QT Interval Analysis in Patients with Chronic Liver Disease

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The prevalance of QT prolongation in chronic viral liver disease is high and the risk of complications is increased. We wanted to study the QT interval prolongation at the patients diagnosed with chronic hepatic disease and also to evaluate some of clinical and biochemical variables. We studied a cohort with 126 patients diagnosed with chronic viral hepatic diseases hospitalised to Cardiology Department, to the County Hospital of Craiova, between Octomber 2016 and January 2018. We aimed to determine the occurrence of QT interval prolongation in a large series of patients with chronic hepatic disease of viral etiology. We wanted to evaluated the QT prolongation to clinical and biochemical variables. The QT interval was measured by a standard 12-lead ECG for each patient, with prolongation defined as 460 ms. Multiple clinical and biochemical variables were evaluated including sex, age, areas (rural/urban) the frequency of arrhythmic events (PACs, PVCs, Atrial fibrillation, Bradycardia, Tachycardia), NT proBNP, Hb,uric acid, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST) , cholesterol, triglyceride, etc. The group of patients was composed by 43 woman and 83 men. From 43 women, representing 65.06% (461.56 ±42.03) and from 83 men, means 66.67% (461.14 ± 45.10) presented interval QT prolongation. Studing the distribution of hepatic etiologies we can see that 34 patients had hepatitis B, 35 patients hepatitis C, 5 patients B and C dual virus infection and 52 patients with chronic liver disease of etiology other than viral. We registered close results about QT interval prolongation on group, sex and origine group of patients. The value of QT interval to our patients was higher compared to other values recorder in other studies, at the patients with chronic hepatic disease, despide the fact we chose a higher value of QT prolongation. The highest value of QT interval was in the group of age between 60 and 69, even if in other studies we notice a prolonged QT interval at patients over 70 years old. The biological and biochemical profile of chronic hepatic disease of the subjects included in our study showed no statistical difference between male and female patients.We found a higher incidence of arrhythmic events, at patients with chronic hepatic disease of viral etiology, especially to premature atrial contraction and atrial fibrillation.We found a couple of correlation between QT interval prolongation and the evolution of chronic hepatic disease of viral etiology. It is very important to develop a strong and complex strategies to prevent and to treat the arrhythmic event presented at the patients diagnosticated with hepatic disease, because of the higher risk of developing life-threatening arrhythmias, includen sudden cardiac death.

Keywords: Hepatic disease, Arrhythmia, QT interval prolongation

Cardiovascular manifestation are related to chronic liver disease unconcerned to hepatic etiology. Three cardiovascularabnormalities remain significant in practice: prolongation of the QT interval, chronotropic incompetence and electromechanical disincronism. The QT interval defined as the time between the onset of the QRS complex and the end of the T wave may be elongated in certain situations for different factors.One of those in which QT interval is prolonged is also the chronic hepatic disease of viral etiology, a disease with increasing impact in our country and which is the subject of this study. Elongation of the QT interval is the result of abnormal myocardial repolarization and may be associated with an increased risk of heart rhythm disorders and sudden death [1].

The prolongation of QT interval is related with an higher cardiovascular risk profile.This is correlate with a strong predictor for a coronary heart disease and cardiovascular morbidity and mortality.[1]There are many studies that

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indicate that elongation of the QT interval should be considered an independent risk factor for sudden cardiac death because of the higher association with the life-threatening arrhythmias [2,3].

In patients with chronic hepatic disease,QTc interval prolongation is correlated with a high predisposition to develop abnormal heart rhythm abnormalities. For investigating these electrophysiological abnormalities a 12-leadelectrocardiogram recording, a simple and advantageous method, can determine the QT interval and the presence of any arrhythmic disorders.

Our study aims to evaluate the QT interval prolongation for the patients with chronic hepatic disease of viral etiology and its association to clinical and biochemical variables and mortality.

Experimental part

Materials and methods

In our study, we included 126 patients admitted to the County Hospital of Craiova, Cardiology Department, between October 2016 and January 2018. The main criteria in our study was the certain diagnosis of hepatic disease, which was based on the clinical examination, laboratory findings including ultrasonography and Fibroscan. We considered only patients with viral etiology, with B and C virus, due to the important prevalence of those patients in our country. The exclusion criteria were: patients with congenital long QT syndrome and patients on treatment with drugs which predispose to influence QT interval.

For determination the QT interval we used a 12 lead ECG so as to the QT interval based on Bazett's formula (QTc) was obtain by a computerized ECG machine. With the help of Bazett's formula the QT interval is measured from the start of the Q wave to the termination of the T wave and then divided by the square root of the R-R interval [4]. For diagnosing QT prolongation to our patients the reference QTc value was 460 ms.

Results and discussions

We analyzed 126 patients with chronic liver disease, female/men = 43/83. From 43 women - 65.06% (461.56 ±42.03), and 83 men - 66.67% (461.14 ± 45.10) had a prolonged QT interval (table 1). The profile of chronic hepatic disease patients included in our study showed no statistical difference between female and male patients.

From our cohort 53 subjects were coming from rural and 73 subjects from urban areas. From 53 patients from rural areas - 66.04%(460.94 ± 42.05) and from the total of patients coming from urban environment- 67.12% (461.53 ± 45.50) presented QT interval prolongation (table 1).

We clasified our sample of patients in 3 groups of age. We had 29 patients under 60 years old, 52 patients with age between 60 and 69 years old and 45 patients with age above 70 years. From these category we registered QT interval prolongation in 68.97% of patients under 60(466.83 ± 45.29) years-old, 73.33%(452.98 ± 34.33) from 60-69 years-old age group and 59.62%(467.31 ± 51.64)older than 70 years-old (table 1). The analysis of the QT interval for our patients revealed that the subgroup with patients with age above 70 years had only 59.62 % of them QT interval prolonged, despide the other subgroups which have 10% more than the others categories.

We observed that from 126 patients with chronic hepatic disease, 84 had prolongation of the QT interval. We had 10 patients with premature atrial contraction, 11 patients with premature ventricular contractions and 52 patients with atrial fibrillation from a amount of 82 patient with QT interval prolonged (table 2).

In order to assess the arrhythmic risk of patients with chronic hepatic disease with viral etiology we focused on

Grup	QT INTERVAL ± D.S.	QT INTERVAL PROLONGED
Total (126)	461.29 ± 43.91	69.77%
WOMEN (43)	461.56 ± 42.03	65.06%
MEN (83)	461.14 ± 45.10	66.67%
RURAL (53)	460.94 ± 42.05	66.04%
URBAN (73)	461.53 ± 45.50	67.12%
<60 YEARS (29)	466.83 ± 45.29	68.97%
60-69 YEARS (52)	452.98 ± 34.33	73.33%
>70 YEARS (45)	467.31 ± 51.64	59.62%

Table 1
ANALYSIS OF THE QT INTERVAL ACCORDING TO SEX, REGIONS AND AGE

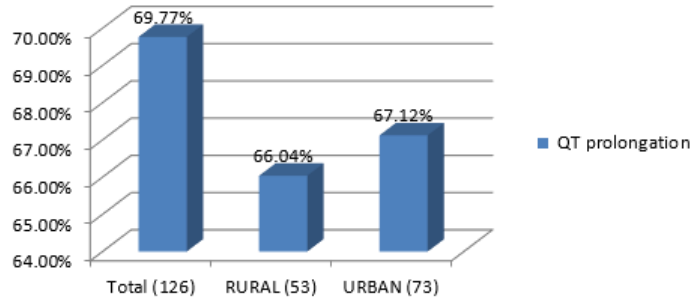

Fig. 1. QT prolongation rural/urban

Table 2
QT INTERVAL PARAMETERS AND ARRHYTHMIC EVENTS

	Total	PACs	PVC	ATRIAL FIBRILLATION
QTc INTERVAL PROLONGED	84	10 (11.90%)	11 (13.10%)	52 (61.90%)
NO QTc INTERVAL PROLONGATION	42	4 (9.52%)	11 (26.19%)	22 (52.38%)
Total	126	14 (11.11%)	22 (17.46%)	74 (58.73%)

PACs= premature atrial contractions
PVC=premature ventricular contraction

Table 3

ANALYSIS OF THE QT INTERVAL ACCORDING TO ETIOLOGY AND ARRHYTHMIC DISORDERS

CATEGORY	NR. SUBJECTS	PACs	PVCs	ATRIAL FIBRILLATION	BRADYCARDIA	TACHYCARDIA
WITHOUT VIRAL ETIOLOGY	52	5.77%	11.54 %	63.46%	11.54%	11.54%
HEPATITIS B	34	20.59 %	29.41 %	50.00%	11.75%	8.82%
HEPATITIS B PLUS C	5	0.00%	60.00 %	100.00%	20.00%	0.00%
HEPATITIS C	35	11.43 %	8.57%	54.29%	5.71%	11.43%
TOTAL	126	11.11 %	17.46 %	58.73%	10.32%	10.32%

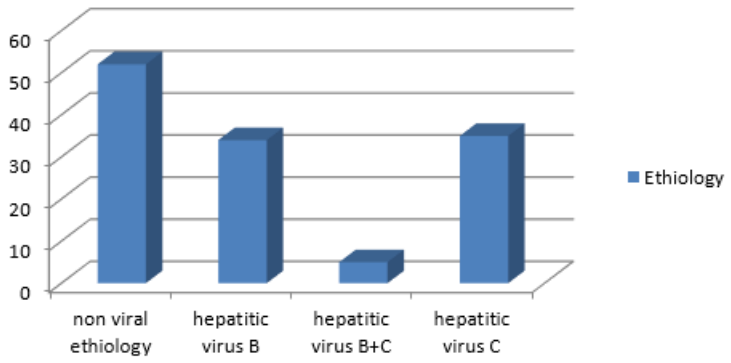

Fig. 2. Ethiology

Table 4

CORRELATIONS BETWEEN THE QT INTERVAL AND THE BIOLOGICAL AND BIOCHEMICAL PARAMETERS

	QT INTERVAL	*NT PROBNP*	*HB*	*Uric acid*	*CREATININA*	*K+*	*NA*	*Alanine aminotransferase (ALT)*	*Aspartate aminotransferase(AST)*	*Cholesterol*
INTERVAL QT										
NT PROBNP	0.08									
HB	-0.17	-0.16								
URIC ACID	0.12	0.05	-0.19							
CREATININE	0.07	-0.22	-0.24	0.27						
K+	-0.06	-0.24	0.07	0.40	0.32					
NA	-0.18	0.18	0.28	-0.10	-0.13	-0.14				
GPT/ALT	-0.06	-0.17	0.12	0.19	0.11	0.19	0.11			
GOT/AST	-0.11	0.06	0.09	-0.11	0.00	0.11	0.10	0.52		
CHOLESTEROL	-0.20	-0.07	0.29	-0.11	-0.22	-0.16	0.11	0.00	-0.13	
TRIGLYCERIDE	-0.30	-0.12	0.34	-0.07	-0.08	-0.03	0.16	0.06	-0.01	0.58

the presence of isolated premature contractions, isolated premature ventricular contractions, atrial fibrillation, bradycardia and tachycardia, arrhythmic events which can lead to sudden cardiac death.The frequency of etiologies of chronic liver disease was 34 patients with hepatitis B, 35 patients with hepatitis C, 5 patients with dual chronic B and C virus infection and 52 patients with chronic liver disease of etiology other than viral.

Pearson correlation coefficient over 0.200 shows a direct correlation between variables, and the lowest of -200 shows the inverse correlation between the variables analyzed ($p<0.5$).

Table 5

ASSOCIATIONS OF QT INTERVAL WITH CHADS-VASC SCORE

QT interval	CHADS-VASC 1 point	CHADS-VASC 2 points
Nr	5	16
Media	**470.00**	**491.25**
Dev.std.	34.84	36.70
p test Student	0.000	- NS

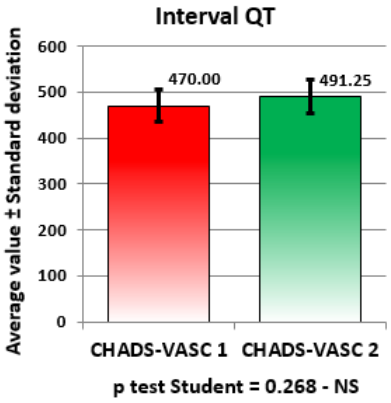

Fig. 3
Correlation between QT interval according to CHADS-VASC Score

Table 6

THE CORRELATION BETWEEN THE VALUE OF QT INTERVAL ACCORDING TO ETIOLOGY

Category	Nr.	Value of the QT interval	Standard deviation
Without Viral Etiology	52	469.48	48.44
B	34	460.44	41.99
B+C	5	505.00	18.79
C	35	443.69	33.35

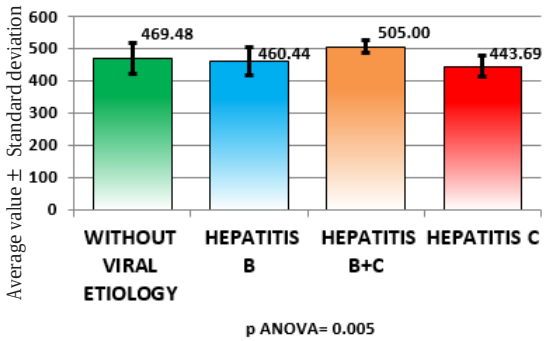

Fig. 4. Analysis of variance of the correlation between the value of QT interval according to etiology

We wanted to analize the correlation between QT interval and a couple of biochemical parameters like hemoglobine, creatinine, triglycerides, alanine amino-transferase, aspartate aminotransferase etc. After using a developed statistic analyze we can say that the values of correlation factor Pearson show us a direct correlation between trygliceride and cholesterol(p=0.58) or between Na^+ values and hemoglobine(p=0.27) . We found a inverse correltation between QT interval and the values of cholesterol(p=- 0.29) or trygliceride.(p= -0.20) (table 4).

From our lot of subjects we had 5 patients with a CHADS-VASC score of 1 point, and 16 patients with a score of 2 points. We noticed that at a bigger score, the QT interval prolongation is higher than for the others.

According to etiology of our subjects we had 34 patients with B virus, 5 patients with both B and C virus and 35 patients with C virus. We observed that having both of the viruses (B and C) interval QT is much more elongated, which can develop a higher risk of arrhythmias and to sudden cardiac death.

It is wellknow that QT interval represents a very important factor for cardiovascular diagnostic, evolution and prognostic.

Scientific studies from international literature consider that prolongation of QT is responsable for many diseases falling to sudden death [5].

Electrophysiological abnormalities are well documented in patients with chronic hepatic disease [6].

The percentage of the patients from our study was higher than other values recorder by other researchers [6] with an standard ECG although we have chosen a higher value (460ms vs.440ms) as a reference for QT interval prolongation [7, 8].

While some studies demonstrate that QTc interval increased with the age [9], we have register the highest value in our second subgroup, between 60 and 69 years (table 1).

A number of studies have revealed the correlation between QT prolongation and severity of arrhythmic risk in patient with chronic hepatic disease [1-15]. Table 2 revealed us that the frequency of arrhythmic events (premature atrial contraction and atrial fibrillation) is much higher in patients with QT prolongation than in patients without QT prolongation. However, in our study the frequency of premature ventricular contraction is the same, at the both categories.

Arrhythmic events occur frequent at patients with chronic hepatic disease [16, 17] and we found atrial fibrillation 100 % present at our patients diagnosed with dual infection (B and C viruses)(table 3.).

It has been reported that QT prolongation can lead to torsades de pointes, a life-threateningabnormal heart rhythm [18].We explored the correlation found between the length of QT interval and the biological and the biochemical parameters, which can lead to possible prolongation of QT interval (table 4).

Also we noticed that in our studied group patients with a score CHADS-VASC higher had a longer QT interval (table 5, fig. 3), than the patients with a lower score and the value of QT interval is higher when the patients have dual infection (table 6, fig. 4), similar as noticed by other researcher [19, 20].

Conclusions

The cardiovascular symptoms represent a very important factor for the evolution and for the prognosis of chronic liver disease.

The existence of QT prolongation at the patients with hepatic chronic disease worse the pharmacological answer and increase the risk of complication including sudden death.

There is very important to have a complex and permanently cardiovascular evaluation of patients diagnosed with liver disease, in order to prevent or to threat both comorbidities.

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