

ORIGINAL ARTICLE

ELECTROPHYSIOLOGICAL CHANGES IN PATIENTS WITH LIVER CIRRHOSIS IN A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN

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Background: Electrophysiological changes in cirrhosis are well known but least investigated especially in our country hence we wanted to see electrophysiological changes especially QT interval in cirrhotic patients. **Methods:** A cross-sectional study was conducted at Aga Khan University Hospital Karachi (AKUH) in which medical records (duration 2008–2010) of cirrhotic patients were reviewed. **Results:** Three hundred and eighty cirrhotic patients' charts were studied, 227 (59.7%) were male and mean age of this cohort was 52.8±12.6 years. The most common cause for CLD was Hepatitis C (CHC) in 260 (68.4%), NBNC in 56(14.7%) and HBV in 51 (13.4%). Only 225 had complete ECG workup, the mean corrected QT interval was 0.44±0.067sec. Among the electrophysiological abnormalities, 79 (35%) had a prolonged corrected QT interval, 7 (3.1%) had a prolonged PR interval (>0.22s) and prolonged QRS duration was seen in 23 (10.4%) patients. QT prolongation was seen in 1 of the 5 patients with Child Class A (20%), 22 of the 73 patients with Child Class B (30.1%), and 25 of the 61 patients with Child Class C (41%). However, this difference however was not statistically significant. (*p* value=.331). **Conclusion:** We conclude that QT prolongation is more frequent in patients with liver cirrhosis especially when the disease is more advanced like in Child C hence these patients are more prone to sudden cardiac death. Moreover, this study shows that the risk associated with QT prolongation is present through all classes of liver cirrhosis. We recommend that routine cardiac screening with ECG of all cirrhotic patients be performed.

Keywords: Cirrhosis; QT interval; child class

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INTRODUCTION

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible if patients decompensate at which point the only option may be liver transplantation.¹ Cirrhosis can be complicated by many conditions like upper gastrointestinal bleeding due to oesophageal varices (EV), hepatic encephalopathy(HE), Ascites with Spontaneous bacterial peritonitis (SBP) and renal impairment.² Cardiac electrophysiological abnormalities are well known entities in liver cirrhosis.

Q-T interval prolongation is the most common abnormality in all electrophysiological abnormalities. Q-T interval represents ventricular electrical systole which is the repolarization phase.^{3,4} Its prolongation provokes very sinister ventricular arrhythmias that can cause sudden death.⁵ This is probably caused by a functional defect as this is reversed after liver transplantation.⁶ QT interval duration can be determined by conventional 12 lead electrocardiographic (ECG) recording from the onset of the QRS complex to the end of the T wave. QT interval varies with heart rate, it decreases when heart rate accelerates.³ Therefore

corrected QT interval is used for the measurement. Initially prolonged QT interval along with increased sudden deaths was identified in alcoholic cirrhotic patients⁷ and then subsequently in cirrhosis of different aetiologies along with the severity of disease.⁵ In cirrhosis, prolonged Q–T interval is significantly related to the severity of the liver disease, portal hypertension, portosystemic shunts and reduced survival.^{8,3} However prolonged QT interval can also be seen in well compensated liver disease.⁹ It is estimated that prevalence of this abnormality in Child Pugh Class A is 25%¹⁰, 51% in CTP class B and 60% in CTP Class C⁵.

Similarly, a study from Pakistan had also shown the higher frequency of prolonged QT interval but on smaller number of patients. That study had shown mean QTc of the cirrhotic group was 0.438±0.015 sec and that of the non-cirrhotic group was 0.432±0.010 sec. The heart rate for the cirrhotic group was 78.34±12.15 and for the non-cirrhotic group was 74.98±8.03 b/min respectively. The mean QTc and HR values were significantly more in the cirrhotic group as compared to the non-cirrhotic with *p*=0.006 and *p*=0.043 respectively.¹¹ Our study aims to further add to this topic, by using a larger sample size and wanted to look for electrophysiological abnormalities like QT interval, PR interval and QRS complex. This topic is poorly researched in Pakistan.

MATERIAL AND METHODS

This study was a cross-sectional study on medical records all patients with known cirrhosis coming in a two year period (2008–2010) at the Aga Khan University, Karachi, Pakistan.

Charts of all established cirrhotic patients of any aetiology (viral as well as non-viral associated cirrhosis) were included. The diagnosis of cirrhosis was made on clinical basis, i.e., history of ascites, upper gastro-intestinal bleed, encephalopathy and ultrasound showing features of cirrhosis like shrunken liver, dilated portal vein, splenomegaly etc.

Patients who were known cases of ischemic heart disease, Renal failure, Hypertension (HTN), bundle branch block (BBB) and patients taking drugs which prolong Q-T interval such as Sotalol and disopyramide, patient with electrolyte abnormalities such Hypokalaemia, Hypocalcaemia, Hypomagnseemia and patients with chronic obstructive pulmonary disease were excluded.

Ethical approval was taken from the Departmental Ethical Committee and the data was collected on predesigned *pro forma*. In all our patients, standard 12 lead ECG was done by the senior technician in the electrocardiographic department. Manual QT interval was measured and then corrected QT (QTc) was calculated by formula:

$$(QTc=QTinterval/\sqrt{RRinterval}).$$

The normal upper limit cut off value for QTc is 440 mili seconds (ms). Currently modern 12 leads ECG gives the calculated value of QT and QTc while it can also be manually measured when all 12 leads are simultaneously recorded.³

The data was analysed using SPSS 19.0. P value for difference between QT prolongation in beta blocker and non-beta blocker group was 0.15. The p value for differences between QT prolongations as we moved from Child class A to C was 0.33.

The effect of beta blocker use on QT interval in the study sample of 225 patients with a complete record was analysed using Pearson's chi squared test.

RESULTS

A total of 380 patients with CLD were admitted; out of which 225 patients had ECG record available. The mean age of this cohort was 52.8±12.6 years.

The QT interval was calculated for a total of 225 patients with a minimum of .20 ms, maximum of .52 ms and a mean of .3682, with the standard deviation being .05423. The QRS complex was calculated for 225 patients with a minimum of .02 ms, maximum of .48ms and a mean of .086±0.03. The PR interval was analysed in 225 patients, and ranged from 0 to .26 ms, with a mean of 0.15±0.03.

The mean pulse calculated from 341 patients was 88.58±19.

Electrophysiological changes showed mean QT interval was 0.37±0.05ms, mean QRS 0.086±0.054, PR interval 0.15±0.03.

Most common electrophysiological abnormality was prolonged QT interval in 79 (35.1%) patients and 23 (10.4%) had prolonged QRS complex.

A total of 139 patients had complete child scoring and ECG performed.

Out of these 139 patients, 5 were in child class A. One out of these 5 patients showed a QT prolongation, none showed PR abnormalities and 1 had QRS prolongation.

Out of the 73 patients in class B, 41 (30.1%) showed QT interval prolongation, 5.5% showed PR abnormalities and 9.7% showed QRS complex abnormalities

From the 61 cases in class C for whom a complete record was available, 41% had QT interval prolongation, 4.9% had PR abnormalities and 11.9% had QRS abnormalities.

The effect of beta blocker use on QT interval was also performed using corrected QT values. Out of the 225 patients with ECGs performed, 76 used beta blockers and 149 did not. Out of the 76 patients using beta blockers, 48(32.9% of the total cases with normal QT) had a QT interval that was normal (from 0 to .46), while 28 (35.4% of those with too long a QT) had a longer than normal QT interval. Amongst the 149 patients not using beta blockers, 98 (67.1% of those with normal QT) had a QT interval that was normal. The other 51 patients not using beta blockers had a prolonged QT, and these account for 64.6% of the patients with a longer than normal QT interval.

The effect of beta blocker use on QRS complex was also analysed among our study sample. Out of the 76 people using beta blockers, 36.8% had an abnormal QRS complex interval.

Table-1: Baseline characteristics

| | n (%) |
|----------------------------|------------|
| Male | 227(59.7) |
| Cause of CLD | |
| HCV CLD | 260 (68.4) |
| HBV | 51 (13.4) |
| HBV/HDV | 13 (3.4) |
| NBNC CLD | 56 (14.7) |
| Child Class (n=228) | |
| A | 8 (3.5) |
| B | 130 (57) |
| C | 90 (39.4) |

DISCUSSION

This study had shown the higher frequency of electrophysiological abnormalities in patients with

cirrhosis. An electrophysiological abnormality in cirrhotic patients includes chronotropic incompetence; electromechanical uncoupling, and electrocardiographic QT interval prolongation.

Their underlying mechanism is unknown but some of these have common alterations at molecular level.³ These mechanisms such as the sympathetic nervous activity influences the heart rate and electromechanical coupling by several mechanisms: Noradrenaline binding to B-receptors, receptor-mediated G protein interaction and, consequently, stimulation of adenylylase, activation of cAMP-dependent phosphokinase A and channel phosphorylation. Several receptor and post-receptor defects have been described in cirrhosis with reduced B-receptor density and sensitivity, and altered G protein and calcium channel functions. All these mechanisms are responsible for these electrophysiological abnormalities.^{2,3}

Our study did have much more males than females, a reflection of the unfortunate reality that men are much more frequently exposed to risk factors for hepatitis infection in Pakistan.¹²

Our study showed a rising trend in the percentage of cases showing a QT prolongation (20–30% to 41%) as we go from class A to C. Although a clearly higher percentage of patients had QT prolongation as we progressed from Class A to C, this difference however was not statistically significant. (p value=.331).

The QT interval was not significantly different between the Beta Blocker and Non-blocker group (0.15 p value), proving that there is no significant effect of beta Blocker on QT prolongation in this cohort of patients.

From the 149 patients not using beta blockers, 34.2% had an abnormal QRS interval. This showed that there was no significant effect of beta blocker usage on QRS complex abnormalities.

The percentages of cases with QRS abnormalities and PR changes, however, did not show any trend as we go from Pugh Child Class A to C. The percentage of cases showing QT prolongation in our study (With Class A 25% to Class B 30.1% to Class C 41%) is slightly lower than that in already published data (which is 25–51 to 60 as we move from Pugh class A to C), however a similar upward trend has been shown.^{5,10}

The clinical significance of the prolonged QT interval is still in the grey zone but in a study by Bernardi M *et al*, it was seen that survival in these patients with prolonged QT interval is shorter as compared to normal QT interval.⁵ The interesting finding in this study was that there was shorter survival in those who are child class A with prolonged QT interval while in rest of the two child

classes are not affected for mortality by prolonged QT.⁵ From this it can clearly be concluded that prolonged QT interval is risk factor for mortality in cirrhotic patient in the earlier stage of disease.

A limitation of our study was that the number of cases in the Child Pugh class A was very small, and that all patients using beta blockers were distributed among classes B and C and none in A. Beta-blockers have the potential to cause QT shortening in patients with prolonged baseline values due¹³, thus partially explaining the lowering effect in the percentage of patients who present with QT prolongation from Child classes B and C.

We also found in our study that the percentage of cases with QT prolongation increases uniformly as we go from class A to C. This is unlike the findings in two previous studies^{13,14} which show that occurrence of QT prolongation in classes B and C is much higher than in class A. This again emphasizes the need for earlier intervention because of a higher risk in class A patients with prolonged QT interval in Southeast Asia compared with the rest of the world.

CONCLUSION

We conclude that QT prolongation is more frequent in patients with liver cirrhosis especially when the disease is more advanced like in Child C, although this difference is not statistically significant, hence these patients are more prone to sudden cardiac death. Moreover, this study shows that the risk associated with QT prolongation is present through all classes of liver cirrhosis.

AUTHOR'S CONTRIBUTION

OM wrote initial synopsis, did analysis and review the final original article, SH provided the supervisory role, while others help in data collection and data entry.

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