
Serum Concentration of Choline Esterase in Chronic Liver Diseases

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ABSTRACT

Background: In biochemistry, cholinesterase is a family of enzymes that catalyze the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid, a reaction necessary to allow a cholinergic neuron to return to its resting state after activation. Chronic liver disease is a health problem that results in the progressive destruction and deterioration of the liver. The disease, which develops at a slow process, lasts for a long period of time; there are various types of chronic liver disease. One of them is cirrhosis of the liver.

Aim: to assess the status of Choline esterase in patients with various chronic liver diseases.

Subject and methods: the present study is a cross-sectional study at Al-Yermouk Teaching Hospital. Include measurement of serum Choline esterase in patients with different chronic liver diseases.

Results: a total of 110 patients with chronic liver diseases were involved in this study, they were classified as following:

- Patients with hepatitis G1: (n=30).
 - Patients with hepatic cirrhosis G2: (n=30).
 - Patients with hepatic carcinoma G3: (n=30).
 - Patients with hepatic carcinoma receiving chemotherapy G4: (n=30).
- A matching group of apparently healthy subjects who were included as controls G5: (n=60).

Serum choline esterase was significantly reduced in patients with chronic liver diseases as compared with the controls ($p < 0.001$) with the lowest reduction in hepatic carcinoma group (G3).

Conclusion: patients with chronic liver diseases have low level of serum choline esterase compared with controls as a part of impairment of hepatic function; however, this reduction was not severing enough to cause neuromuscular blockade, the above results were supported by the significant low level of s. choline esterase; which can be used to monitor hepatic function.

Key words: choline esterase, chronic liver diseases.

Introduction:

In biochemistry, cholinesterase (ChE) is a family of enzymes that catalyze the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid, a reaction necessary to allow a cholinergic neuron to return to its resting state after activation.¹

There are two types:

- Acetylcholinesterase (EC 3.1.1.7) (AChE), also known as *RBC cholinesterase*, *erythrocyte cholinesterase*, or (most formally) *acetylcholine acetylhydrolase*, found primarily in the blood and neural synapses. Acetylcholinesterase exists in multiple molecular forms. In the mammalian brain the majority of AChE occurs as a tetrameric (G4) form with much smaller amounts of a monomeric (G1) form.²
- Pseudocholinesterase (EC 3.1.1.8) (BChE or BuChE), also known as *plasma cholinesterase*, *butyrylcholinesterase*, or (most formally) *acylcholine acylhydrolase*, found primarily in the liver.³

The difference between the two types of cholinesterase has to do with their respective preferences for substrates: the former hydrolyses acetylcholine more quickly; the latter hydrolyses butyrylcholine more quickly.³

The half-life of pseudocholinesterase is approximately 8–16 hours. Pseudocholinesterase levels may be reduced in patients with advanced liver disease. The decrease must be greater than 75%

before significant prolongation of neuromuscular blockade occurs with succinylcholine.^{3,4}

Chronic liver disease is a health problem that results in the progressive destruction and deterioration of the liver. The disease, which develops at a slow process, lasts for a long period of time. There are various types of chronic liver disease. One of them is cirrhosis of the liver.^{4,5}

This study was conducted to assess the status of ChE in various chronic liver diseases (CLD).

Subjects & Methods:

A-Subjects

The study was a cross-sectional study carried out at Al-Yarmouk Teaching Hospital, during the period from October, 2007 till the end of September, 2008.

B. Blood samples:

Five milliliters of random venous blood were withdrawn from each patient, in supine position, without application of tourniquet. Samples were transferred into clean new plain tube, left at room temperature for 15 minutes for clotting, centrifuged, and the separated serum was transferred into Eppendorf tube and was used for measurement of ChE. The tubes were stored at -20°C until analysis, which was done within one month after collection.^{6,7}

C-Methods

Measurement of serum ChE (Butyrylcholinesterase) was done by ELISA Kits (Enzyme-linked immunosorbent assay Kits)⁷.

D. Statistical analysis:

Statistical analysis was done using Excel system version 2003 and includes descriptive statistics (mean and standard deviation) and inferential statistics (*t-test*) to test the significance of mean difference. When P-value was less than 0.05, the difference is considered statistically significant, and the difference is considered highly significant when P-value was less than 0.001.

Results:**A-Subjects:**

A total of 120 patients with CLD were enrolled in this study: Thirty of them (G1) were infected with viral hepatitis (B or C): age range was 32-45 years, mean age $\pm$ SD was 37 ± 4.8 years; equal sex distribution; total serum bilirubin (TSB) ranges between 17-25.5 $\mu\text{mol/L}$, mean TSB $\pm$ SD was 20.2 ± 3.3 $\mu\text{mol/L}$; other 30 patients (G2) were complaining from hepatic cirrhosis: age range was 38-56 years, mean age $\pm$ SD was 52 ± 8 years; equal sex distribution; total serum bilirubin (TSB) ranges between 23.5-28.2 $\mu\text{mol/L}$, mean TSB $\pm$ SD was 24.1 ± 3.5 $\mu\text{mol/L}$; the remaining 60 patients were suffer from hepatic carcinoma: thirty of them (G3) were newly diagnosed their age range was 48-61 years, mean age $\pm$ SD was 54 ± 6 years; equal sex distribution; total serum bilirubin (TSB) ranges between 20.8-47.4 $\mu\text{mol/L}$, mean TSB $\pm$ SD was 40.9 ± 13.6 $\mu\text{mol/L}$, 30 patients of them (G4) receive chemotherapy: age range was 46-55 years, mean age $\pm$ SD was 50 ± 4 years; equal sex distribution; total serum bilirubin (TSB) ranges between 21.5-38.2 $\mu\text{mol/L}$, mean TSB $\pm$ SD was 27.1 ± 6 $\mu\text{mol/L}$. These results are shown in table 1.

The study included another 60 apparently healthy subjects who serve as healthy controls (G5); they were matched with patients' groups for age and sex: age range was 30-50 years, mean age $\pm$ SD was 44 ± 5 years with equal sex distribution, TSB range was between 9.58-12.6 $\mu\text{mol/L}$, mean TSB $\pm$ SD was 10 ± 3 $\mu\text{mol/L}$ as in table 1.

Any patient with history of chronic exposure to insecticides was excluded from the study.

B-Serum Choline Esterase:

Serum ChE was significantly reduced in all patients (G1, G2, G3 & G4) compared with healthy controls (G5) [$P < 0.001$] with the lowest reduction in patients with hepatic carcinoma (G3). Moreover, serum ChE was significantly lower in hepatic carcinoma group (G3) when compared with those who receive chemotherapy (G4) [$P < 0.05$]. However, serum ChE was lower in patients with liver cirrhosis (G2) when compared to those infected with viral hepatitis (G1) but this reduction not reach to a statistical significant level [$P > 0.05$] as in Table 2.

Discussion:

The differential diagnostic importance of ChE determination in searching for and observing the course of liver diseases is emphasized in the literature within the small and large enzyme pattern. In chronic hepatitis and cirrhosis normal or almost normal values suggest a favorable prognosis. Greatly reduced ChE points to limitation of liver function and a severe form of the disease suggesting toxic influences and considerable deficiency. Rapidly falling ChE activity both in acute hepatitis and in chronic inflammations of the liver point to the danger of threatening hepatic coma.^{4,8}

Whatever the origin, only deficits of more than 50% modify significantly the metabolism of succinylcholine or mivacurium.⁸

In this study, although serum ChE was moderately decreased in CLD, it did not reach to sever reduced level that points to limitation of hepatic function and indicate a favorable prognosis. Our results are in accordance with other studies like: Lejus et al⁸, Uete et al⁹, Prellwitz et al¹⁰

In conclusion, the present study indicates the usefulness of sequential monitoring of serum choline esterase activity for assessing hepatic disease, particularly cirrhosis, and for monitoring the course of hepatic disease.

Table (1): Clinical criteria of patients' groups with Chronic Liver Diseases & Control (presented as range and mean $\pm$ SD).

Group	G1	G2	G3	G4	G5
No	30	30	30	30	60
Age / year (Mean $\pm$ SD)	37 ± 4.8	52 ± 8	54 ± 6	50 ± 4	44 ± 5
Age range (years)	32- 45	38-56	48-61	46-55	30- 50
Sex	Equal distribution				
TSB ($\mu\text{mol/L}$) (mean $\pm$ SD)	20.2 ± 3.3	24.1 ± 3.5	40.9 ± 13.6	27.1 ± 6	10 ± 3
TSB Range($\mu\text{mol/L}$)	17-25.5	23.5-28.2	20.8-47.4	21.5-38.2	9.58- 12.6

(G1): Patients with Chronic Liver Diseases (Chronic Hepatitis).

(G2): Patients with Chronic Liver Diseases (Hepatic Cirrhosis).

(G3): Patients with Chronic Liver Diseases (Hepatic Carcinoma).

(G4): Patients with Hepatic Carcinoma on Chemotherapy.

(G5): Healthy Controls.

Table (2): The mean serum Choline Esterase in different patients with chronic liver diseases and controls (presented as mean $\pm$ SD).

Variable	G1	G2	G3	G4	G5
serum Choline Esterase (IU/L)	6.5 $\pm$ 1.1*	6.3 $\pm$ 1.03*	5.8 $\pm$ 0.9*	6.3 $\pm$ 1.1	13.6 $\pm$ 3.04

(G1): Patients with Chronic Liver Diseases (Chronic Hepatitis).

(G2): Patients with Chronic Liver Diseases (Hepatic Cirrhosis).

(G3): Patients with Chronic Liver Diseases (Hepatic Carcinoma).

(G4): Patients with Chronic Liver Diseases (On Chemotherapy).

(G5): Healthy Controls.

* t-test: G1, G2, G3 and G4 versus G5, $p < 0.001$

§ t-test: G2 versus G1, $p > 0.05$, §§ t-test: G3 versus G4, $p < 0.05$

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