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Original Article

Subclinical ventricular repolarization abnormality in uncontrolled compared with controlled treated hypertension

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ABSTRACT

Background: Antihypertensive medications have variable effects on the duration of the QT interval. This study aims to demonstrate the subclinical ventricular conduction defect in treating hypertensive patients taking in consideration the status of the blood pressure control with the antihypertensive agents.

Methods: This cross-section study was performed at the Departments of Physiology and Pharmacology, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq. A total number of 97 hypertensive patients (30 males and 67 females) were eligible to enroll in the study. The patients were grouped into controlled hypertension (Group I) and uncontrolled hypertension (Group II). Each participant is subjected to the electrocardiograph (ECG) investigation. A QT nomogram plot used to identify the patients who are vulnerable or at risk of developing cardiac arrhythmias.

Results: There were no significant differences in the values of the electrocardiogram determinants between Group I and Group II. Abnormal prolonged QTcB interval observed in 18 out of 80 (22.5%) patients of Group II compared with 4 out of 17. The JT index value of ≥ 112 was observed in 20 out of 80 (25%) patients of Group II compared with 6 out of 17 (35.3%) patients of Group I. A significant correlation between the QTcB duration with JT index observed in both Groups I and II.

Conclusion: Patients with hypertension have variability in ventricular repolarization (QTcB and JT) irrespective of their blood pressure control putting them at higher risk of cardiac arrhythmias.

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1. Introduction

The duration of the QT interval is one of the ventricular repolarization markers that can predict malignant arrhythmias in several diseases, including hypertension.¹ The QT interval is considered as one of the predictors of the risk of both coronary events and cardiovascular death in patients with hypertension.² In patients with uncomplicated hypertension, a prolonged corrected QT (QTc) interval is accompanied with a twofold increase in the risk of cardiac events after adjusting the other risk factors.³ In elderly subjects the duration of the QT interval is considered as a prognostic marker as Dimopoulos et al. found a high blood pressure (systolic and diastolic), and cardiac arrhythmias are associated with a higher value of the QTc dispersion.⁴ Prolonged ventricular repolarization found to be a risk factor of cardiac morbidity and mortality in patients with resistant hypertension

after adjusting the systolic blood pressure while in pregnancy induced hypertension, the duration of the QT interval found to be within the normal range of the healthy women.⁵ In hypertension associated with obesity, the duration of QTc interval is prolonged and tended to be decreased after blood pressure control and weight loss.⁶ Antihypertensive drugs (angiotensin converting enzyme inhibitors and angiotensin receptor blockers) reduced the duration of QT interval due to their effects on the left ventricular mass which increases in hypertension.^{7–9} Beta-adrenoceptor blockers may also reduce the duration of the QT interval in a dose-dependent manner without having any effect on the blood pressure^{10,11} while calcium channel blockers (dihydropyridine) do not exert a beneficial effect on QT interval.¹² High ceiling diuretics and thiazides may prolong QT interval due to electrolyte disturbances¹³ while potassium sparing diuretics shortened the QTc interval.¹⁴ The duration of JT interval is also a marker of ventricular repolarization and it is of more benefit than QT interval because the Bazett's formula of QTc exaggerates heart rate-dependency of ventricular repolarization intervals.¹⁵ Li et al. demonstrated the association between metabolic syndrome and prolonged QT and JT intervals and these

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intervals significantly correlated with the number of the metabolic derangement.¹⁶ Hypertensive patients treated with different antihypertensive drugs may have abnormal cardiac electrophysiology, in addition, the status of blood pressure control may also influence the duration of ventricular repolarization. Therefore, this study aims to demonstrate the subclinical ventricular conduction defects in treating hypertensive patients taking in consideration the status of the blood pressure control.

2. Materials and methods

This cross-section study was performed at the Departments of Physiology and Pharmacology, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Scientific Committee. The study included hypertensive patients who were followed up with a diagnosis of essential hypertension at the private clinics between January 1, 2014 and January 30, 2015. All patients provided informed consent to participate in the study. The criteria of inclusion were essential hypertension treated with antihypertensive drugs. The criteria of exclusion included secondary hypertension, diabetes mellitus, pregnancy, renal and hepatic failure. From each patient, the subjective data related to the current medical and the other associated illnesses were obtained. Each patient was examined clinically and the blood pressure was measured on sitting position. The mean of three readings of the blood pressure was taken. The mean arterial blood pressure was determined using the following equation: Mean arterial blood pressure (mmHg) = Diastolic + (1/3) pulse pressure. The pulse pressure is equal to systolic minus diastolic blood pressure.

Controlled hypertension was diagnosed as systolic and diastolic blood pressure <140 mmHg and <90 mmHg, respectively while a systolic and/or diastolic blood pressure \geq 140 mmHg and/or 90 mmHg was diagnosed uncontrolled hypertension at the time of the current use of antihypertensive drugs.

Each participant is subjected to the electrocardiograph (ECG) investigation. Specifications of the ECG machine are: 12 standard leads, the sensitivity is 10 mm/mV, the record speed is 25 mm/s. The ECG records of patients who were in sinus rhythm are obtained. All ECG waveforms were verified by visual inspection.¹⁷ The ECG record strips were scanned and the scanned picture was magnified by PC windows photo-viewer to zoom. From each ECG record strips, the following data were obtained: heart rate (beats/min); R-R interval (s); P-R interval (s); QRS wave duration (s); QTm (QT measured) interval (s); QTc (QT corrected) interval (s); JTm (JT measured) interval (s); Jtc (JT corrected) interval (s) and JT index.

QTc (QT corrected) interval (s): it is calculated by using the following formulae¹⁸:

$$\text{Bazett formula}(QT_cB) = QTm/\sqrt{RR}$$

The cutoff point of QTcB value is used according to Goldberg et al.¹⁹ with a modification of children and adolescent age that instead of <15 years, \leq 18 year old is considered (Table 1).

The JTm (s) was calculated by subtracting QRS complex duration from QT interval and the corrected (JTc) was calculated by subtracting of the duration of QRS complex from QTcB. The JT index = JTm (heart rate + 100)/518, and a cutoff value of \geq 112 indicated a prolonged duration of ventricular repolarization in ventricular conduction defect.²⁰ A QT nomogram plot that developed by Chan et al., used to identify the patients who are vulnerable or at risk of developing cardiac arrhythmias.²¹ The QT-nomogram plot represented a plot of heart rate against the QT interval and any point out of the curve indicated that the patient is vulnerable to cardiac arrhythmias.

Table 1

Cut-off value of QTcB according to age and gender.

Category	Children and adolescent <18 years	Adult male	Adult female
Normal	<0.44 s	<0.43 s	<0.45 s
Borderline	0.44–0.46 s	0.43–0.45 s	0.45–0.47 s
Prolonged	>0.46 s	>0.45 s	>0.47 s

A total number of 97 hypertensive patients (30 males and 67 females) were enrolled in this study. Seventeen of them have a blood pressure of less than 140 (systolic) and less than 90 (diastolic), and this group represented as controlled hypertension and assigned Group I. Eight patients have either high systolic, or diastolic or both and represented as uncontrolled hypertension and assigned Group II.

Six patients have a systolic blood pressure \geq 140 mmHg and a diastolic blood pressure <90 (Group IIA), 12 patients have a diastolic blood pressure \geq 90 mmHg and a systolic blood pressure <140 (Group IIB), and 62 patients have a systolic and diastolic blood pressure \geq 140 and 90 mmHg respectively (Group IIC).

2.1. Statistical analysis

The statistical analysis was performed by using SPSS v.20.0 for Windows (IBM Corp., Armonk, NY, USA). The results are expressed as a number and mean \pm SD. The difference between percentage tests was used to compare categorical variables. The differences in means were analyzed by using the two tailed unpaired *t*-test and a simple correlation test was used to determine the relationship between hematological indices and the variables related to the mean blood pressure and the other metabolic derangement determinants. The level of statistical significance was set at $p \leq 0.05$.

3. Results

Table 1 showed that there are insignificant variation in age and duration of hypertension between the groups. The habit of current smoking is observed in a significant high percent in Group II compared with Group I. Previous history of stroke and ischemic heart disease observed in a significant high frequency in Group II compared with Group I (Table 2). Variability in the prescription of antihypertensive drugs observed in Group II compared with group I. At the time of entry, significant high systolic, diastolic, and both systolic and diastolic blood pressure observed in 6, 12, and 62 patients, respectively (Group II) compared with 17 out of 97 patients were under control blood pressure (Table 3) Accordingly the pulse pressure and the mean arterial blood pressures were significantly differed from the corresponding values of Group I. (Table 3). There were no significant differences in the values of the electrocardiogram determinants between controlled hypertension (Group I) and uncontrolled hypertension (Group II) (Table 4). Abnormal prolonged QTcB interval observed in 18 out of 80 (22.5%) patients of Group II compared with 4 out of 17 (23.5%) patients of Group I, the difference did not reach a significant level. The JT index value of \geq 112 was observed in 20 out of 80 (25%) patients of Group II compared with 6 out of 17 (35.3%) patients of Group I, the difference did not reach a significant level (Table 4). Fig. 1 shows that 8 patients (1 belonged to Group I and 7 belonged to Group II) were vulnerable to cardiac arrhythmias, the difference did not reach to the significant level (5.9% versus 8.8% respectively). Fig. 2 shows significant correlations between the QTcB interval with JT index in both Groups I and II. The coefficient factors were 0.841 and 0.742 for Groups I and II respectively. The frequency of borderline-pathological prolonged QTcB interval observed in 13 out of 43 patients using antihypertensive drugs in term of

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