Original Article

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COMPARISON OF QTc DURATION ON ELECTROCARDIOGRAM BETWEEN PATIENTS OF LIVER CIRRHOSIS AND NON CIRRHOTIC CONTROLS

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ABSTRACT

Objective: To compare the QTc duration on electrocardiogram (ECG) of patients of cirrhosis (hep B and C origin) with non cirrhotic controls.

Study Design: Case control study.

Place and duration of study: The study was carried out at the Department of Medicine, Military Hospital, Rawalpindi, from 8th Feb 2009 to 8th Aug 2009.

Material and Method: After meeting the exclusion and inclusion criteria, 80 cirrhotic patients were enrolled in group-I and equal number of non cirrhotic controls were enrolled in group-II. Three 12 lead ECG recording were taken for each patient, 5 minutes apart, and QTc value was calculated for each ECG and then mean of the three was used for the analysis. A QTc value more than 0.44 seconds was taken as prolonged.

Results: The mean QTc interval on electrocardiogram in group-I i.e. cirrhotic was 0.4603 seconds (SD±0.1312) and mean QTc interval on electrocardiogram in group-II i.e. noncirrhotic was 0.407 seconds (SD±0.029). These findings were statistically significant (p value < 0.001).

Conclusion: Cirrhotic patients have prolonged QTc interval as compared to noncirrhotic controls.

Key words: Cirrhosis, Electrocardiogram, QTc interval.

INTRODUCTION

Cirrhosis is the end result of hepatocellular injury, it is the tenth leading cause of death world over and is a very common ailment in Pakistan[1]. In our population cirrhosis is mostly secondary to chronic hepatitis B and C viral infection. Cirrhosis can lead to various complications which include portal hypertension, gastroesophageal varices, ascites and hepatorenal syndrome, these complications are well recognized and thoroughly studied. The effect of cirrhosis on cardiovascular and circulatory system is a field which still needs to be explored[2]. Cirrhotic cardiomyopathy is a clinical entity which includes baseline increase cardiac output, attenuated systolic contraction or diastolic relaxation in response to physiological, pharmacological and surgical stress and electrical conductance abnormality. Increased QTc interval is a part of this clinical entity which can potentially lead to sudden cardiac death and ventricular arrhythmias[3]. The drugs which cause prolongation of QTc interval add further insult in cirrhosis which may lead to fatal arrhythmias. The prevalence of cirrhotic cardiomyopathy remains unknown at present, mostly because the disease is generally latent and gets clinically significant when patient is subjected to stress such as exercise, drugs, infections, hemorrhage and surgical procedures such as insertion of transjugular intrahepatic portosystemic shunts (TIPS) or therapeutic paracentesis.

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PATIENTS AND METHODS

This was a case control study done in the Department of Medicine, Military Hospital (MH) Rwp, from Feb 2009 till Aug 2009. It is a tertiary care hospital with entitlement of officers, junior commissioned officers and other ranks of Armed Forces. Patients from all parts of the country are referred to this medical facility. Keeping in view expected frequency of QT abnormality in normal population at 5.9%[4] and that in cirrhosis at 37%[5], a sample size was estimated.

Using purposive, non probability sampling where bias was minimized by rigorous matching, 80 cirrhotic patients who were HBsAg or anti HCV Ab positive with USG finding of coarse liver echotexture, increased portal vein diameter, and ascites were considered as cases and included in group-I. Eighty patients who were coming to the medical OPD or admitted in medical wards with any complaints other than cirrhosis were considered as controls, and included in group II. Patients already taking drugs such as beta blockers, Ca channel blockers, antiarrythmic, macrolides were excluded from both groups. Patients of ischemic heart disease, hypertension, hyperkalemia, heart failure and valvular heart diseases were also excluded from both groups.

An informed consent was obtained from all patients for subjecting them to a special investigation and using their data for research. Demographic information was collected in name, age, and gender. Three 12 lead ECG recordings were taken for each patient, 5 mins apart and QTc interval was calculated for each ECG using formula QTc = QT / $\sqrt{RR}$[6]. Mean of three readings were used for analysis. A QTc interval more than 0.44 sec was taken as prolonged. Data had been analyzed using SPSS version 15. Mean of QTc of 2 groups were compared by independent sample "t-test". The *p*-values were calculated with significance level set at 0.05.

RESULTS

A total of 80 cirrhotic patients were enrolled in group I as cases and 80 non cirrhotic patients were enrolled in group II as control. Group wise gender description of patients is given in figure.

Mean age of group I was 55.04 yrs (SD±4.08) while mean age of group II was 54. 7 years (SD±3.86). Both the groups were comparable with respect to age (p> 0.05) and gender (p> 0.05)

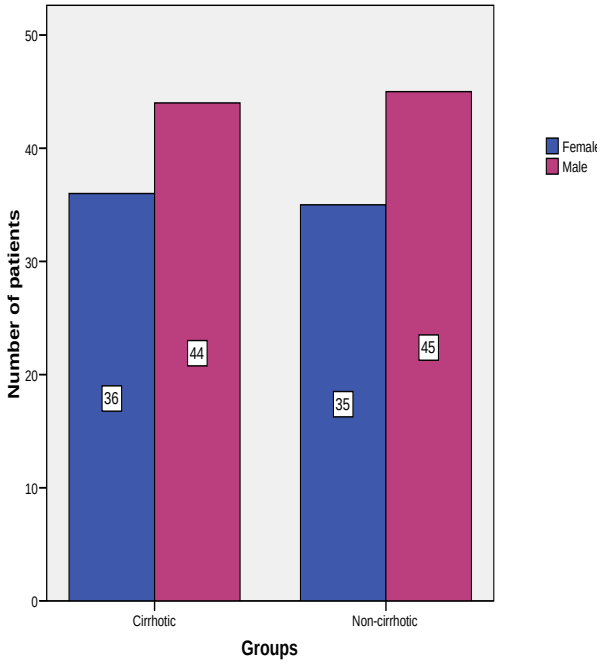

Figure: Group-wise gender description of patients

The mean QTc interval on ECG in group I i.e cirrhotic was 0.4603 seconds (SD±0.1312) and mean QTc interval on ECG in gp II ie non cirrhotic was 0.407 seconds (SD±0.029).

These findings were statistically significant as shown in table.

DISCUSSION

In 2005 a panel of expert hepatologists and cardiologists met at world congress of gastroenterology and proposed a working definition of cirrhotic cardiomyopathy according to which it is a form of chronic cardiac dysfunction in patients with cirrhosis characterized by blunted contractile responsiveness to stress, and / or altered diastolic relaxation with electrophysiological abnormalities in the absence of any other known cardiac disease[7]. Currently, it is

Table: Description of age and QTc interval on ECG

Variables	Cirrhotic (n = 80)		Non-cirrhotic (n = 80)		*p*-value
	Mean	SD	Mean	SD	
Age (years)	55.04	4.08	54.47	3.86	> 0.05
QTc interval on ECG (seconds)	0.4603	0.1312	0.4047	0.0290	< 0.001

formulated that cirrhotic cardiomyopathy includes prolongation of QTc interval, increased heart rate, decreased myocardial contraction force and diastolic dysfunction.

In experimental cirrhosis of rats, in which cirrhosis was introduced either by bile duct ligation or exposure to carbon tetra chloride, several abnormalities in beta adrenergic signaling pathway have been identified for example decrease in beta adrenergic receptor density, reduction in G5 proteins and increase in adenylate cyclase activity with resultant decrease in cAMP generation, all of which have negative effect on cardiomyocyte contractility[8]. Electrophysiological abnormalities in cirrhosis are due to a combination of plasma membrane changes, beta adrenoceptor and postreceptor pathway defects and generalized ion channel dysfunction. All above mentioned abnormalities in membrane fluidity and beta adrenergic signaling pathway in cirrhosis can lead to a delay in electrical excitation and its mediation of the mechanical contraction, resulting in impaired electromechanical coupling.

This study was merely concerned with QTc interval as evidence of cirrhotic cardiomyopathy and it clearly documents significant prolongation of QTc interval on ECG in 46% patients of cirrhosis as compared to non cirrhotic controls. This result has wide spread clinical implications because various drugs e.g erythromycin, antiarrythmic drugs, psychotropic medication such as haloperidol, when given to cirrhotic patients add further insult to injury and can cause fatal arrythmias.

Dr Henriette and colleagues[9] conducted a study to measure QTc interval of patients of liver cirrhosis in relation to severity of portal hypertension and they measured QTc interval in cirrhotic patients with hepatic venous pressure gradient HVPG < 12 mm Hg and compared it to patients of liver cirrhosis who have HVPG > 12 mm Hg. They concluded that 52 % of cirrhotic patients irrespective of severity of increase in HVPG has prolonged QTc duration and thus QTc interval is more related to liver dysfunction rather than severity of portal hypertension.

Zambruni and colleagues[10] assessed the effects of beta blockers administration on QTc interval in a cohort of cirrhotic patients with varying degree of decompensation. They noted reduction in QT interval only in patients with a baseline prolonged QT interval, but there was lengthening of QT interval in those with normal baseline QT interval. Furthermore they found no correlation between the change in QT interval with beta blockade and reduction in portal pressure, implicating that portal hypertension and shunting were not involved in QT prolongation.

One local study conducted by Dr Zuberi and colleagues[11] regarding comparison of QTc interval and heart rate in patients of liver cirrhosis and non cirrhotic controls, concluded that mean of heart rate and QTc interval were significantly higher in cirrhotic patients as compared to non cirrhotic control which is exactly similar conclusion as our study

Local and international literature agrees with the findings of our study, but certain avenues still need to be explored e.g effect of drugs which prolong QTc interval on cardiac rhythm in patients of cirrhotic cardiomyopathy, and comparison of other aspects of cirrhotic cardiomyopathy e.g diastolic dysfunction with non cirrhotic controls, treatment options of cirrhotic cardiomyopathy, and effects of QTc prolongation on cardiac functioning, which we intend to pursue in near future.

CONCLUSION

Cirrhotic cardiomyopathy is a new clinical entity, which includes prolongation of QTc interval, as documented in our study. This has widespread clinical implications such as drugs which increase QT interval

should be avoided in patients of liver cirrhosis.

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