Evaluation of Serum Cholinesterase Level as A diagnostic Marker in Chronic Liver Disease

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Abstract

Background: Liver is the main source of Butyrylcholinesterase (serum cholinesterase). It is a non-specific cholinesterase that is reduced in patients with advanced liver diseases. Measurement of serum Butyrylcholinesterase activity serves as a sensitive indicator of synthetic capacity of the liver.

Objective: To evaluate serum cholinesterase levels in chronic liver disease patients.

Patients and methods: In this study serum cholinesterase level was evaluated in chronic liver disease patients by a colorimetric kinetic assay method. Thirty cirrhotic subjects and thirty non-cirrhotic hepatic disease subjects were compared to 20 normal individuals. This study was done at Al-Azhar University Hospitals in the period between June 2018 and August 2020.

Results: A significant decrease in serum Cholinestrease level was observed in all patients of chronic liver disease as compared to control group.

Conclusion: Serum cholinesterase is a better diagnostic and prognostic marker than the conventional liver function test that are raised in other liver disease also.

Keywords: Serum cholinesterase, Albumin, Viral hepatitis, Liver cirrhosis.

INTRODUCTION

Liver disorders are the major leading cause of morbidity and mortality worldwide. Biochemical tests for the assessment of liver function (commonly referred to as liver function tests) includes measurement of serum total bilirubin, serum aspartate and alanine transaminases serum alkaline phosphatase, serum protein and albumin *(Kumar and Keerthana, 2016).*

Liver function tests are raised in non-liver diseases, e.g. transaminase levels in heart diseases, alkaline phosphatase levels in bone diseases etc. So, there is a need for a test which should be more specific, and sensitive for diagnosis of liver disease *(Chowdhry and Kaushik, 2017).*

Cholinesterase is a family of enzymes that catalyze the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid, an essential process for the restoration of the cholinergic neurotransmission *(Gülçin et al., 2016).*

There are two types of cholinesterases, acetylcholinesterase (AChE) or erythrocyte cholinesterase, which is most concentrated in the central nervous system, striated muscle and erythrocyte membrane, and butyrylcholinesterase (BChE) or plasma cholinesterase, which is most abundant in plasma *(Fonseca et al., 2020).*

Cholinestrase has a serum half-life between 8 and 12 days*(Amin et al., 2017).*

Cholinesterase is synthesized mainly in hepatocytes and released into the blood. Cholinesterase activity is reduced in liver

dysfunction due to reduced synthesis. The predominant hepatic source of serum cholinesterase, the marked decrease in its synthesis with hepatocyte dysfunction and restoration of synthesis with hepatocyte recovery suggests that serum cholinesterase activity might be a more specific indicator of liver dysfunction than the traditional liver function test *(Roshankumar et al., 2019)*.

This study was performed to evaluate serum cholinesterase levels in chronic liver disease patients.

SUBJECTS AND METHODS

This study was done at Al-Azhar University Hospitals during the period between June 2018 and August 2020 on a total of 80 individuals (age and sex matched). Those individuals were divided into 2 groups: group1 (60 patients) and group 2 (20 control). The patients group was subdivided into two equal subgroups: *Group 1(A)* and *Group 1(B)* hepatic disease subjects. Control group were apparently healthy individuals.

Inclusion criteria: Patients presented with cirrhotic liver disease and non-cirrhotic hepatic disease aged between 40-65 years.

Exclusion criteria: Patients with congenital liver disorder, chronic malnutrition, organophosphorus poisoning, muscular dystrophy and pregnancy.

Methods:
I. Full history taking and clinical examination.
II. Sample Collection: Ten ml venous blood was withdrawn from all participants of the study (both patients and controls) ; 2ml on EDTA for routine CBC which was done using Sysmex Kx-21 automated cell counter, 2ml on Na citrate for Prothrombin time and the remaining amount in plain tube was left for clotting, and then centrifuged. Separated serum was divided in 2 aliquots, one for routine biochemical tests performed by an enzymatic colorimetric reaction using a Modular P analyzer (Roche Diagnostics) while the other aliquot was stored deeply frozen at - 20°C for estimation of serum cholinesterase**.**

Serum Cholinesterase was done using a Biolis 50i Superior analyzer by a colorimetric

kinetic assay method using a commercially available kit supplied by BEN – BIOCHEMICAL ENTERPRISE, Milano, Italy.

Statistical analysis:

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 2, IBM Corp. U.S.A. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. P-value ≤ 0.05 was considered significant.

For all analyses, Chi-squared (X^2) test, Fisher's exact test, one way ANOVA test and Kruskal Wallis test were used.

RESULTS

Our study included a total of 80 individuals. 60 patients recruited to Al-Azhar university hospitals and 20 apparently healthy individuals.

Table (1) showed the demographic characteristics of study population in control and Chronic Liver Disease patients:

- Statistically significant difference (**p-value < 0.05**) between studied groups as regard ALP.
- Statistical significant difference (**p-value < 0.001**) between studied groups as regard ALT, AST, Albmin, Bilirubin (T & C), PT & INR.
- Statistical significant difference (**p-value < 0.001**) between studied groups as regard TLC, PLTs & Hb.
- No statistical significant difference (**p-value > 0.05**) between studied groups as regard HBs Ag.
- Statistically significant difference (**p-value < 0.05**) between studied groups as regard HCV Ab.
- Statistically significant difference (**p-value < 0.05**) between studied groups as regard AFP.
- Highly statistical significant difference (**p-value < 0.001**) between studied groups as regard Cholinesterase.

Table (1): Demographic and laboratory data of all studied groups.

Groups / Parameters		Group IA (n = 30)		Group IB (n = 30)		Control (n = 20)		P-value
Sex	**Male**	18	60%	13	43.3%	12	60%	0.251
	Female	12	40%	17	56.7%	18	40%	
Age (Years)	**Mean ±SD**	56.7	± 5.7	53.9	± 4.4	55.1	± 4.2	0.091
ALT (U/L)	**Mean ±SD**	46.1	± 5.6	49.8	± 6.1	23.7	± 5.3	< 0.001
AST(U/L))	**Mean ±SD**	55.6	± 11.3	57.9	± 8.7	28.9	± 5.0	< 0.001
ALB (g\dl)	**Mean ±SD**	2.9	± 0.5	3.6	± 0.3	4.3	± 0.5	< 0.001
ALP (U/L)	**Median - IQR**	215.4 (158.8 – 278.8)		163.3 (135 – 194)		184.7 (145.8 – 220.5)		0.008
T Bil. (mg/dL)	**Median – IQR**	2.11 (1.47 – 2.4)		0.78 (0.63 – 0.9)		0.73 (0.61 – 0.87)		< 0.001
C. Bili. (mg/dL)	**Median - IQR**	0.84 (0.46 – 1.03)		0.14 (0.08 – 0.16)		0.13 (0.1 – 0.16)		< 0.001
PT (sec)	**Mean ±SD**	16.8	± 1.2	12.4	± 0.3	12.1	± 0.2	< 0.001
INR	**Mean ±SD**	1.7	± 0.2	1.0	± 0.0	1.0	± 0.0	< 0.001
TLC (x10ˣ3/ul)	**Mean ±SD**	4.7	± 1.2	6.5	± 1.5	7.2	± 1.7	< 0.001
PLTs (x10ˣ3/ul)	**Mean ±SD**	117.4 (93.3 – 134)		184.8 (165.3 – 192.5)		287.8 (206.8 – 365)		< 0.001
Hb (g/dl)	**Mean ±SD**	9.7	± 0.8	12.0	± 1.3	13.1	± 1.0	< 0.001
HCV Ab	**Negative**	4	13.3%	1	3.3%	20	100%	< 0.001
	Positive	26	86.7%	29	96.7%	0	0%	
HBs Ag	**Negative**	26	86.7%	28	93.3%	20	100%	0.210
	Positive	4	13.3%	2	6.7%	0	0%	
AFP (IU/ml)	**Mean ±SD**	31.9 (2.9 – 11.1)		2.66 (1.77 – 3.4)		2.6 (1.65 – 3.35)		< 0.001
Cholinesterase (U/L)	**Mean ±SD**	2036.0	± 342.0	3643.3	± 400.2	7507.2	± 1249.1	< 0.001

DISCUSSION

This study showed that Serum Cholinesterase level markedly decreased in patients with liver cirrhosis followed by patients with chronic hepatitis when compared with controls. The difference in the mean was highly statistically significant.

The results of this study were matched with that of *Chowdhry (2014)* who found that serum cholinesterase levels were found to be significantly decreased in majority of cases of liver disease. Mean serum cholinesterase level was very much lowered in cirrhosis patients as compared to other liver diseases.

Also, this study was consistent with the study done by *Abbas and Abbas (2017)* who found that mean serum cholinesterase decreased with reduced hepatic reserves. Cholinesterase levels predict survival in patients with parenchymal cirrhosis, distinguish between liver disease and non-liver disease aberration in liver function tests and differentiate cirrhosis from non-cirrhosis.

However, *Dhungana (2014)* found that butyrylcholinesterase (BChE) level markedly decreased in carcinoma of liver followed by cirrhosis of liver, infective hepatitis, obstructive jaundice when compared with controls. The difference in the mean was statistically significant. Regarding liver diseases, a decreased BChE activity reflects hepatocellular impairment; similarly, recovery was evidenced by a gradual increase of BChE levels.

However, *Gokani et al. (2014)* found that, the difference between the mean serum cholinesterase activity of liver diseases and control group was statistically significant with 90% sensitivity and 100% specificity, suggesting that reduced serum cholinesterase activity strongly indicate liver dysfunctions. Morever, *Ramachandran et al. (2015)* found that median serum ChE in cirrhotics was 1590 IU/L compared to controls 7886 IU/L, p<0.001. Furthermore, *Meng et al. (2013)* showed that the level of cholinesterase is closely correlated with the damage severity of liver

cells and may respond to the liver reserve function of cirrhotic patients.

CONCLUSION: There is a strong relationship between lower level of serum cholinesterase in patients with more advanced disease, indicating that reduced serum cholinesterase level is most likely the result of reduced of synthesis from hepatocytes. Cholinesterase can be used as a routine diagnostic test besides other liver function tests for investigation of liver disorders and a prognostic parameter in patients with liver cirrhosis.

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تقييم مستوى الكولين استراز فى المصل كدلالة تشخيصية
فى أمراض الكبد المزمنة

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خلفية البحث: يعتبر الكبد هو المصدر الرئيسي لتصنيع الكولين استراز، لذلك هناك ارتباط بين مستوى الكولين استراز فى المصل وقدرة الكبد على أداء وظيفته التصنيعية حيث ينخفض مستوى الكولين استراز فى المصل فى المرضى الذين يعانون من أمراض الكبد المزمنة، كما ان درجة إنخفاض مستوى الكولين استراز فى المصل تتناسب طرديا مع درجة الضرر الذى لحق بالكبد.

الهدف من البحث: تقييم مستوى الكولين استراز فى المصل كدلالة تشخيصية فى أمراض الكبد المزمنة.

المرضى وطرق البحث: تم أخذ عينات الدم من ستين مريض بأمراض الكبد المزمنة المحجوزين بقسم الباطنة العامة بمستشفى الحسين الجامعى، فى الفترة من يونيو ٢٠١٨ إلى أغسطس ٢٠٢٠ ، وتم فصل المصل وإستخدامه لتحليل مستوى الكولين استراز في مصل الدم.

النتائج: وجد إختلاف ذو قيمة إحصائية بين المجموعات فيما يخص الكولين استراز، وكانت النتائج طبيعية للمجموعة الضابطة أما المرضى فكان لديهم إنخفاض فى مستوى الكولين استراز.

الاستنتاج: يعتبر قياس مستوى الكولين استراز فى المصل فى أمراض الكبد المزمنة علامة تشخيصية وإنذارية أفضل من اختبارات وظائف الكبد التقليدية التي ترتفع في أمراض أخرى.