

PROLONGED DISPERSION OF QT AND QT_C IN THALASSEMIA MAJOR PATIENTS

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Abstract- Thalassemia major patients require repeated transfusions of packed cell and their lysis lead to iron deposition especially in the cardiac walls such as septum and posterior wall, so make thickening and cause cardiac disorders. In this case-control study, our object was to appoint if QT and QT_C and T_e dispersions were predictors of cardiac disorders in thalassemia major patients or not. 34 thalassemic patients who had no cardiac sign or symptom and 34 normal subjects between 16-18 years old of age were referred for evaluation of their QT, QT_C, and T_e dispersions in their ECGs. All standard 12-lead ECGs were obtained from them and were digitized by a single observer blinded to the assigned groups. As references, QT and T_e were measured and QT_C was calculated by Bazett's formula. Results showed highly significant differences in QT and QT_C dispersions between thalassemic patients and control group (P-value = 0.004 and 0.001 respectively); but it was moderate for T_e (P-value = 0.086). About the means of QT, QT_C and T_e, there were highly significant differences between two groups too (P-value = 0.001, 0.000, and 0.000 respectively). QT and QT_C dispersions are significantly higher in thalassemic patients than normal persons and may be predictors of cardiac disorders such as arrhythmias or sudden death in thalassemic patients in future.

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Key Words: β -thalassemia, QT, QT_C dispersion

INTRODUCTION

Thalassemia is a common genetic disorder which causes severe anemia in its major type. Thalassemia major patients require repeated transfusions of packed cell (P.C.). Lysis of transfused packed cell releases much iron which is not excretable. Iron depositions in their body organs especially in the heart, the kidney, and the brain are main reasons for these organ failures and cause death during the second decade (1). Many of the previous data support cardiovascular disorders such as structural changes and thicknesses of septum and posterior wall and reduction of shortening fraction and ejection fraction (2). It has been shown that ventricular wall thickening may be altered by pathologic factors such as iron deposition. For these reasons we determined to know whether QT and QT_C dispersions altered in thalassemia major patients or not. QT dispersion is defined as the difference between the maximum and minimum QT intervals of the 12 leads of ECG (3). It has been suggested that QT dispersion reflects regional variation in ventricular

recovery (4). It is an index of inhomogeneity of repolarization. It is usually expressed as the difference or the range of the various repolarization measurements obtained from a heart (5). Increased QT dispersion is a predictor of sudden death and ventricular arrhythmias in the patients with chronic heart failure (CHF), remote myocardial infarction (6), hypertrophic obstructive cardiomyopathy, non insulin dependent diabetes mellitus, peripheral vascular disease, arrhythmogenic right ventricular cardiomyopathy and essential hypertension. In this study for the first time we determined QT dispersion in a group of thalassemia major patients and would follow the program for determination of differences of QT dispersions and its relation to cardiac disorders in a large group of thalassemic patients.

MATERIALS AND METHODS

Study population

Thirty-four patients were referred for evaluation of the QT dispersions in their ECGs. The mode of sampling was non-randomized. We selected these patients between the age range of 16-18 years in order to decrease growth leaping effects, which might have influence on variables. Past five years history of thalassemic patients managements showed that they had almost good managements by packed cell transfusions and iron chelator infusions. These

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patients had no history of cardiac disorders, arrhythmias, or use of drugs related to cardiac disorders, caffeine, digitalis, alcohol, cigarette or narcotic analgesics in the month before the test had been done. The control group included 34 normal high school students between 16-18 years of age without any exclusion criteria as mentioned above and any previous history of cardiac disorder.

Site and time

The patients were selected from thalassemic patients referring to Tadjrish Mofid and Ahari Children Medical Center hospitals of Tehran, Iran. ECGs and echocardiographies were obtained in Ahari Children Medical Center Hospital and other tests were done in Cardiovascular Research Center clinical lab. Subjects of control group were selected from three schools near to these centers regarding inclusion and exclusion criteria. ECGs were obtained from them at the same time as the patients.

ECG recording

All 12-lead ECGs were obtained at 50mm/s speed with standard lead position. All ECGs were digitized by a single observer blinded to the assigned control or case groups. The QT interval was measured from the beginning of QRS complex to the end of T wave defined as the return to T-P baseline. When U wave was present, the QT interval was measured to the nadir of the curve between the T and U waves. QT intervals were measured in all leads if possible. The QT intervals could be measured in at least eight leads in all patients in the study. For each lead three consecutive cycles were measured and the arithmetic mean of QT intervals for that lead was used in all future calculations for QT dispersion.

QT intervals were corrected (QT_C) with Bazett's formula to compensate for its known dependence to heart rate: $QT_C = QT / RR^{1/2}$.

Dispersion of QT and QT_C were calculated as the difference between the longest and the shortest values measured in each of the ECG leads (QT_{max} - QT_{min} and QT_{Cmax} - QT_{Cmin}).

The QT_{apex} (QT_a) interval was measured from the onset of QRS to the apex of T wave. The T_{apex} to T_{end} (T_e) interval (from the apex of T wave to its end) was calculated from this formula: $T_e = QT - QT_a$.

Also, the mean of QT intervals in 12 leads of ECG of each person was measured and calculated. The means of QT_C and T_e intervals were calculated too. Regarding the errors of manual measurement of QT

interval, we used 50mm/s speed and standard features to reduce errors.

Statistical Analysis

The T-test was used for estimation of the differences in the data between case and control groups. For evaluation of correlation between T_e dispersion and QT or QT_C dispersions, r-Pearson was calculated. These tests were analyzed by SPSS 9 software. A value of P < 0.05 was considered as significant.

RESULTS

Patients comprised of thirty four thalassemia major patients (20 males and 14 females) and 34 normal controls (19 males and 15 females). QT, QT_C and T_e means: QT and QT_C dispersions differed significantly between two groups of thalassemics and normals (Tables 1 and 2). The means of QT, QT_C and T_e had significant differences between the case and the control groups (P= 0.001, 0.000 and 0.000 respectively). There were highly significant differences of QT and QT_C dispersions between thalassemic patients and control subjects (P= 0.004 and 0.001 respectively). Also there was moderate difference between the patients and the controls about T_e dispersion (P= 0.086).

We compared males to females in each group of thalassemics and normals. There weren't any significant differences of mean QT, mean QT_C and mean T_e, between males and females in each group of thalassemics and normals except for mean T_e. The mean T_e of the males was significantly higher than the females of normal group (P= 0.014).

The QTD, QT_CD and T_eD did not have any significant difference between two subgroups of males and females in each groups of the thalassemics and the normals. T_e dispersion correlations to QT or QT_C dispersions were calculated too (Table 3). We separated two subgroups of males and females. T_e dispersion to QT or QT_C dispersions did not have any significant correlation in each of male or female subgroups of thalassemics. There was not any significant correlations in normal females too. But T_e dispersions to QT and QT_C dispersions had highly significant correlations in the male subgroup of normals (r= 0.714, P= 0.001 and r= 0.700, P= 0.001 respectively).

Table 1. Means of QT, QT_C, and T_e

Parameter	Case	Control	P-value
Mean QT (mean±SD)	398.1729±33.8093	373.4747±15.0851	0.001
Mean QT _C (mean±SD)	436.0624±23.0307	408.6676±15.0851	0.000
Mean T _e (mean±SD)	104.7880±13.5840	93.4120±8.0800	0.000

Table 2. QT, QT_C, and T_e dispersions

Parameter	Case	Control	P-value
QTD (mean±SD)	51.7644±23.5766	37.0588±16.2161	0.004
QT _C D (mean±SD)	55.7021±21.9988	40.0256±16.0532	0.001
T _e D (mean±SD)	45.9021±22.0518	38.2062±32.1659	0.086

Table 3. T_e dispersion to QT and QT_C dispersions correlations

Parameter	Group	Gender	N	r-Pearson	P-value
T _e D to QTD	Thalassemics	Male	20	0.050	0.834
		Female	14	0.221	0.448
	Normals	Male	19	0.714	0.001
		Female	15	0.263	0.343
T _e D to QT _C D	Thalassemics	Male	20	0.020	0.932
		Female	14	0.125	0.671
	Normals	Male	19	0.700	0.001
		Female	15	0.202	0.469

DISCUSSION

Results of present study show significant difference between QT dispersion and other indices related to it between thalassemia major patients and normal persons. Manual measurement of QT interval is significantly altered by paper speed, electrocardiogram gain and T wave amplitude. We used 50 mm/s speed to reduce rate of standard errors. Standard QT dispersion from ECG correlate significantly with dispersion of repolarization measured from myocardium. Many studies showed that QTD could be a predictor of cardiac disorders. QRS dispersion (≥ 40 ms) has been the strongest independent predictor of sudden death in arrhythmogenic right ventricular cardiomyopathy (ARVC). QT dispersion > 65 ms was one of the arrhythmic risk stratification in these patients (20). In patients with sustained ventricular arrhythmias, QT interval dispersion may be a further non-invasive

marker of susceptibility to ventricular arrhythmias (7). Also QT_C dispersions are excellent predictors of cardiac death in non-insulin dependent diabetes mellitus. QT dispersion predicts cardiac death in patients with peripheral vascular disease or essential hypertension too.

In post myocardial infarction patients, the prognostic significant difference of QTD-V (QTD in ventricular beats) more than QTD-S (QTD in sinus beats) was reported. QTD-V was significantly greater in the group of patients with arrhythmic events than in group without arrhythmic events. QT dispersion is increased after MI and the level is higher in the patients with ventricular fibrillation (6).

QT dispersion reflects regional variation in ventricular recovery (4). A prolonged and shortened mean QT_C interval over 24 hours was associated with more than two-fold risk of sudden death compared with intermediate mean QT_C values (400- 440ms).

There are two main hypotheses to explain the electrophysiological basis of QT dispersion. The local hypothesis explaining QTD with spatial differences in action potential duration mirrored in the various QT

intervals compete with the global hypothesis explaining the variation in surface ECG measurements with different projections of a common T wave vector (5). By these results and our study it may be thought that QT dispersion and related markers may be cardiac predictors in thalassemic patient; especially about cardiac ischemia and sudden death related to cardiac disorders in them. The present population based on cross-sectional study of thalassemia major patients showed that QT, QT_C and T_e dispersions are increased in thalassemic patients in comparison with normal persons. In some previous articles there are appointments about the effects of aging and gender on QT dispersion (8). Also there are other articles mentioning that there are no significant differences in QT, QT_C and RR dispersions between girls and boys (9-10). We didn't find any significant differences of QT and QT_C dispersions between males and females in our case and control groups. Only T_e dispersion to QT or QT_C dispersions had highly significant correlations in male subgroup of normals.

One previous study showed that LVH⁺ patients (with left ventricular hypertrophy) had longer ventricular internal diastolic diameter and atrial diameter and thicker interventricular septa and left ventricular posterior wall. QT_C was significantly broader in LVH⁺ patients compared with LVH⁻ patients (without left ventricular hypertrophy).

Increased QT_{apex} and T_e are associated with a susceptibility to ventricular fibrillation even when the extent of the coronary heart disease and use of β blockers are taken into consideration (11). On the other hand local ischemia of the hypertrophied ventricular myocyte may be one potential mechanism for the increased dispersion of repolarization and it is shown that QT_a maximum interval tended to be longer in LVH⁺ patient as compared with LVH⁻ patients. This hypertrophy of myocytes may partly contribute to the increased QT_a dispersion. Some studies showed increased thickness of posterior wall, dimension of atrium and aortic root and left ventricular systolic and diastolic dimensions in thalassemic patients (2). They can be some reasons of increased QT dispersion in thalassemic patients.

Regarding this study and others mentioned above, we concluded that QT and QT_C dispersions significantly varied in thalassemic patients versus normal persons. If QT and QT_C dispersions are potent predictors of sudden death in other diseases affecting the heart, the questions about prediction of sudden

death in thalassemics following prolonged QT and QT_C dispersions remain. We think that it is important and valuable to continue and expand this study. A large trial of coordinated multicenter concentric investigations should assess about QT and QT_C dispersions in thalassemics to have more accurate results of sufficient confidence. It may provide a predictor of other cardiac disorders such as arrhythmias and sudden death in thalassemic patients.

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