Section: General Medicine

Research

CORRECTED QT DISPERSION AND ITS CORRELATION WITH SEVERITY OF CHRONIC LIVER DISEASE IN COMPARISON WITH MELD-NA SCORE

S. Mahaesh[1], N. Jayaprakash[2], R. Thilakavathi[3], Haridoss Sripriya Vasudevan[2]

[1]Assistant Civil Surgeon, Department of General Medicine, Maduranthakam Government Hospital, Tamilnadu, India.
[2]Associate Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.
[3]Professor, Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, Tamilnadu, India.

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Corresponding Author:
Dr. Haridoss Sripriya Vasudevan
Email: sripriyaharidoss@yahoo.co.in
ORCID: 0000-0002-7806-8924

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Abstract

Background: ECG abnormalities, especially QT interval prolongation are common in chronic liver disease (CLD). Model for End-Stage Liver Disease-Serum Sodium (MELD-Na) score has a decisive effect on the complication grade after liver failure for Acute-On-Chronic liver failure. Present study was aimed to correlate corrected QT dispersion with severity of chronic liver disease in comparison with MELD-Na score. **Materials and Methods:** Present study was performed from January 2021 to June 2021 on 185 patients with chronic liver disease admitted in the ward. QTc dispersion and MELD-Na score calculated. In present study optimal MELD-Na cut-off was >32.14, the sensitivity and specificity for the prediction of 3-month mortality were 77.40 and 83.33%, respectively. A QTc dispersion > or = 60 ms had a 92% sensitivity and 81% specificity in predicting cardiac death, QTc dispersion in patients with diffuse coronary artery disease was significantly ($P < 0.05$) greater than in those with no disease or disease affecting one, two, or three vessels. **Result:** In present study patients with Serum Bilirubin 10 - 15 mg/dl had highest mean QTcd of 88.9 ms. Patients with Serum Bilirubin 5 - 8 mg/dl were recorded with maximum mean QTcd of 71.7 ms. Prothrombin time (PT) in range of 30 – 35 secs showed increase in QTcd. QTcd was reported to be high with increase in the INR value in our study. An increase in CLD duration increases the QTcd duration reported. MELD Na score correlation with QTcd value was found statistically significant ($p<0.05$). **Conclusion:** Corrected QT interval along with MELD-Na score were found to be good predictor of outcome in chronic liver disease in our study.

INTRODUCTION

Nowadays the incidence of liver diseases found to be increased worldwide due to modern lifestyle and food habits, increase intake of alcohol even in younger age groups. The mortality found to be in increasing trend in developing countries.[1] Nearly 1.54 BILLION people found to have chronic liver disease worldwide. Out of which two third were men and one third were women. It is one of the leading causes of mortality and morbidity.[2] Chronic liver disease (CLD) contributes about 2.2 to 2.5 % of mortality and 1.5% of disability adjusted life years. Risk factors such as obesity and alcohol consumption found to be the key risk factors. Most common cause of chronic liver disease includes viral hepatitis, alcoholic liver disease, NASH, biliary tract causes. But effective prevention of viral hepatitis, approach in reduction of alcohol consumption have widely reduced the incidence of mortality due to chronic liver disease.[1,3] Patients usually die of complications of liver disease such as hepatic encephalopathy, bleeding varices, hepatorenal syndrome, infections, but sudden death due to cardiac arrhythmia has also been frequently reported.[4] Several studies have demonstrated that QT interval in standard electrocardiogram is prolonged in patients with chronic liver disease which may lead to sudden death and poor survival of chronic liver disease patients.[5] The QT interval reflects the total duration of myocardial depolarization and repolarization. The various factors implicated in QT prolongation are increased bilirubin levels, low testosterone levels, autonomic

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neuropathy leading to decreased sensitivity of baroreceptor and heart rate variability, high sympathetic activity, electrolyte imbalance.[6] Corrected QT dispersion (QTcd) has been defined as inter lead QT interval variability (difference between maximum and minimum QT interval). Increased QTcd is a direct reflection of disparity in myocardial recovery, and determination of QTcd may help to predict arrhythmic events in chronic liver disease patients. Several studies in the past have documented prolongation of QT interval in chronic liver disease, unfortunately very few studies have been done regarding QT dispersion in chronic liver disease.[5,6] Model for End-stage Liver Disease (MELD) score has been used to rank and prioritize liver transplant (LT) candidates in the Eurotransplant region. The MELD score estimates disease severity in LT candidates based on serum creatinine, bilirubin, and the International Normalized Ratio (INR) of the prothrombin time.[7] To improve the survival prediction and allocation by the MELD score, the addition of the serum sodium (Na) concentration was proposed, as hyponatremia is an independent prognostic factor in patients with cirrhosis. In CLD like cirrhosis, portal hypertension leads to systemic vasodilatation, secondary neurohormonal compensation and less renal excretion of solute-free water. The severity of portal hypertension is inversely related to the serum Na concentration. Clinically, Na levels influence the outcomes of LT candidates before and possibly even after LT. MELD-Na score has been used to predict the severity of liver disease.[8,9] Present study was aimed to compare the effectiveness of MELD-Na score and Corrected QT dispersion in determining the severity of chronic liver disease.

MATERIALS AND METHODS

A prospective cross sectional study was carried out at Department of General Medicine, Government Stanley Medical College and Hospital, Chennai, South India. Present study was performed from January 2021 to June 2021. In our study 185 CLD patients (n=185) were enrolled. Written consent and Institutional ethical committee approval taken before start of the study

Materials

Questionnaire with Basic demographic details of the patient such as name, etc. Laboratory investigations, ECG, Echocardiogram, USG Abdomen and Pelvis are required for the study.

Methodology

QTc dispersion is calculated from the ECG and MELD - Na score calculated for the eligible patients with chronic liver disease admitted in the general medical wards.

Using an optimal MELD-Na cut-off >32.14, the sensitivity and specificity for the prediction of 3-month mortality were 77.40 and 83.33%, respectively. A QTc dispersion > or = 60 ms had a 92% sensitivity and 81% specificity in predicting cardiac death, QTc dispersion in patients with diffuse coronary artery disease was significantly ($P < 0.05$) greater than in those with no disease or disease affecting one, two, or three vessels.

Inclusion Criteria

Patients who have given consent for the study with chronic liver disease. Hemodynamically stable patients in Age group of more than 18 years

Exclusion Criteria

Hemodynamically unstable patients with hepatic encephalopathy, GI bleed, spontaneous bacterial peritonitis. Patients with Systemic hypertension, diabetes mellitus, drugs causing QT prolongation, structural heart disease, metabolic disturbances such as hypocalcaemia, hypomagnesemia. Patients with pre-existing arrhythmia like bundle branch block, atrial fibrillation.

Sample Size

Based on the reference study done by as per Bernardi et al[10] Total sample size was calculated as N=185

Statistical Analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean and S.D were used for continuous variables. To assess the agreement between the variables Intra Class Correlation and Pearson's correlation was used represented with Scatter plot. In the above statistical tools, the probability value 0.05 is considered as significant level.

RESULT

Present study was carried out on 185 patients with CLD. The majority of patients 50 (27%) were in age group of 31 to 40 years with mean age of 48±13 years. Male patients were much higher 135 (73%) than female patients 50 (27%) [Table 1].

Table 1: Demographic variables of patients

Variables	Frequency (Number of Patients) (N)	Percent (%)
Gender		
Male	135	73
Female	50	27
Age Group		
Up to 30 years 31 -	12	6.5
40 years	50	27.0

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41 - 50 years	46	24.9
51 - 60 years	43	23.2
61 - 70 years	26	14.1
71 - 80 years	6	3.2
Above 80 years	2	1.1

QTcd was reported significantly higher in patients with raised bilirubin indicating the severity of disease. Patients with Albumin 2.5 – 3 gm/dl had the highest increase in QTcd, followed by 3.5-4 gm/dl. Prothrombin time (PT) in range of 30 – 35 secs have an increase in QTcd but only 2 patients were available in this group. PT in range of 20 – 25 secs have a mean QTcd of 102.1 ms QTcd. The higher INR value were found with higher QTcd values in present study. The serum sodium level 130-135 was reported with highest QTcd value (Table 2). [Table 2].

Table 2: Comparison of different variables of CLD patients with QTcd

Variables	Frequency (Number of Patients)	QTcd(ms)Mean± SD
Serum bilirubin (mg/dl)		
2 - 5	64	52.3±15
5 - 8	63	71.7±31.6
8 - 10	51	67.8±30.9
10 - 15	7	88.9±37
Serum Albumin (g/dl)		
2 - 2.5	54	67.7±24.7
2.5 - 3	53	73.9±32.5
3 - 3.5	68	53.9±26.7
3.5 - 4	10	69.8±12.6
PT (sec.)		
10 - 15	74	55.8±17.6
15 - 20	69	51.6±23
20 - 25	26	102.1±24.9
25 - 30	9	94.9±13.9
30 - 35	5	106.0±0.97
35 - 40	2	106.0±1.10
INR (mg/dl)		
1 - 1.5	65	49.7±16.3
1.5 - 2	75	60.5± 26.6
2 - 2.5	17	72.5 ±17.8
2.5 - 3	16	93.0 ±22.7
3 - 3.5	3	114.0 ±0.0
3.5 - 4	9	122.9± 3.3
Serum Sodium (mmol/l)		
120 - 125	7	88.0 ±0.0
125 - 130	19	103.5± 25.0
130 - 135	108	55.8 ±26.5
135 - 140	51	65.3 ±21.2

In our study an increase in CLD duration increases the QTcd values. The 1-5 years CLD duration was found with 51ms mean QTcd whereas more than 10 years CLD duration was reported with 67ms mean QTcd. MELD Na score was evaluated with QTcd value and their correlation was found statistically significant ($p<0.05$) [Table 3]. The interclass correlation was also found statically significant ($p<0.05$) with average value of 0.36 and lower limit of 0.145 and upper limit 0.521 at 95% confidence interval [Table 4].

Table 3: Evaluation of duration of CLD with respect to QTcd

Duration of CLD (in years)	QTcd	
	Frequency (N)	Mean± SD
1 - 5 yrs	30	51.60 ±19.39
> 5 yrs	155	67.04 ±29.36

Table 4: Correlation of QTcd with MELD-Na Score

Correlation of QTcd with MELD-Na Score				
	MELD-Na Score			
QTcd	r-value	0.597		
	p-value	0.005		
	N	185		
Intra-class correlation coefficient				
Average measure	ICC	LB	UB	Sign.
	0.36	0.145	0.521	0.001

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DISCUSSION

The majority of patients 50 (27%) were in age group of 31 to 40 years with mean age of 48±13 years. Male patients were predominant 135 (73%) than female patients 50 (27%). Amanuel et al., in their study reported mean age of 42.4±13 with 67.5% male patients which similar to our study observations.[11] QTcd was reported significantly higher in patients with raised bilirubin indicating the severity of disease. It is well known fact that raised serum bilirubin concentration is associated with liver disease. Different studies have already reported serum bilirubin higher concentration with CLD. Patients with Albumin 2.5 – 3 gm/dl had the highest increase in QTcd, followed by 3.5-4 gm/dl. Yovita et al., in their investigation also reported similar findings.[12] Prothrombin time (PT) in range of 30 – 35 secs have an increase in QTcd but only 2 patients were available in this group. PT in range of 20 – 25 secs have a mean QTcd of 102.1 ms QTcd. The higher INR value were found with higher QTcd values in present study. Prothrombin is a protein made by the liver. The PT is one way of measuring how long it takes blood to form a clot, and it is measured in seconds. When the PT is high, it takes longer for the blood to clot. This usually happens because the liver is not making the right amount of blood clotting proteins, so the clotting process takes longer. A high PT usually means that there is serious liver damage or cirrhosis. In our study increase PT and INR values indicated CLD thereby high QTcd values which is comparable to earlier reported studies.[13,14] The serum sodium level 125-130 mmol/l was reported with highest QTcd value. Intractable ascites, severe hyponatremia, and decreased arterial pressure are clinical findings seen in patients with advanced cirrhosis. These conditions occur as a result of reduced solute-free water clearance.[15] According to several recent studies, hyponatremia occurring as a result of a reduced solute-free water clearance was a key prognostic factor in patients with liver cirrhosis when hyponatremia was incorporated into the MELD score.[16,17] Hyponatremia is a common abnormal finding in approximately 57% of hospitalized patients with chronic liver disease and in 40% of outpatients with liver disease.[18] In present study sodium level 130-135mmol/l showed highest QTcd values thereby indicated CLD. MELD-Na score was evaluated with QTcd value and their correlation was found statistically significant ($p<0.05$). The interclass correlation was also found statically significant ($p<0.05$) with average value of 0.36 and lower limit of 0.145 and upper limit 0.521 at 95% confidence interval. Kim et al reported comparable results in their investigation where 53% patients showed serum sodium level below 135 mmol/l of which 23% died due to cirrhosis.[19]

In our study higher CLD duration was found with increases QTcd value. The 1-5 years CLD duration was found with 51ms mean QTcd value whereas more than 10 years CLD duration was observed with 67ms mean QTcd. Puthumana et al., found observation similar to our findings where long duration liver disease was found to be associated with high QTcd values.[20]

Limitation of Study

The study design of this study was cross-sectional. So that it will be difficult to see the exact effects of independent variables on an outcome. The other limitation was less sample size of the study since it was 185.

CONCLUSION

Corrected QT dispersion along with MELD- Na score might be an additional prognostic means to identify patients with an increased mortality risk among patients with chronic liver disease. We speculate that besides the severity of cirrhosis, the evaluation of QT dispersion data in cirrhotic patients may be of greater importance in assessing life expectancy.

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