases were females, so the male : female ratio was 1:1.27 (graph1).
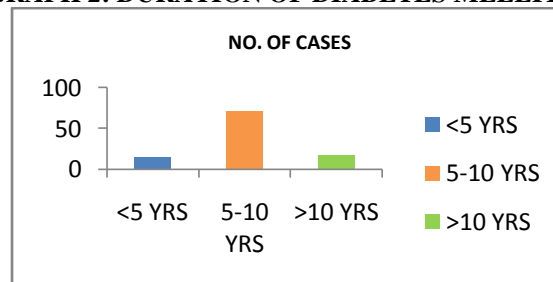
TABLE 3: TYPE AND FAMILY HISTORY OF DM

Type of DM	No. of cases	Family history of DM
Type 2 DM	82	60 (73.17%)
Type 1 DM	18	0

TABLE 4: DURATION OF DIABETES MELLITUS

Duration of years	No of cases
< 5 years	14
5 – 10 years	70
>10 years	16
Total	100

GRAPH 2: DURATION OF DIABETES MELLITUS

From table 3, 82 cases were suffering from type 2 DM. From table 4, most of the patients (70%) had duration of 5- 10 years.

As evidenced from table 1, valsalva ratio, deep breath test, 30:15 beat ratio, postural hypotension test and SHGT were abnormal in 28%, 46%, 34%, 8% and 12% of cases respectively. The

scoring for CAN showed that 28% cases were having score 4 and 2% of cases had score 1. Regarding grading, 52%, 24%, 2%, 22% had grade I, II, III and IV CAN, respectively (table 5).

Our study also showed that 46 cases had QTc>440 msec, while the remaining 54 cases had QTc< 440 msec (Table 6). In type 2 DM, 42 cases

were having grade I CAN and none of them had QTc> 440 msec. 24 patients having grade II CAN were associated with QTc>440 msec. 2 case with grade III CAN was having QTc> 440 msec and also 14 patient had grade IV CAD and all of these patients had QTc>440 msec (graph 3)
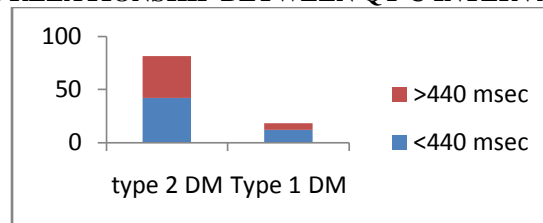
TABLE 5: GRADING OF CAN

GRADE	I	II	III	IV	No of cases
Type 2 DM	42	24	2	14	82
Type 1 DM	10	-	-	8	18

TABLE 6: QTC INTERVAL IN DIABETIC PATIENTS

QTc	<440 msec	>440 msec
Type 2 DM	42	40
Type 1DM	12	6
Total	54	46

GRAPH 3: RELATIONSHIP BETWEEN QT C INTERVAL AND DM

Regarding type 1 DM , 10 cases were of grade I autonomic neuropathy and none had QTc>440 msec. there was no case of grade II and III CAD, but had 8 cases of grade IV autonomic neuropathy with QTc>440 msec. there was no case with score 2 or 3 having QTc>440 msec. There are 14 cases of type 2 DM having < 5 years of duration belonged to grade I autonomic neuropathy with QTc>440 msec. 50% of patients with 5-10 years duration having grade I,II and IV CAN respectively with QTc>440 msec. 14 cases with >10 year of duration had grade II,III,IV CAN respectively. Considering QTc prolongation as an indicator of CAN, it was observed to have sensitivity of 46% and specificity of 100% with no false positive response.

IV. DISCUSSION

100 diabetic patients were subjected to standard autonomic function tests to determine CAN and also to establish the relationship between CAN and QTc interval. Out of 100 patients, 42 patients belong to age group 41-50 years and the mean age studied was 41.6 years. Patients with type II DM had family history of diabetes. The majority (70%) of patients had diabetes of 5-10 years of duration. Valsalva ratio: 28% of cases had

an abnormal response (i.e. <1.10). Previous studies by Ewing's et al, Bathwal et al [11] and lakhotia et al had abnormal response of 26%, 22.3% and 20% respectively. Deep breath test: 46% patient had abnormal response and it was 12% in Ewing's et al[12],42% in Bathwal et al and it was 38.3% in Lakhotia et al. 30:15 ratios: Our study had 38% with abnormal response and it was 38% abnormal in Ewing's et al and 17% in Bathwal et al. Postural hypotension: Our study had 8% cases with abnormal response and it was 16% in Ewing's et al, 44% in lakhotia et al. SHGT: 12% cases had an abnormal response in this study and it was 14% abnormal in Ewing's et al,26% in Lakhotia et al.

Duration of type 2 DM had a definitive predictive value for both CAN and QTc prolongation. Considering QTc prolongation as an indicator of CAN, it was observed to have sensitivity of 46% and specificity 100% with no false positive response. Our study was comparable with Gonin JM et al et al[13]., which showed 89% specificity with sensitivity of 57%, Veglio et al[14] has found specificity to be 89% with sensitivity as low as 15%. Our study shows that the development of autonomic neuropathy typically involves the parasympathetic fibers before the sympathetic fibers [15]. Based on our findings QTc has been

clearly established as a predictor of sudden cardiac arrest. Considering the above fact it is prudent that diabetic patients must have an optimal control of blood glucose, since prolonged QTc interval has been clearly established as a predictor of sudden cardiac death. So diabetic patients should be screened for CAN regularly and those with abnormal QTc should be closely monitored. Hence, there is a strong need for earlier and regular evaluation of autonomic nervous system function in type 2 diabetics to prevent further complications.

V. CONCLUSION:

The result of the investigation indicates that there was prolongation of QTc in DM patients with different degree of CAN. A battery of standard tests could be effective in detecting CAN. Further research on a large sample size is required to evaluate the findings of this study and effectiveness of QTc prolongation may be taken as a direct evidence of CAN in diabetics.

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