

QTc prolongation - a predictor for autonomic neuropathy in diabetic patients

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Abstract

Introduction: ECG is an important tool to assess the electrical activity of the heart. It is like any other investigation which can be done on bedside. In this study we have assessed the prolongation of QT interval (QTc), which is a marker for assessment of autonomic neuropathy (AN), in diabetic patients. The probability of autonomic neuropathy is high if the QT interval is prolonged. **Material and Methods:** All patients of Type I and Type II Diabetes Mellitus of various age groups studied in the period of 1 year. **Results:** As per the discussion QTc can be considered as the predictor of autonomic neuropathy (AN) in a patient if it is prolonged (>440 msec.). **Conclusion:** Instead of doing the tests for AN which are more cumbersome a simple QTc can predict AN in a patient. The thumb rule tests definitely stand to grade and assess the AN in a patient, but QTc is inexpensive, more tolerated and easier tool to label the patient as having AN.

Keywords: QTc interval, Type I Diabetes, Type II Diabetes Mellitus, Autonomic Neuropathy, ECG.

Introduction

Diabetes is one of the most ancient diseases known to man. The magnitude of population that suffers from this disease along with the morbidity and mortality associated with the illness has enticed a galaxy of research workers.

The Earliest description dates around 400 BC as Honey Urine, and was around 3000 years ago. Diabetes involves cardiovascular system in various ways especially the coronary arteries, to develop the Coronary artery disease (CAD), the silent myocardial infarction (MI) & dilated cardiomyopathy (DCM). Cardiac autonomic nerves have the sympathetic and parasympathetic components, both of which can be involved in case of Diabetes. In the ECG the QT interval measures the ventricular activity and is the time period from starting of the Q wave till the end of the T wave. The correction of the QT interval is done in comparison with the heart rate and is called the QTc. This requires the use of the Bazett's formula [1]. Prolongation of QTc is the marker for sudden cardiac death [2]. Similar studies have been done in this regard [3][4]. Central respiratory depression and increased frequency of sudden death is also documented [5]. Cough reflex threshold, a vagus mediated respiratory protective

reflex was raised suggesting the denervation of respiratory tract [6]. Hence the use of respiratory depressants and anesthetics in diabetes should be judicious. Other tests used are Valsalva, Deep Breath test, 30 : 15 ratio, Postural hypotension and SHGT (Ewing et al 1920), are difficult from the point of view of the patient's cooperation. QTc can easily be performed, is patient friendly, nearly 100% specific [7]. QTc is a valuable bed-side tool for the assessment of the patient, their routine evaluation and timely intervention. Refer to all the studies.

Aims and Objectives

1. To study the Frequency of QTc prolongation in Diabetes subjects.
2. To study the relationship between QTc prolongation and Cardiac autonomic neuropathy in diabetic subjects.
3. To study the relationship of cardiac autonomic neuropathy with duration and type of diabetes mellitus.
4. To study the relationship between QTc prolongation with degree of Cardiac autonomic neuropathy in diabetic subjects.
5. To study the relationship between QTc prolongation with other complications of Diabetes Mellitus.

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Materials and Methods

- 50 Patients were selected, exclusive of age, sex, type and duration of Diabetes.
- Time frame of 1 year from July 2013 to June 2014.
- Selection criteria included the Inclusion Criteria and Exclusion Criteria as Under:

a. **Inclusion criteria:**

- All cases of Type I DM and Type II DM admitted in the Hospital.
- All cases of various age groups.

b. **Exclusion Criteria:**

- Patients with anti arrhythmic drugs.
 - Class 1 A – Quinidine, Dysopyramide, Procainamide, Tricyclic antidepressants, Phenothiazines.
 - Class III – Amiodarone, Sotalol.
 - Hypothermia. [8]
 - Intracranial Bleed.
 - Hypocalcaemia.
 - Acute Myocarditis (Clinically)
 - Acute myocardial Infarction.
 - Hypertrophic Cardiomyopathy.
 - Advanced or complete AV block.
 - Hereditary –
 - Jervell-Lange Nelson Syndrome.
 - Romano-ward Syndrome.

7. Scoring

Done as per criteria of A Score of 2 or more denoted definite cardiac autonomic neuropathy [4]

Name of the test	Normal (0)	Borderline(1)	Abnormal (2)
Valsalva ratio (Longest R-R/shortest R-R)	≥ 1.21	1.11 – 1.20	≤ 1.10
Deep Breath Test (E:I ratio, beat / minute)	≥ 15	11 – 15	≤ 10
30 : 15 ratio	≥ 1.04	1.01 – 1.03	≤ 1.0
Postural Hypotension (fall in systolic BP on standing, (mm of Hg))	≤ 10	11 – 29	≥ 30
SHGT (Increase in diastolic BP on sustained hand grip (mm of Hg))	≥ 16	11 – 15	≤ 10

4. History:

Detailed clinical history was taken and more emphasis on Symptoms of autonomic Neuropathy (Postural Dizziness, Impotence, Gustatory Sweating, Atonic Bladder, Gasteroperesis, Constipation, Diabetic Diarrhoea etc.)

5. Clinical Examination :

Detailed clinical examination was done and Cardiac Dysautonomia assessment was done by non-invasive response to autonomic function tests. That includes Valsalva Ratio 30:15, Diastolic BP rise with sustained hand grip and postural hypotension, [9].

6. Tests:[9]

- Valsalva Ratio:** (Heart rate response to Valsalva maneuver)
- Deep Breath test:** (Heart rate (R-R interval) variation during deep breathing)
- 30:15 ratio:** (Immediate Heart rate response to standing).
- Postural hypotension:** (Blood pressure response to standing)
- SHGT:** (Blood pressure response to sustained handgrip)

8. Gradation

Done from 0-IV, and Grade I onwards being definite autonomic neuropathy[10].

Grade	Particulars	Result of parasympathetic tests	Result of sympathetic tests
0	Normal sympathetic and Parasympathetic functions	All normal or one borderline	Normal
I	Mild parasympathetic dysautonomia	One abnormal or two or more borderline	Normal
II	Moderate parasympathetic dysautonomia	Two abnormal or one abnormal and two borderline	Normal
III	Severe parasympathetic dysautonomia	more than two abnormal tests	Normal
IV	Combined parasympathetic and sympathetic dysautonomia	Any parasympathetic abnormality	One abnormal or two borderline.

9. QTc:

- Subject with definite cardiac autonomic neuropathy, was graded [10] and subjected to resting ECG. QTc was calculated by Bazett's formula.[1]
- Bazett's formula is $QTc = QT / \sqrt{R-R}$ interval
- QTc of more than 440 msec, was considered prolonged.

Results

The inference of the thumb rule tests indicate the accuracy of the tests, but the same are also the predictor of autonomic neuropathy in diabetic patients.

Table 1: Autonomic neuropathy scoring in different individuals

Sl. No	Score	No. of Cases	Percentage (%)
1.	2	9	18
2.	3	12	24
3.	4	14	28
4.	5	6	12
5.	6	6	12
6.	7	2	4
7.	8	1	2

The study showed the maximum cases having a score 4 (n=28)

Table 2: Result of Grading of Autonomic Neuropathy

Grade	I	II	III	IV	Total
Type II DM	21	12	1	7	41
Type I DM	5	-	-	4	9
Total	26	12	1	11	50

Most of the cases had Grade I Autonomic Neuropathy (n=21)

Table 3: Result of relation between QTc Interval and type of DM

QTc	< 440	≥ 440
Type II DM	21	20
Type I DM	6	3
Total	27	23

In the study majority of the cases of type II DM had QTc prolonged than 440 mili sec as compared to Type I DM (n=20).

Table 4: Result of comparison of Relation of Degree of Autonomic Neuropathy with QTc

A) Type II DM:

Grade	Total No. of Cases	QTc \geq 440 msec	Percentage
I	21	-	-
II	12	12	100
III	1	1	100
IV	7	7	100

In the study all the patients, belonging to Grade II to IV AN had QTc \geq 440 msec.(n=20)

B) Type I DM:

Grade	Total No. of Cases	QTc \geq 440 msec	Percentage
I	5	-	-
II	-	-	-
III	-	-	-
IV	4	3	75%

In the study patients with grade IV AN with prolonged QTc are 03(n=3)

Table 5: Result of the Relation of Autonomic Score with QTc

S No.	Score	No. of Cases	QTc < 440	QTc \geq 440
1.	2	9	9	-
2.	3	12	12	-
3.	4	14	6	8
4.	5	6	-	6 (100%)
5.	6	6	-	6(100%)
6.	7	2	-	2(100%)
7.	8	1	-	1(100%)

The study showed all the patients with score more than 5 had prolonged QTc (n=15).

Table 6: Relation of Duration of Diabetes Mellitus type II with Autonomic Neuropathy and QTc

Duration in Years	Number of cases	Grade				QTc \geq 440
		I	II	III	IV	
< 5	7	7	-	-	-	-
5 – 10	26	13	11	-	2	13
> 10	8	1	1	1	5	7
Total	41	21	12	1	7	20

The above shows the patients with more than 5 years duration of DM had prolonged QTc (n=20).

Table 7: Relation of diabetes Mellitus with QTc Prolongation

QTc	< 440	\geq 440
Type II DM	21	20
Type I DM	6	3
Total	27	23

In this study the QTc is prolonged in 46% of cases (n=23)

p-value for Type I DM and Type II DM in for prolonged QTc was 0.08, which is true.

The thumb rule tests are cumbersome and need the cooperation and the patient, which is a difficult task, instead a simple ECG can be a predictor of AN in a diabetic patient. The QTc measured was significant in 23 out of 50 Diabetic cases, which infers that the test can be considered as the predictor of autonomic neuropathy if the QTc is more than 440 msec.

Discussion

Diabetes Mellitus is one of the common diseases. There are several complications of diabetes. The complications get worsened with the duration of Diabetes and with uncontrolled hyperglycemia. Neuropathy is one of the major complications of Diabetes Mellitus. Autonomic neuropathy can be detected by thumb rule tests, which are cumbersome for the patient. A simple bed side ECG test can be performed and the corrected QT (QTc) can be determined which can be an indicator for autonomic neuropathy. The study included 50 diabetic patients. The thumb rule tests were, performed and corrected QT (QTc) was studied.

Out of 50 patients, majority of the patients belonged to age group 41 – 50 years and females were more in number. Type II DM were more in prevalence than the type I. Majority of the patients were of more than 5 years duration. Postural dizziness was the commonest symptom in our study whereas the Impotence was the common symptom among the males. Diabetic diarrhoea was the least common, in contrast to Ewing et al 1973 [11]. In the symptom of peripheral neuropathy numbness was the commonest. With the impairment of Deep Tendon Reflexes, Chuttani et al.[12]. The study also implicated that when there is a prolongation of QTc [13] the signs of peripheral neuropathy, retinopathy and nephropathy were also observed. Maximum number of the patients with duration of DM more than 5 years and with autonomic score more than 5 had prolonged QTc (>440msec).

Conclusion

Corrected QT (QTc) interval prolongation has been shown to be an independent predictor of mortality in many clinical settings and is a common finding in hospitalized patients. Instead of doing all the thumb rule tests for autonomic neuropathy, in a diabetic patient, only a simple ECG can be done on the bed-side, by which the QT interval can be calculated. If prolonged (i.e. QTc >440 msec.), this can be a predictor of Autonomic neuropathy, in a Diabetic Patient. The other thumb rule tests can then be performed, to assess the grade of Autonomic Neuropathy.

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