Qtc and Qtd Intervals in Patients with Type 2 Diabetes Complicated by Peripheral Sensory Neuropathy

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ABSTRACT:

BACKGROUND:

QT interval reflects depolarization and repolarization of the left ventricle, both QT interval and QT dispersion in surface 12 leads ECG of diabetic patients increase with progression of cardiac autonomic neuropathy(CAN) and this may lead to increase risk of dangerous dysrhythmias, it was found that there was association of this phenomenon with other complications of diabetes as ischemic heart disease and microalbuminuria.

OBJECTIVE:

To asses the relation of QTc and QTd to age ,duration of disease, gender, body mass index (BMI), and to presence of peripheral distal symmetrical sensory neuropathy.

METHODS:

A longtudinal study of 38 diabetic patients type 2 complaining of distal sensory neuropathy , 12 leads ECG done for all and QTc and QTd are measured with classical method, data collected from patients about age, gender, duration of diabetes and their weight and high for body mass index (BMI).

RESULTS:

The result of this study declare that the sample mean age is 46.18 years, mean duration of diabetes is 8.5 years, 57.9% are female , 42.1% male and 60% of them had BMI above 25 kg/m2. 31.6% of the patients had prolong QTc and 42.1% had prolong QTd. 50% of those over 50 years had prolond QTc and 85% of those over 40 years had prolong QTd inspite of that relation of prolongation to age is not significant statistically(P more than 0.05), while the relation of QT intervals to duration of disease is significant statistically, female gender show clear association to prolongation of both QTc and QTd which is significant statistically (P less than 0.05) and inspite of the relation of prolongation of QT intervals to increase in BMI but was not significant statistically.

CONCLUSION:

QTc and QTd prolongation is more common in diabetics who is complaining of symmetrical peripheral sensory neuropathy specially if duration of diabetes is more than 5 years and more in females than males.

KEYWORDS : QT interval,diabetes,sensory neuropathy**.**

INTRODUCTION:

QT interval represent depolarization and repolarization of the left ventricle, QTc is corrected QT to heart rate while QTd is the QT dispersion(the difference between the largest and smallest QT). Approximately 16% of type 1 diabetics and 26% of type 2 diabetics have QT prolongation. Increased QTd has been reported as 7% in type 1 and 33% in type 2 diabetes[1]. Diabetic patients with more pronounced QT abnormalities tend to have a higher age and blood pressure and they tend to have cardiovascular complications. Even in recently diagnosed diabetes mellitus QT interval is prolonged in the absence of CHD and autonomic neuropathy. Prolonged QTc (corrected QT interval) and QTd(QT dispersion interval) are independent markers of CHD and are predictors of sudden cardiac death[2].

A role of autonomic neuropathy in duration of Q-T interval in diabetic patients has been proposed, because diabetic patients with autonomic neuropathy show longer QTc compared with those without autonomic neuropathy [2]. The relation between QTc prolongation and autonomic neuropathy was not observed in women [2].

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It has been suggested that the interlead variability of QTc is a better predictor of arrhythmias and death than QTc duration [3]. This has been confirmed in the general population [4] and groups of outpatients with recently diagnosed diabetes [5], nephropathy [6], or type 2 diabetes [7]. However, in recent prospective studies of type 2 diabetic patients , QTc but not QTd was the predictor of mortality[8]. QTc prolongation and increased QTd were significantly related. However, the hypothesis that the two parameters provide different information is supported by the observation that a significant proportion of men and women with normal QTd (<0.08 s) have a prolonged QTc (>0.44 s). Furthermore, in patients with long QT syndrome, QTd is more predictive of the efficacy of antiarrhythmic drugs than QTc [9].

A role of cardiac ischemia in Q-T interval dispersion is suggested by the observation that QTd is prolonged in patients immediately after an acute myocardial infarction and tends to reduce thereafter [10].

Increased QTc, QTd are seen also as isolated syndrome, in chronic heart failure, peripheral vascular disease[12], hypertension, hypertrophic cardiomyopathy , myocardial infarction and drugs[13]. Some of the drugs which prolong QT interval are Sparfloxacin, Pentamidine, Haloperidol, Probucol, Cisapride, Amiodarone, Disopyramide, Flecainide, Amitriptylline, Doxepin, Imipramine, Astemizole, Terfenadine, Gatifloxacin and Halefentrine[14].

PATIENTS AND METHODS:

Between march and October 2007, a longtudinal study of 38 patients, 22 females an 16 males diabetics type 2 according to WHO criteria on diet or metformin therapy or both , who all had features of symmetrical sensory neuropathy confirmed with nerve conduction study by a neurologist are included. Those on insulin ,glibinclamide and other drugs that affect QT interval as(Sparfloxacin, Pentamidine, Haloperidol, Probucol, Cisapride, Amiodarone, Disopyramide, Flecainide, Amitriptylline, Doxepin, Imipramine, Astemizole, Terfenadine, Gatifloxacin and Halefentrine), and those with hypertension, heart failure, cardiomyopathy, CRF, and overt ischemic heart disease were excluded.

For all, standard resting 12-lead ECGs were recorded with the same equipment and response frequencies at 25-mm/s paper speed and 10-mm/mV amplitudeR-R and Q-T intervals were measured with a ruler on the resting ECG tracing: five consecutive beats were considered on lead V_5. The Q-T interval was measured from the beginning of the QRS complex to the end of the downslope of the T wave (crossing of the isoelectric line); when a U wave was present, the Q-T interval was measured to the nadir of the curve between the T and U waves. The Q-T interval corrected for the previous cardiac cycle length (QTc) was calculated according to Bazett's formula : $QTc = QT/(RR)^{1/}$The dispersion of QT was calculated using the difference between the maximum and minimum QT in any thoracic lead . A QTd >0.080 s was considered abnormally increased.

Statistical analysis using SPSS program version 11 is used to find the statistical significance.

RESULTS:

38 diabetics type 2 with peripheral symmetrical sensory neuropathy confirmed by nerve conduction study (NCS), their mean age is 46.18 SD_+ 7.5 years, mean duration of diabetes is 8.5 SD_+ 6.5 years, 22(57.9%) are females and 16(42.1%) are males, 23(60.5%) had body mass index(BMI) above 25kg/m2 and 17(44.7%) had duration of disease over 5 years.

All of them had no history of present clinical or ECG features of ischemic heart disease or heart failure neither taking any drug known to interfere with QT intervals. It was found that prolonged QTc in 12 (31.6%) and prolonged QTd in 16 (42.1%) of them.

Table 1 show the relation of QTc and QTd to the age, it is clear that 50% of those with prolong QTc are more than 50 years age, while more than 85% of those over 40 years of age had prolong QTd, inspite of that regression analysis show insignificant association between age and both QTc and QTd intervals.

The relation of duration of diabetes to abnormalities in QTc and QTd are shown in table 2, this table show that both QTc and QTd occur more frequently with increase duration of diabetes and this fact is significant statistically

Table 3 show the relation of gender to abnormalities in QTc and QTd , where female show clear association with the prolongation of both QTc and QTd which is significant statistically.

Table 4 is for the relation of BMI to QTc and QTd intervals abnormalities, while the percentage of intervals abnormalities are higher in those with BMI above 25 but that was not significant statistically.

The relation between QTc and QTd are assessed in table 5 which show strong association that is significant statistically.

Table 1:Relation of age to QT intervals

	QTc				QTd			
	Normal		Prolong		Normal		Prolong	
age	No.	%	No.	%	No.	%	No.	%
31-40 y	7	27%	1	8.33%	6	27.70%	2	12.50%
41-50 y	14	53.80%	5	41.67%	12	54.55%	7	43.75%
51-60 y	5	19.20%	6	50%	4	18.18%	7	43.75%
Total	26	100%	12	100%	22	100%	16	100%
P. Value > 0.05								

Table 2:Relation of duration to QT intervals

	QTc				QTd			
	Normal		Prolong		Normal		Prolong	
duration	No.	%	No.	%	No.	%	No.	%
Less than 5 y	16	61.5%	5	41.67%	16	72.77%	5	31.25%
More than 5 y	10	38.5%	7	58.33%	6	27.27%	11	68.75%
Total	26	100%	12	100%	22	100%	16	100%
P. Value < 0.05								

Table 3:Relation of gender to QT intervals

	QTc				QTd			
	Normal		Prolong		Normal		Prolong	
gender	No.	%	No.	%	No.	%	No.	%
female	13	50%	9	75%	9	41%	13	81.25%
male	13	50%	3	25%	13	59%	3	18.75%
Total	26	100%	12	100%	22	100%	16	100%
P. Value < 0.05								

Table 4:Relation of body mass index to QT intervals

	QTc				QTd			
	Normal		Prolong		Normal		Prolong	
BMI	No.	%	No.	%	No.	%	No.	%
normal	11	42.3%	4	33.33%	10	45.54%	5	31.25%
High	15	57.7%	8	66.67%	12	54.5%	11	68.75%
Total	26	100%	12	100%	22	100%	16	100%
P. Value > 0.05								

Table 5:Relation of QTc to QTd

	QTc			
	Normal		Prolong	
QTd	No.	%	No.	%
Normal	19	86.36%	7	43.75%
Prolong	3	13.64%	9	56.25%
	22	100%	16	100%
P. Value < 0.05				

Table 6:Companism of results of our study and the study of veglio.

Interval	Diabetes type2 percentage (veglio study)	Diabetes type2 with neuropathy percentage
QTc	26%	31.6%
QTd	33%	42.1%

DISCUSSION:

The EURODIAB investigators point out that prolongation of the QT interval corrected for heart rate (QTc) is a strong risk factor "for all-cause and cardiovascular mortality in apparently healthy people, as well as in people with various conditions, including diabetes[1]. Prolonged QTc interval may be a marker of subclinical undetected atherosclerotic process[15], and QTd has been shown to predict mortality in type 2 diabetic patients[5,8]. prevalence of prolong QTc and QTd increase in diabetics than control non diabetics[16]. Autonomic neuropathy and distal neuropathy associated more with prolongation of QT intervals[2].

In this study 38 patients with diabetes type 2 who all are complaining with symmetrical distal sensory neuropathy proved by NCS, 12 leads ECG show that 31.6% had prolong QTc and 42.1% had prolong QTd while Veglio found the prevelance to be 26% and 33% consequetivly in diabetics type 2 in general[1] as shown in table 6.

This study declare that 50% of those with age over 50 years had prolong QTc and 85% of those who are over 40 years had prolong QTd inspite of that association of age to QT interval was insignificant, this is also the result of Veglio, but Sara Gianti found significant relation to older patients but in type 1[17].

Relation of duration of diabetes to prolongation of QTc and QTd are assessed and it is found that a duration of more than 5 years is significantly associated with increase prevelance of both in diabetics while Veglio show no relation to duration in type 1[18].

This study confirm relation of prolongation of both QTc and QTd intervals to female gender significantly which is also found by Bruno[19] Sex-based or sex hormone–associated differences in myocardial cell function have been documented, while veglio show no association with gender in type 2 diabete [1].

BMI relation to prolongation of both QTc and QTd is not significant in this study while Giunti stated that a BMI 21.5-23.2 is a modifiable protective risk factor for QTc [17] but not for QTd.

The relation of prolongation of QTc to prolongation of QTd is very significant in this study, prolong QTc and increase QTd are independent markers for CHD in diabetes and predictor of cardiac death even in newly diagnosed diabetes type 2[18,5].

CONCLUSION:

prolongation of QTc and QTd appear to be more common in diabetics type2 who complain of symmetrical distal sensory neuropathy than in diabetics as whole, more common with age female gender and obese, there is strong association between QTc and QTd.

Recommendation:

Every patient with diabetes type 2 specially female with long duration and those with peripheral sensory neuropathy should have ECG and measurement of QTc and QTd intervals for any abnormality to anticipate the future risk.

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