ORIGINAL ARTICLE

COMPARISON OF HEART RATE AND QTc DURATION IN PATIENTS OF CIRRHOSIS OF LIVER WITH NON-CIRRHOTIC CONTROLS

Bader Faiyaz Zuberi, Shahid Ahmed*, Nabiha Faisal*, Salahuddin Afsar, Abdul Rauf Memon, Inayat Baloch and Rashid Qadeer

ABSTRACT

Objective: To compare QTc duration and Heart Rate (HR) in patients with cirrhosis with non-cirrhotic controls.
Design: Cross-sectional analytical study.
Place and Duration of Study: Civil Hospital and Lyari General Hospital, Karachi, from March 2004 to February 2006. **Patients and Methods:** Confirmed patients of cirrhosis were selected and allocated to Group-I. An equal number of non-cirrhotic patients were taken as control and were allocated to Group-II. ECG was recorded and values of HR and QTc were calculated. Comparison of increased frequency of HR and prolongation of QTc were done using Chi-square test or Fisher's Exact Test with significance level at • 0.05. ROC curves of HR and QTc were plotted for the presence of cirrhosis. **Results:** Seventy-eight confirmed patients of cirrhosis of liver were inducted in Group-I with same number of non-cirrhotic patients as control in Group-II. The mean ± SD of QTc of Group-I was 0.438 ± 0.015 sec and that in Group-II was 0.432 ±0.010 sec and that for HR in Group-I and II were 78.34 ±12.15 and 74.98 ± 8.03 b/min respectively. The mean QTc and HR values were significantly more in Group-I as compared to Group-II with p = 0.006 and p = 0.043 respectively. **Conclusion:** Means of both HR and QTc were significantly higher in cirrhotic patients as compared with non-cirrhotic controls.

KEY WORDS: *Cirrhosis. Heart rate. QTc. Circulation. Cirrhotic cardiomyopathy.*

INTRODUCTION

Cirrhosis is a very common ailment in Pakistan,[1,2] mostly caused by viral hepatitis B and C.[3] Its prevalence is still very high despite measures to control the viral infections. Many complications can occur as a result of cirrhosis, out of which ascites, portal hypertension and varices are well-known. Many new complications are being recognized which include hepatopulmonary and sleep-apnoea syndromes.[4] The affects of cirrhosis on cardiovascular and circulatory system are not well studied.[5] The use of new investigative modalities has shown several lines of evidence of impaired cardiac contractility and performance in patients with cirrhosis and has led to the introduction of the new clinical entity, cirrhotic cardiomyopathy.[6] Although it was first described in 1953, but was forgotten and not much work was done on it.[6] Changes in Heart Rate (HR) and QTc duration are part of this new syndrome. A prolonged QTc duration in chronic liver disease could potentially lead to ventricular arrhythmias and sudden cardiac death.[7-9] There is no report regarding HR and QTc disorders in cirrhosis from our area. The aim of this study was to compare the HR and QTc duration in patients of cirrhosis with non-cirrhotic controls.

PATIENTS AND METHODS

It was a cross-sectional study conducted at medical wards of Civil Hospital and Lyari General Hospital, Karachi, affiliated with Dow University of Health Sciences from March 2004 to February 2006.

Keeping in view of expected frequency of QT abnormalities in normal population reported at 5.9% [10] and that in cirrhosis at 37%,[11] a sample size was estimated for difference between two population proportions, using confidence level (1-a) of 95% and precision (d) of 0.085 to be of 156.

Using convenience sampling, confirmed patients of cirrhosis were inducted after taking informed consent. All the selected patients were allocated to Group-I. An equal number of non-cirrhotic patients admitted in the ward for other reasons were taken as control and were allocated to Group-II. Group-I was further sub-classified into Group-IA, IB and IC according to Child's classification.

Patients with ischemic and valvular heart disease, conduction defects, cardiac failure, hypertension, hyperkalemia and patients taking b-blockers, calcium channel blockers, anti-arrhythmic and cardiac glycosides were excluded.

Clinical details were recorded of all the selected patients on a proforma. Three 12 lead ECG recordings were taken of each patient, 5 minutes apart, and HR and QTc were calculated for each ECG and then mean of the three were calculated and used for the analysis.

QTc values were calculated for all patients by the formula: QTc = QT/÷R-R.[12,13]

Heart rate were calculated on ECG by formula. HR=1500/R-R[14]

A mean value of QTc > 0.44 seconds was taken as prolonged, while the HR > 100 was taken as increased. Blood sample

Department of Medicine, Dow University of Health Sciences, Karachi.
*Department of Medicne, Lyari General Hospital/DUHS, Karachi.

Correspondence: Dr. Bader Faiyaz Zuberi, C-404, Al-Habib Pride, CL-8/5, Civil Lines, Karachi-75530, Pakistan. E-mail: bder@zuberi.com.pk

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was taken for complete blood counts, urea, creatinine, electrolytes, LFTs, albumin, and prothrombin time.

Means of HR and QTc were compared by independent samples 't-test' between the two groups. 95% confidence intervals and p-values were calculated with significance level set at • 0.05. Frequency of high HR and prolonged QTc was determined by recoding the patients with HR > 100 and QTc > 0.44 into separate variables for frequency estimations. Comparison of increased frequency of HR and prolongation of QTc were done using Chi-square test or Fisher's Exact Test with significance level at • 0.05. Receiver Operative Characteristic (ROC) curves were plotted using HR and QTc as Test Variables and presence of cirrhosis as State Variable. SPSS version 15.0 was used for statistical analysis.[15]

RESULTS

Seventy-eight confirmed patients of cirrhosis of liver were inducted in Group-I with same number of non-cirrhotic patients as control in Group-II. The mean age in Group-I was 34.4 years and that in Group-II was 35.2 years (Table I). Patients of

Table I: Demographic profile of patients according to groups.

		Group-II	Group-IA	Group-IB	Group-IC
Gender	Female	33	2	7	12
	Male	45	4	12	41
Age	Mean years	36.29	26.17	37.00	36.53

Group-I were sub-classified into Groups IA, IB and IC according to the Child's Classification as under: IA = 6, IB = 19 and IC = 53 patients. The mean ± SD of QTc on Group-I was 0.438 ± 0.015 sec and that in Group-II was 0.432 ±0.010 sec (Figure 1) and that for HR in Group-I and II were 78.34 ± 12.15 and 74.98 ± 8.03 b/min (Figure 2) respectively. Comparing the mean QTc values of the two groups by independent samples 't-test', gave the SED= 0.002; 95% CI[2] = 0.001751 to 0.009993; with p = 0.006. Similar comparison testing for HR revealed SED = 1.65; 95% CI = 0.10545 to 6.62019 with p= 0.043. Means of both HR and QTc were significantly higher in Group-I as compared with Group-II. Comparison of frequency of increased HR > 100 /min between the two groups showed no significant difference, 4 (5.1%) and 2 (2.6% two sided Fisher's Exact Test = 0.681). Similar calculations of frequency of prolonged QTc > 0.44 sec gave significantly increased frequency of prolonged QTc in Group-I; 15 (19.2%), as compared to Group-II; 4 (5.1%). Chi-square test with continuity correction = 0.014. ROC curves were plotted to see the area under the curve for HR and QTc for the presence of cirrhosis and it is shown in Figure 3. The area under the curve of QTc was 0.61 with p= 0.021 and 95% CI = 0.52 and 0.70. The area under the curve of HR was 0.55 with p= 0.253 and 95% CI = 0.46 and 0.64.

The area under the curve for QTc was significantly more in cirrhotic patients, while the area under the curve for HR is not significantly increased in cirrhotic patients as compared to non-cirrhotic controls.

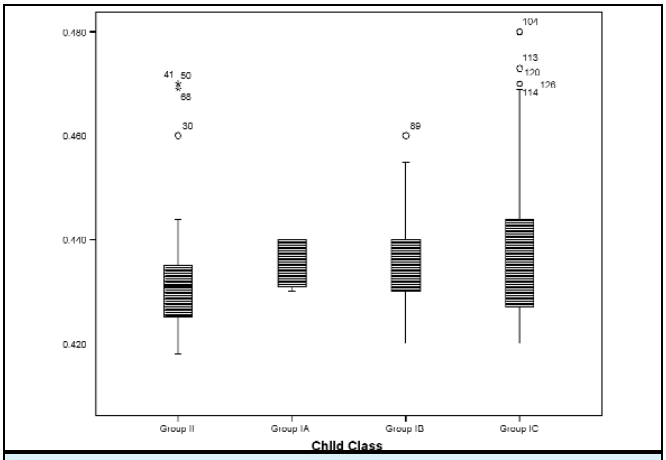

Figure 1: Box plot of QTc according to groups.

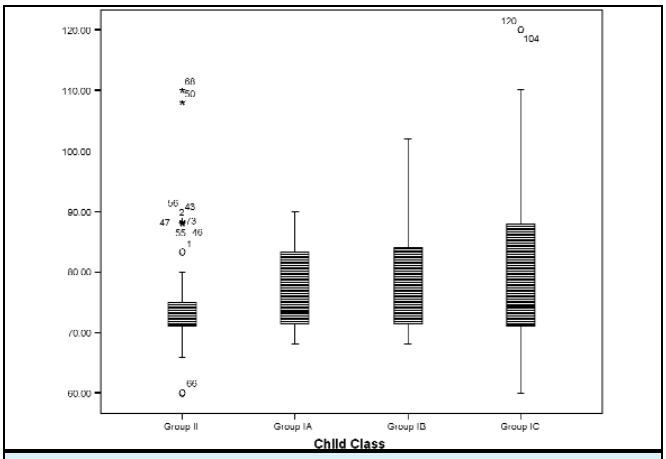

Figure 2: Box plot of HR[3] according to groups (HR[3] Heart rate).

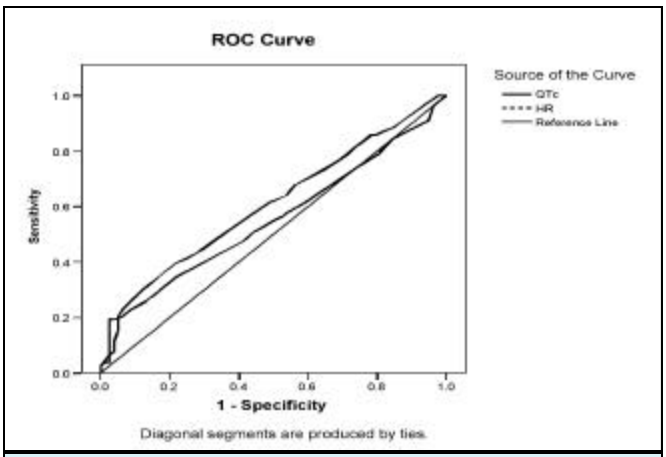

Figure 3: Roc curves or HR[4] and QTc for presence of cirrhosis (HR[4]=Heart rate).

DISCUSSION

Cirrhotic cardiomyopathy is a new clinical entity, which is diagnosed infrequently because of relative unawareness regarding this entity. It has many features including prolongation of QTc, increased HR, decreased myocardial contraction force and diastolic dysfunction.[7,16] The current study documents significant prolongation of QTc in patients with 19.2% of cirrhosis in our population, although, figures as high as 37% have been reported. Several electrophysiological

mechanisms for the conductance abnormalities and impaired cardiac contractility have been suggested, these include reduced beta-adrenoceptor density, postreceptor signal defects, abnormal excitation-contraction coupling, and molecular abnormalities.[17,18] Beta-receptor density and sensitivity is reduced in cirrhosis,[16] along with altered G protein and calcium channel functions.[19] This results in both impaired chronotropic responses and electromechanical uncoupling.[20] The coupling between the cardiac output and arterial compliance is an important factor affecting the left ventricular stress and work done by it.[21] Ascending and arch of aorta can contain the stroke volume without excessive change in systemic arterial pressures. On the other hand, a too compliant arterial system will hamper prompt and timely delivery of blood to different parts of the body and also delay flow in important vascular beds. These effects will be more marked in the patients with large cardiac output, stroke volume and vascular beds of varying vascular resistance as in cirrhotic cardiomyopathy.[9] It has also been reported that patients with essential hypertension become normotensive on development of cirrhosis.[22]

In our study, we found significant increase in mean values of HR between the two groups but when we tested the frequency of patients having heart rate of more than 100 beat/min we did not find significant difference in the frequency of tachycardia in two groups. The area under the curve was estimated by the ROC curves that were plotted for both HR and QTc for presence of cirrhosis. The area under the curve was greater with QTc (Figure 3). In the current study, the frequency of QTc prolongation was also studied according to the Child's Class and it was found that the frequency of QTc prolongation increases with the severity of liver disease. However, as the sample size was not estimated for the sub-group analysis; reliable inference could not be made in this regard. Prolongation of QTc interval has been shown to be related to the severity of liver disease and survival.[18,23] Improvement in the QTc interval has been documented with improvement in liver functions, beta-blockers and liver transplantation.[20]

Conclusion

HR and QTc changes were documented in our study, at present no universal or consensus guidelines are available for their management.

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