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CORELATIONS BETWEEN THE VALUE OF SERUM CHOLINESTERASE AND CHILD-PUGH AND MELD-NA SCORES IN CIRRHOTIC PATIENTS

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Abstract

A variety of laboratory tests are used in the evaluation of the hepatic patients. Serum cholinesterase is reduced in liver disfunction in contrast with other enzymes. The aim of this study was to assess the value of serum cholinesterase in evaluation of the liver reserve function in cirrhotic patients. A total of 70 patients were divided into 3 groups according to the Child-Pugh Score. Using corelation analysis, the correlation between serum cholinesterase and albumin and serum plasma prothrombin time was analysed. Cirrhotic patients were grouped into A, B and C grades as per Child-Pugh score.

The results showed that cholinesterase levels tend to decrease according to the Child-Pugh score. The cholinesterase correlated with the albumin serum levels, value of Child-Pugh score and MELD-Na score and didn't corelate to INR. In conclusion, correlated with the damage severity of the liver cells cholinesterase may respond to liver reserve function.

Keywords: *serum cholinesterase, liver cirrhosis, Child-Pugh Score, albumin, MELD-Na score.*

Rezumat

O multitudine de teste de laborator sunt utilizate în practică pentru evaluarea pacienților cu hepatopatii. Colinesteraza serică are un nivel scăzut în disfuncția hepatică, în contrast cu alte enzime. Scopul acestui studiu este de a stabili dacă valoarea colinesterazei serice se poate corela cu rezerva funcționala hepatică, în cazul pacienților cirotici. Un număr de 70 de pacienți cunoscuți cu ciroză hepatică au fost împărțiți in 3 grupuri, conform scorului Child-Pugh. Analiza statistică a urmărit corelațiile dintre colinesteraza serică, albumină, INR și scorurile Child-Pugh și MELD-Na. Pacienții au fost împărțiți în grupurile A, B si C conform scorului Child-Pugh.

Rezultatele au arătat că nivelul colinesterazei tinde să scadă corespunzător cu scorul Child-Pugh. Valoarea colinesterazei serice se corelează cu nivelul albuminei, valoarea scorului Child-Pugh și a scorului MELD-Na, însă nu se corelează cu valoarea INR. În concluzie, corelată cu nivelul insuficienței hepatice, colinesteraza poate estima rezerva funcționala hepatică.

Cuvinte cheie: *colinesteraza serică, ciroza hepatică, Scorul Child-Pugh, albumina, scorul MELD-Na.*



Introduction

Laboratory tests, often known as liver function tests (LFTs), are useful in the evaluation and treatment of patients with hepatic dysfunction, comprising serum aspartate and alanine transaminases, alkaline phosphatase, bilirubin and albumin[1]. These tests often reveal abnormal results in patients with clinical problems other than liver dysfunction[2]. Tests of biosynthetic capacity of the liver include serum albumin, ceruloplasmin, ferritin, alfa1-antitrypsin, lipoproteins and blood clotting factors. These substances are synthetised in the liver for transport into the circulation. Cholinesterase is synthetised mainly in the hepatocytes and is released into the blood[5].

Serum cholinesterase activity is reduced in liver dysfunction due to reduced synthesis. This contrasts with other serum enzymes associated with the clinical assessment of liver function whose activities increase because of enhanced release from their cellular sources following cell membrane damage[3].

In gastroenterology, the Child-Pugh score (also known as the Child-Turcotte-Pugh score) is used to assess the prognosis of chronic liver disease, mainly cirrhosis. Although originally used to predict mortality during surgery, the Child Pugh score is now used to predict prognosis as well as the required strength of treatment, and the necessity for liver transplantation. As two main clinical measures in Child-Pugh score, serum protein and blood-clotting factors are important in evaluating the liver reserve function of cirrhotic patients[4]. However, the cirrhotic patients, particularly those with Child grades B and C with ascites or haemorrhagic tendency, are usually treated with albumin or blood transfusions, which may affect the real numeric value for calculating the Child-Pugh Score[5].

Additionally, serum cholinesterase is not easily affected by this treatment. We therefore compared serum cholinesterase with the Child-Pugh score to evaluate the liver reserve function of cirrhotic patients. Moreover, since serum cholinesterase, albumin and blood-clotting factors are synthesized by the liver with different half-life[6], we also monitored the correction between cholinesterase, albumin and INR.

Patients and methods

Patients. A total of 70 patients presenting to the Fundeni Clinical Institute (Bucharest, Romania), 28 male medium age and 42 females between 2017 and 2018 were included in the present study. Inclusion criteria for the study were: a diagnosis of liver cirrhosis based on histology, clinical or ultrasonographic signs or on transient

Descriptive Statistics								
		Valid	Missing	Mean	Std. Deviation	Minimum	Maximum	
Age	female	42	0	68.357	8.150	46.000	84.000	
Age	male	28	0	63.643	12.749	33.000	82.000	

Table 1. *Demographic characteristics of the study population*

Descriptive Statistics						
	Valid	Missing	Mean	Std. Deviation	Minimum	Maximum
Age	70	0	66.471	10.416	33.000	84.000
Sex	70	0				
Albumin	70	0	3.471	1.046	1.800	5.200
Cholinesterase activity	70	0	6462.871	2651.086	1131.000	11982.000
Child Pugh Score	70	0	7.157	3.264	5.000	16.000
MELD-Na Score	70	0	11.129	7.089	6.000	32.000
Total Bilirubin	70	0	2.572	5.592	0.270	30.900
Encephalopathy grade	70	0	0.371	0.705	0.000	2.000
Ascites grade	70	0	0.300	0.667	0.000	2.000
Creatinine	70	0	0.950	0.402	0.400	3.300
ALAT	70	0	63.029	38.464	11.000	190.000
INR	70	0	1.243	0.434	0.890	3.010
Na	70	0	137.971	5.217	122.000	147.000
Hb	70	0	13.523	2.261	3.500	17.200
PLT	70	0	176.443	75.188	31.000	348.000
Leu	70	0	6.599	2.473	3.100	18.000

Note. Not all values are available for Nominal Text variables.
Table 2. *Clinical and laboratory characteristics of the study population*



elastography (FibroScan, Echosens, Paris, France).

Exclusion criteria were history of albumin or blood transfusion in the last 4 weeks prior to enrolment, clinical evidence of variceal bleeding at enrolment, history or clinical evidence of hepatocellular carcinoma and history of liver transplantation. Informed consent was obtained from patients included in the study.

Measurement of biochemical serum markers. Blood samples were collected with minimal venostasis. Serum was obtained from clotted blood by centrifugation within 1 h from sampling. LFTs comprising serum albumin and prothrombin time (INR) were carried out. Serum cholinesterase activity was determined using a chemiluminescent method using a Cobas e601 Roche automatic analyser in 2 hours of sample separation.

Statistical analysis. Database management and statistical analysis were performed using JASP 0.16.3 Software for Windows11. Descriptive results were expressed as the mean ± standard deviation (SD) or number (percentage) of patients with a condition. Multiple comparisons for the ANOVA test were used to compare the mean data. The Pearson correction test was applied for comparison of cholinesterase, albumin and serum prothrombin times (INR). The tests were two-tailed and $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 70 patients mean age 66.47±10.41 years were included. 28 patients were male with a mean age of 63,64±12,74 Years and 42 females with a mean age of 68.35±8,15 years. The main demographic data of the patients are summarized in Table 1 and the clinical and laboratory data in Table 2. Child-Pugh class A group was present in 43 patients (61,42%), class B in 13 patients (18,57%) and class C in 14 patients (20%) (Table 3).

Serum cholinesterase in various Child-Pugh score groups. The cirrhotic patients were strictly grouped into A, B and C groups, based on their Child-Pugh score. The results showed that serum cholinesterase tended to decrease significantly in the three grades: Child A (8055.465±1709.092U/l), Child B (5415.769±1109.270 U/l) and Child C (2543.643±838.512 U/l) (Table 4). Difference between the mean serum cholinesterase activity in the Child A, B and C groups was statistically significant, as was the difference between the mean values for the Child B and C groups (Table 3, Figure 1, Figure 2).

Correlation between the serum cholinesterase, albumin and INR. Cholinesterase was

Descriptive Statistics			
	Cholinesterase activity		
	A	B	C
Valid	43	13	14
Missing	0	0	0
Mean	8055.465	5415.769	2543.643
Std. Deviation	1709.092	1109.270	838.512
Range	6719.000	2950.000	2820.000
Minimum	5263.000	4342.000	1131.000
Maximum	11982.000	7292.000	3951.000

Table 3. *Cholinesterase activity in the Child-Pugh groups of cirrhotic patients*

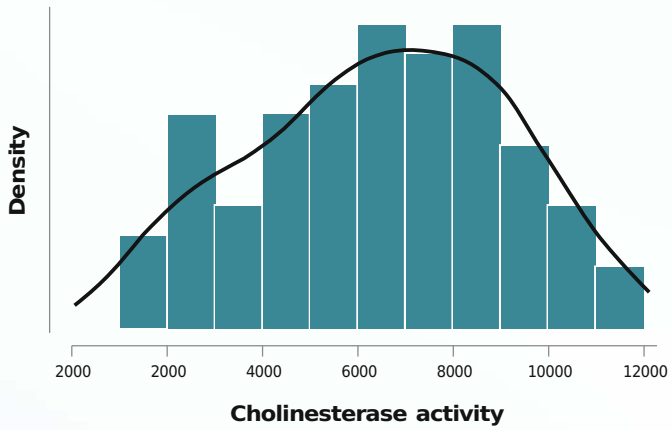


Figure 1. *Distribution Plots of cholinesterase activity*

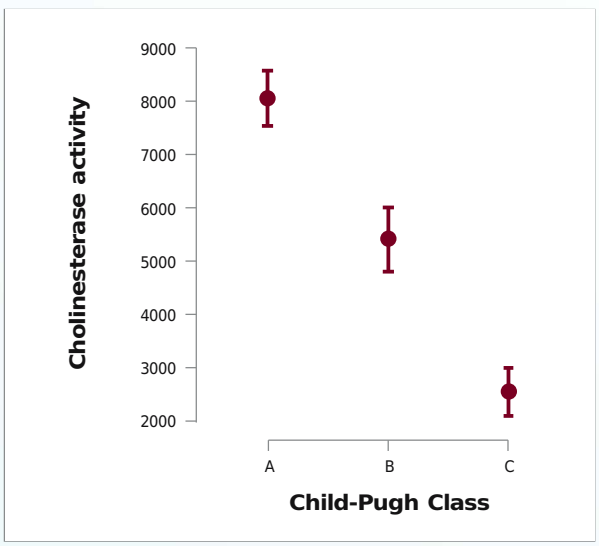


Figure 2. *Interval plots*



positively correlated with albumin (r=0.633, P<0.001) and negatively correlated with INR (r=-0.404, P<0.001) in the cirrhotic patients, confirming that those substances were synthesized in the liver and reduced in the liver disfunction due to reduced synthesis. Cholinesterase and INR (r=-0.404, p=0.001) have a negative strong correlation. Albumin and INR (r=0.782, p=0.001) have a strong positive correlation (Table 4, Table 5, Table 6).

Correlation between the serum cholinesterase, Child-Pugh Score and MELD-Na. Cholinesterase and Child-Pugh Score have a negative, strong correlation (r =-0.696, p =0.001). Cholinesterase and MELD-Na score (r =-0.548, p =0.001) have the same negative strong correlation. Between the Child-Pugh score and MELD-Na score (r =-0.783, p =0.001) we have a strong significative correlation that validates the data (Table 4, Table 5, Table 6, Table 7).

Discussion

In biochemistry, cholinesterase is a family of enzymes that catalyses 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[7].

There are two types of cholinesterases: acetylcholinesterase (AChE), also known as RBC and erythrocyte cholinesterases or acethylcholine acetylhydrolase, found primarily in the blood and neural synapses. AchE exists in various molecular forms. In the mammalian brain the majority of AChE occurs as tetrameric, G4 form. Pseudocholinesterase, also termed as plasma cholinesterase (BCHE), butyrylcholinesterase or acylcholine acylhydrolase, is found primarily in the liver[8,9]. Estimation of the level of activity of the cholinesterase found in serum was first suggested by McArdle in 1940[10], as a useful means for differentiating hepatic from post hepatic jaundice.

The evidence which has accumulated suggests that cholinesterase activity is an assessment indicator for liver function in patients with liver disease. In China, cholinesterase has been included in scores to distinguish hepatitis severity by society of liver disease[11].

However, few studies are available regarding the value of cholinesterase in evaluating liver reserve function in cirrhotic patients. The Child-Turcotte-Pugh scoring system is the first of its kind in stratifying seriousness of end-stage liver disease, mainly cirrhosis[12]. In our study 70 patients were grouped into A, B and C grades, as per Child-Pugh score. The results show that cholinesterase tended to significantly decrease in the three grades. In the Child A group, the value of serum cholinesterase was 8055.46U/l with a SD

Related pairs	Correlation index	P-value
BCHE: Alb	r=0.153	0.328
BCHE: INR	r=-0.027	0.862
Alb: INR	r=-0.114	0.357
BCHE, cholinesterase; Alb, albumin; INR International Normalized Ratio		

Table 4. *Correlations between cholinesterase, albumin and INR in the Child A group of cirrhotic patients*

Related pairs	Correlation index	P-value
BCHE: Alb	r=0.881	0.001
BCHE: INR	r=0.564	0.045
Alb: INR	r=0.732	0.004
BCHE, cholinesterase; Alb, albumin; INR International Normalized Ratio		

Table 5. *Correlations between cholinesterase, albumin and INR in the Child B group of cirrhotic patients*

Related pairs	Correlation index	P-value
BCHE: Alb	r=0.169	0.564
BCHE: INR	r=-0345	0.227
Alb: INR	r=0.716	0.004
BCHE, cholinesterase; Alb, albumin; INR International Normalized Ratio		

Table 6. *Correlations between cholinesterase, albumin and INR in the Child C group of cirrhotic patients*

Related pairs	Correlation index	P-value
BCHE: Alb	r=0.663	0.001
BCHE: INR	r=-0.404	0.001
Alb: INR	r=0.782	0.001
BCHE: Child-Pugh Score	r=-0.696	0.001
BCHE: Meld NA	r=-0.584	0.001
Child-Pugh Score: Meld-Na score	r=0.783	0.001
BCHE, cholinesterase; Alb, albumin; INR International Normalized Ratio		

Table 7. *Correlations between cholinesterase, albumin and INR in all patients*



1709.09U/l, in the Child B group the mean value of serum cholinesterase was 5415.76U/l with SD of 1109.27 and in the Child C the mean value of serum cholinesterase was 2543.64U/l with a SD of 838.51U/l.

The result agrees with the findings of Gu and Zhong[13]. Their data demonstrated that the levels of cholinesterase in the three grades were: Child A (5978±535U/l), Child B (3957±454U/l) and Child C (2267±332U/l). The Child-Pugh score is calculated from the values of five clinical measures of liver disease, among which ascites and encephalopathy are subjective measures[14]. Liver cirrhosis is classified into Child-Pugh class A-C, employing the added score from above. Compared with the Child-Pugh score, cholinesterase has the advantage that is easier and more objective in evaluating the liver reserve of cirrhotic patients.

The liver performs an important role in protein biosynthesis. Cholinesterase, albumin and blood-clothing factors are synthetised in the liver than transported into the circulation. Thus, liver function tests include cholinesterase, albumin and prothrombin time (INR) and may provide useful information concerning the state of a cirrhotic patient´s liver. In our study, in cirrhotic patients, cholinesterase was positively correlated with albumin and negatively corelated with INR, confirming that those substances were synthesized by the liver and reduced in liver disfunction due to reduced synthesis. In decompensated cirrhotic patients, albumin and blood transfusions are usually used, which may affect the real numerical value to calculate the Child-Pugh score[15] If surgery is needed as a treatment the risk calculated on the Child-Pugh score may be inaccurate[16]. In their study, Gu and Zhong[13] demonstrated that three cirrhotic patients (two Child B and one Child A score patient) suffered hepatic encephalopathy following portal azygos disconective operation, with cholinesterase levels of under 2000U/l.

Thus, those authors suggested that cirrhotic patients with cholinesterase <2000U/l may have higher risk for liver failure, if undergoing abdominal surgery. Thus, the combination of Child-Pugh score may be more subjective and accurate in evaluating the liver reserve function of cirrhotic patients, which is useful for surgeons to decide on surgery timing.

Conclusions

Findings of the present study have demonstrated that the level of cholinesterase is closely correlated with the damage severity of the liver cells and may respond to the liver reserve function of cirrhotic patients. Compared with the Child-Pugh score and MELD-Na score, serum cholinesterase is less

complex and not easily affected by treatment for decompensated cirrhosis or other disease. The combination of cholinesterase with Child-Pugh score or MELD-Na score may be more subjective and accurate in evaluating the liver reserve function of cirrhotic patients.

Conflict of interest: none

References

1. Fanping M, Xiaojuang Y, Xuemei M, Xiao-Dong G, Bo J, Hanwei Li. Assesment of the value of serum cholinesterase as a liver function test for cirrhotic patients. Biomedical reports. Beijing: Pathological Diagnosis and Research Center, 2013, pp. 265-268.

2. RS, Weisinger. Laboratory tests in liver disease and approach to the patient with abnormal test. Goldman L. and Bennett. In Cecil Textbook of Medicine. JC(eds.) 21st edition. Philadelphia: WB Saunders, 2000, pp. 775-777.

3. Zhou X., Tu ZG. Clinical Biological Chemical and Biological Chemical Inspection 3rd edition. Beijing: People's Medical Publishing House, 2003, pp. 325-328.

4. KariyoneK, Shimatani Y, Kurihara T, Fujita Y, Uesugi M. Establishing indicators for Cholinergic crisis. Rinso: Byori, 2010, pp. 972-978.

5. Lu Z, Zhong NS. Internal Medicine. 7th edition. Beijing: People's Medical Publishing House, 2008. p. 453.

6. Zou Z, Xin S, Li B. Relationship between cholinesterase, prothrombin activity and albumin and the pathology of the liver. Beijing: Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi, 2001.

7. Sinha SN, Keresztes-Nagy S, Frankfater A. Studies on the distribution of cholinesterase: Activity in the human and dog heart. s.l.: Pediatr Res 10, 2006.

8. Kondo M, Hada T, Fukui T. Enzyme-linked immunosorbent assay (ELISA) for aleuria aurantia lactin-reactive serum cholinesterase to diferentiate liver cirrhosis and chronoc hepatitis. s.l.: Clin Chim Acta 243, 1995, pp. 1-9.

9. AI, Ogunkeye OO and Roluga. Serum cholinesterase activity helpsto distinguish between liver disease and non-liver disease in liver function tests. Pathophysiology. 2006, pp. 91-93.

10. B, McArdle. The serum cholinesterase in jaundice and diseases of the liver. s.l.: Quart J Med, 1940, p. 107.

11. Association of Infectious and Parasitic Epidemiology Branch of Learning Branch of Liver Disease: viral hepatitis prevention and treatment plan. s.l.: China J Inter Med, 2001, pp. 62-68.

12. Wang I, Gao XI, Bay YZ. Patients with cirrhosis serum cholinesterase clinical research. s.l.: Chin J Med Guide, 2005, p. 68.

13. Gu YJ, Zhong YB. Cholinesterase determination of evaluation of patients with liver cirrhosis of the liver reserves significance. s.l.: Chin J Med Guide, 2010, pp. 649-650.

14. Prakash R, Mullen KD. Mechanics, diagnosis and management of hepatic encephalopathy. s.l.: Nat Rev Gastroenterol Hepatol, 2010, pp. 515-525.

15. Chromy V, Svachova L, Novosad L. Albumin based or albumin-linked calibration cause o positive bias in serum proteins assayed by the buiret method. s.l.: Clin Chem Lab Med, 2009, pp. 91-101.

16. Garg H, Kumar A, Garg V, Sharma P, Sharma BC, Sarina SK. Clinical profile and predictors of mortality in patients of acute-on-chronic liver failure. s.l.: Dig Liver Dis, 2012, pp. 166-171.

17. D, Vincent. Transaminases, or nithinecarbamyl transferase, arginase, cholinesterase, etarylesterase. Lyon: Lyon Med 232, 1974, pp. 267-273.