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INCIDENCE OF PROLONGED QT IN CIRRHOTIC PATIENT

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ABSTRACT: This study performs to assess the prevalence of various types of cardiovascular abnormalities which presents as prolonged QcT and its relation with severity of liver disease. From 48 cirrhotic patients and 48 persons taken as control biochemical blood tests and ultrasonography is done. Severity of liver disease with respect to the criterions of CHILD &MELD in the group of patients is determined. QT interval and QcT were measured in both groups of case and control. χ^2, T-test and Mann–Whitney U test use for analysis. An abnormality of blood biochemical tests was more often in cirrhotic patients than control group. Prolonged QcT was significantly more prevalent in patients than in controls' group. Prolongation of QcT in patients' group did not have any significant relation to the severity of liver disease according to criteria of CHILD &MELD which could be explained by the following reasons. The first reason was probably due to the low volume of sample and heterogeneous distribution of three groups of CHILD (A, B and C) in cirrhotic patients and another reason was the probability of association between QcT and the rise of portal pressure and gradient of portacaval pressure which were independent from the severity of liver dysfunction. Prevalence of prolonged QcT in cirrhotic patients reflects the higher incidence of cardiac arrhythmias in these patients. Therefore diagnosis of cardiac conduction abnormalities and arrhythmias with their precipitating factors and avoiding prescription of medications exacerbating their occurrence has a vital importance in patients with cirrhosis.

Keywords: Cirrhosis, Prolonged QT, CHILD, MELD, Electrocardiography (ECG).

INTRODUCTION

QT interval includes the period of time between the onsets of ventricular depolarization to the end of repolarization. In fact, the QT interval shows the period of ventricular systole therefore it includes the complete electrical events of ventricles. With respect to the period of time QT is more related to the ventricular repolarization than its depolarization therefore its prolongation predisposes ventricular arrhythmia [1]. Predisposing factors of prolonged QT are namely as electrolyte abnormalities (e.g., hypocalcemia, hypomagnesemia & hypokalemia), acute myocardial infarction and side effect of some medicines and congenital abnormalities [2].

As a result of chronic liver injuries and release of various cytokines like IL-6, IL-7 & TNF-α gradual susceptibility to develop fibrosis and finally cirrhosis is made [3]. This disease is usually irreversible when it reaches its advanced stages and liver transplantation is unavoidable in them.

After liver transplantation in cirrhotic patients, cardiovascular abnormalities including delayed cardiomyopathy, hyperdynamic circulation and abnormalities of ventricular repolarization (diagnosed as prolongation of QT) develops of which the commonest one is a prolonged QT whose prevalence is even reported up to 56% in cirrhotic patients [4,5]. Although the main mechanism of QT prolongation in cirrhotic patient is unknown but the sympathetic hyperactivity and autonomic dys function which are usual abnormalities in liver cirrhosis are considered to be of possible mechanisms [5,6]. In other words prolongation of QT in cirrhosis is related to the pathophysiology of cirrhosis itself and not to any special predisposing factor of cirrhosis [6].

Prolonged QT can result in serious arrhythmias like VT, VF, Torsade depoints causing sudden death in both of acquired and congenital etiologies. These predisposing factors in patients with cirrhosis along with the rise of biliary salts in plasma can result in cardiac dysfunction [7].

In this study the prevalence of QT interval prolongation and its incidence in patients suffering from chronic liver disease, according to the criterions of CHILD & MELD in liver dysfunction, was assessed. Besides, the prolongation of QT in these patients was studied in respect to its prevalence, sexual differences, age variabilities, stage of liver dysfunction and different etiologies of liver injury.

MATERIALS AND METHOD:

This was conducted on 48 patients with cirrhosis as a case group and 48 persons devoid of any liver disease and cardiovascular abnormalities as the control group. Coagulation tests (including PT, INR) and biochemical blood tests (including bilirubin total, direct, AST, ALT, Alb and creatinine) were done for both case control groups and registered in their identification forms. 12 leads ECG was taken from both groups. In the medical records of patients history of encephalopathy and presence or absence of ascites based on the clinical examination of liver and its ultrasonography were studied. Patients with electrolyte abnormalities or medications affecting the cardiac rhythmand/or beta blockers were excluded from the study. Patients were divided according to the criterions of CHILD (to three groups of A, B and C) and MELD and the study was conducted. QT of patients from their ECG and the QcT according to the formula of Bazett ($QcT=QT/\sqrt{RR}$) in respect to the heart rate was calculated.

STATISTICAL ANALYSIS:

Data analysis and interpretation was performed by using the statistical analysis of χ^2, T-test and Mann–Whitney U test in the software of SPSS-16. AP ≤ 0.05 was considered statistically significant.

RESULTS

This study was conducted on 48 patients with cirrhosis and 48 healthy individuals. 34 patients were male (70.8%) and 14 were females (29.2%). Age groups above 60 years old were more prevalent in both groups and with respect to table (1) there was a significant statistical difference between the two groups (P<0.05).

Between the QT interval, QcT, Criteria of CHILD, levels of AST, albumin, creatinine, PT, INR, bilirubin in both group there was a significant difference, except for the level of albumin, these levels were reported to be more in the patients' group in comparison to that of control (P<0.05) but between the level of ALT, criteria of MELD in both groups of QT (normal & prolonged) and criteria of CHILD in both groups of QcT (normal and prolonged) in both groups of patient and control there was no statistically significant difference (P<0.05) table 1 & 2.

QcT was normal in 32 patients (66.7%) and 44 persons (91.7%) and prolonged QT was found in 16 patients and 4 persons accordingly. Encephalopathy and ascites were reported to be present in 22 patients (45.8%) and 43 patients (89.4%) respectively.

Cause of cirrhosis was reported to be autoimmune in three patients (6.2%), HCV in 17 patients (35.4%), HBV in 16 patients (33.3%) and cryptogenic in 12 patients (25%).

Table 1. Characteristics of Patients With Cirrhosis (n=48) and Controls (n=48).

	Case	Control	P value
Age (year)	63.62±12	50.85±16.9	0.001
PT	15±2.2	13±1.01	
INR	1.54±0.39	1.11±0.14	
Albumin	3.06±0.47	4.05±0.314	
Creatinine	1.34±0.78	1.03±0.52	0.025
AST	54.17±32.2	25.44±8.4	
ALT	35.27±23.7	29.56±9.41	
Bilirubin	2.62±1.34	0.86±0.25	
Ascites	43(89.6%)	-	
Encephalopathy	22(45.8%)	-	
MELD	17.6	17	
Child	8.77±1.74	5.04±0.202	0.001
A	6(12.6%)	48(100)	
B	24(50%)	-	
C	18(37.4%)	-	

QT	388.31±50.41	353.25±35.38	0.001
QcT	429.61±36.4	394.38±39.5	0.001

Table 2. Severity of liver cirrhosis

	Normal QcT	Prolonged QcT	P value
CHILD Mean	8.6±1.69	9±1.8	0.564
MELD Mean	17±5.3	17.6±5.4	0.622

DISCUSSION

In our study association between ECG, QcT prolongation was evaluated in both control and cirrhotic patients groups whose result is definitely supporting the higher prevalence of prolonged QcT in cirrhotic patients (P value 0.001) in comparison to that of control. All biochemical tests supporting the liver dysfunction (Alb, INR and PT) and also prevalence of ascites and hepatic encephalopathy was more in the group of cirrhotic against the control group as was expected to be so because of study design employed. Higher level of AST against ALT in patients with cirrhosis is probably deemed to be due to the rise of AST to ALT when liver cirrhosis generally develops. In our study although these was a significant difference in QcT between the groups of cirrhotic and controls but based on criteria of CHILD and MELD which shows the severity of hepatic dysfunction, there was no statistically significant difference between the severity of liver dysfunction and QcT. Explanations for this issue can be presented in two ways. Probably the major issue is the association between the prolonged QcT with the rise of portal pressure and portacaval gradient and QT is longer in patients with portal hypertension therefore the QcT does not have any association to liver dysfunction [1,7-9]. But a better explanation could be the insufficient volume of sample in different groups of CHILD & MELD, therefore a study with higher number of sample for the comparison of different groups of liver dysfunction is recommended.

Clinical association of QT interval in patients with cirrhosis is also in need of more evaluations and studies. Despite of reports based on the occurrenceof sudden death associated with the prolongation of QT and ventricular arrhythmia, still it is deemed that sudden death is unusual in cirrhotic patients [10,11]. Since the complications of cirrhosis are not taken to be serious therefore cardiac monitoring of patients with cirrhosis is rarely being done, even when these patients develop complications like gastrointestinal bleeding and bacterial infections. Probably in these conditions which sudden rise of sympathetic system results change for ventricular repolarizationis considered to be a life threatening condition in patients.

CONCLUSION

Based on this cohort study it seems that cardiologic evaluations in all cirrhotic patients before the prescription of antiarrhythmic medicines and/or drugs affecting the sympathetic system is necessary.

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