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Research Article

Serum cholinesterase as diagnostic marker of liver disease

Ruchi Gokani[*1], Pranay Jadav[2], Nadeem Shaikh[3], Rita Shah[4], Mitul Chhatriwala[5] and Bhavita Patel[6]

[1,3,5]*Resident,* [6]*Ph.D. Student,* [4] *Professor & Head, Department of Biochemistry, S.B.K.S MI & RC, Piparia, Vadodara, Gujarat*
[2]*Assistant Professor, Department of Community Medicine, GMERS Medical College, Gandhinagar, Gujarat*

***Correspondence Info:**
Dr. Ruchi Gokani
Resident,
Department of biochemistry,
S.B.K.S MI & RC, Piparia, Vadodara, Gujarat
E -mail: dr.ruchi135@gmail.com

Abstract

Background: Liver disease is leading cause of morbidity and mortality worldwide. Cholinesterase is a family of enzymes that catalyse the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid. It is an enzyme synthesized by hepatocytes and its serum levels reflect the synthetic function of liver.

Objectives: To estimate serum cholinesterase in liver disease patients and to compare serum cholinesterase level with other liver function tests like SGOT, SGPT, ALP and Bilirubin levels.

Methodology: The present cross sectional study was conducted at the Biochemistry department of tertiary care institute. Thirty patients with liver disease were included in the group A and 30 healthy patients not having liver disease were enrolled in group B as control .Serum cholinesterase and Liver Function Tests were estimated in all participants.

Results: The levels of cholinesterase were significantly lower in liver disease patients. Serum cholinesterase was 3424.77 ± 2149.30 in group A vs.7320.77 ± 1577.26 in group B ($P<0.05$). It is 90% sensitive and 100% specific.

Conclusion: From the present study it is concluded that serum cholinesterase can serve as better diagnostic marker of liver disease.

Keywords: Serum cholinesterase, Liver Function Test, Sensitivity.

1. Introduction

Liver is the largest vital organ in our body. As liver has wide range of functions it is prone to many diseases which are very commonly seen in India. Liver disease is any disturbance of liver function that causes illness. It is also referred to as hepatic disease[1]. It is 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 aspartate and alanine transaminases, serum bilirubin, serum albumin, serum protein and alkaline phosphatase but these tests are often abnormal in patients with clinical problems other than liver dysfunction[2]. The activities of serum transaminases may be raised due to increased release from non-liver tissue sources in various pathologies. Increased serum alkaline phosphatase activity may result from physiological or pathological enzyme production and release from non-liver tissue sources. Serum bilirubin may be raised because of increased erythrocyte breakdown rather than because of failure of hepatic clearance. Albumin concentration may be reduced for reasons other than failure of liver synthesis[3]. As a result, none of these tests can individually confirm liver dysfunction. Therefore there is a need for a test which should be specific as well as sensitive for liver diseases. Cholinesterase is a family of enzymes that catalyse the hydrolysis of the neurotransmitter acetyl choline into choline and acetic acid. The 2 types of cholinesterase found in the human blood are acetyl cholinesterase ("true" cholinesterase) in red cells and butyryl cholinesterase (non-specific, pseudo cholinesterase) in serum[4].

Cholinesterase (ChE) is synthesized mainly in hepatocytes and released into the blood. Serum ChE activity is reduced in liver dysfunction due to reduced synthesis[5]. 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 tests[6].

The present study was conducted to estimate serum cholinesterase in liver disease and to compare it with other liver function tests.

2. Material and Methods

2.1 Study setting & study type

The present cross sectional study was conducted at the Biochemistry department of Dhiraj Hospital, Piparia, Vadodara after approval from institutional ethical committee.

2.2 Study participants & study period

During August 2014 patients having liver diseases in the age group of 20-70 years of either sex attending the OPD or admitted in ward were included in Group A or case group and Healthy subjects without liver disease were enrolled in Group B or control group.

2.3 Inclusion criteria

Patients with any liver disease (any four of SGPT, SGOT, ALP, Bilirubin, albumin were abnormal) like hepatitis, liver cirrhosis, jaundice, liver abscess were included in this study**.**

2.4 Exclusion criteria

The patients with age <20 or >70 years, having acute infection, chronic malnutrition, poisoning from organophosphates were excluded. Females having pregnancy or using oral contraceptive pills were excluded from the study.

2.5 Sample size and sampling

Purposively 30 patients with liver disease were included in the group A and 30 healthy patients not having liver disease were enrolled in group B.

2.6 Data collection

Written consent was taken from all participants before entering in the study. First brief socio demographic information from all participants was collected. Blood samples of participants were taken from cubital vein and collected in plain tubes. Serum Cholinesterase (reference range:4850-12000U/L) was estimated by enzymatic method[7] on Erba semi auto analyzer. Total bilirubin (reference range:0.2 – 1.0 mg/dl)and direct bilirubin(reference range:0.1 – 0.4 mg/dl) were estimated by diazo method[8], Total Protein (reference range:6 – 8 gm/dl)was measured by Biuret method[9] and Albumin (reference range:2.7 – 5 gm/dl) by BCG method[10] on Erba EM-200 fully automated analyzer. Serum Glutamic Oxaloacetic Transaminase (SGOT) (reference range: up to 40 U/L), Serum Glutamate-Pyruvate Transaminase (SGPT) (reference range: up to 40 U/L)[11] and Alkaline Phosphatase (ALP) (reference range: Adult: 80 – 290 U/L, Child: 245 – 770 U/L)[12] were estimated by enzymatic method on Erba EM-200 fully automated analyzer.

3. Statistical Analysis

The data were entered in Microsoft excel 2007. Statistical analysis was done by Epi info 7. Continuous variables were expressed as mean ± Standard Deviation and categorical variables were expressed as percentages. Statistical analysis of different biochemical parameters was performed by Students' *t*-test. Chi square or fisher's test were used for categorical analysis accordingly. A value of $p< 0.05$ was considered as statistically significant.

4. Results

The mean age in both the groups was 50.50 ± 12.54. Out of 30 subjects in group A 24 (80%) were male and 6 (20%) were female, in group B 25 (83.3%) were male and 5 (16.7%) were female. Out of 30, 14(46.7%) were taking alcohol in group A and 8(26.7%) in group B. Serum cholinesterase level were found to be low in 27(90%) patients in group A and normal in 3(10%) patients while in group B it was normal in 30(100%) persons. (Table -1)

Table 1: Socio demographic information of the both groups

Characteristics of participants	Group A-Cases (n=30)	Group B- Control (n=30)
Age distribution		
20-30 years	2 (6.7%)	2 (6.7%)
31-40 years	4 (13.3%)	4 (13.3%)
41-50 years	7 (23.3%)	7 (23.3%)
51-60 years	10 (33.3%)	10 (33.3%)
61-70 years	7 (23.3%)	7 (23.3%)
Sex		
Male	24 (80%)	25 (83.3%)
Female	6 (20%)	5 (16.7%)
Literacy		
Literate	22 (73.3%)	24 (80%)
Illiterate	8 (26.7%)	6 (20%)
Marital status		
Married	28 (93.3%)	29 (96.7%)
Unmarried/single/divorced	2 (6.7%)	1 (3.3%)
Smoking		
Yes	11 (36.7%)	9 (30%)
No	19 (63.3%)	21 (70%)
Drinking alcohol		
Yes	14 (46.7%)	8 (26.7%)
No	16 (53.3%)	22 (73.3%)
Serum cholinesterase level		
Low	27 (90%)	0 (0%)
Normal	3 (10%)	30 (100%)
High	0 (0%)	0 (0%)

In the present study the level of cholinesterase were significantly lower in liver disease patients, mean being 3424.77 U/L as compared to controls. (Table 2).Total bilirubin , direct bilirubin and indirect bilirubin were significantly higher in Group A as compared to Group B. SGPT, SGOT and ALP were also significantly higher in patients with liver disease as compared to control (Table 2). Serum total protein and serum albumin were significantly lower in cases compared to controls. (Table -2)

Table 2: Comparison of Means of laboratory parameters in both groups

Variables	Group A-Cases (n=30)	Group B- Control (n=30)	P value
Serum cholinesterase	3424.77 ± 2149.30	7320.77 ± 1577.26	<0.05
Total bilirubin	4.33 ± 3.40	0.78 ± 0.50	<0.05
Direct bilirubin	2.82 ± 2.57	0.40 ± 0.38	<0.05
Indirect bilirubin	1.50 ± 1.17	0.39 ± 0.24	<0.05
SGPT	99.96 ±93.33	37.73 ± 35.15	0.002
SGOT	88.90 ± 76.36	43.30 ± 34.58	0.005
ALP	313.20 ± 97.15	206.13 ± 73.06	<0.05
Total protein	5.29 ± 1.09	6.22 ± 0.98	0.001
Serum albumin	2.66 ± 0.79	3.46 ± 0.81	<0.05

(SGOT - Serum Glutamic Oxaloacetic Transaminase, SGPT - Serum Glutamate Pyruvate Transaminase, ALP - Alkaline Phosphatase)

Out of 30 cases of liver disease patients 27 cases had cholinesterase values less than 4850 U/L. While in control group all the participants had values above 4850 U/L. 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.

Out of 30 cases of liver disease patients 25(83.33%) cases had bilirubin values more than 1.0 mg/dl. While in control group 5 (16.66%) had bilirubin values more than 1.0 mg/dl, showing sensitivity and specificity of 83.33%. (Table-3)

Table 3: Individual sensitivity and specificity of Biochemical markers of Liver disease

Variables	Liver disease (n=30)	No liver disease (n=30)	Sensitivity	Specificity	p-value
Serum cholinesterase					
< 4850	27	00	90%	100%	<0.001
≥4850	03	30			
Total bilirubin					
> 1.0 g/dl	25	05	83.33%	83.33%	<0.001
≤1.0 g/dl	05	25			
SGPT					
>40 U/L	24	04	80%	86.67%	<0.001
≤40 U/L	06	26			
SGOT					
>40 U/L	22	10	73.33%	66.67%	0.004
≤40 U/L	08	20			
ALP					
>290 U/L	18	05	60%	83.33%	0.001
≤290 U/L	12	25			
Total protein					
<6.0 g/dl	23	12	76.67%	60%	0.008
≥6.0 g/dl	07	18			
Serum albumin					
<2.7 gm/dl	20	05	66.67%	83.33%	0.0002
≥2.7 gm/dl	10	25			

(SGOT - Serum Glutamic Oxaloacetic Transaminase, SGPT - Serum Glutamate Pyruvate Transaminase, ALP - Alkaline Phosphatase)

Out of 30 cases of liver disease patients 24(80%) cases had SGPT values more than 40 mg/dl. While in control group 4(13.33%) had SGPT values more than 40 mg/dl, showing sensitivity 80% and specificity of 86.67%.Out of 30 cases of liver disease patients 22(73.33%) cases had SGOT values more than 40 mg/dl. While in control group 10(33.33%) had SGOT values more than 40 mg/dl, showing sensitivity 73.33% and specificity of 66.67%. Out of 30 cases of liver disease patients 18(60%) cases had ALP values more than 290 U/L. While in control group 5(16.66%) ALP values more than 290 U/L, showing sensitivity 60% and specificity of 83.34%. (Table-3)

Out of 30 cases of liver disease patients 23(76.66%) cases had protein values less than 6 g/dl. While in control group 12(40%) had protein values less than 6 g/dl, showing sensitivity 76.67% and specificity of 60%.Out of 30 cases of liver disease patients 20 (66.66%) cases had albumin values less than 2.7 g/dl. While in control group 5(16.66%) had albumin values less than 2.7 g/dl, showing sensitivity 66.67% and specificity of 83.33%. (Table-3)

5. Discussion

Estimation of the level of activity of the cholinesterase found in serum was first suggested by McArdle (1940)[13], 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.

Present study was conducted to find out the effectiveness of serum cholinesterase enzyme to correctly diagnose liver diseases. Serum cholinesterase appears to originate in the liver and is closely associated with the synthesis of serum albumin[14,15,16]. It has been shown that even very low pre-liver transplant serum cholinesterase levels improve by second week after a successful liver transplantation, thus confirming the hepatic origin of this enzyme. It is synthesized mainly in hepatocytes and released into the blood. Serum ChE activity is reduced in liver dysfunction due to reduced synthesis; in contrast to other serum enzymes associated with the clinical assessment of liver function whose content increases a result of increased release from their cellular sources following cell membrane damage[5].

Data from study conducted by Khan[17] pointed that 100% patients with cirrhosis had lower serum cholinesterase level and he also showed that there was close relationship between the severity of cirrhosis and level of serum cholinesterase enzyme.

Our study is in accordance with the study of Ogunkeye[18], he also reported lower level of serum cholinesterase level in liver disease patients. William Burnett also found serum cholinesterase is useful both as a liver function test and in the diagnosis of jaundice[19].

Ramachandran *et al* found Median serum ChE in cirrhotics was 1590 IU/L (110-8143) compared to controls 7886IU/L (2022- 21673), p<0.001. Serum ChE levels below 3506 had a 98.7% sensitivity and 80.3% specificity in predicting cirrhosis found serum ChE is an excellent biomarker of cirrhosis with good sensitivity and specificity[20].

6. Conclusion

In this study comparison of serum cholinesterase levels versus conventional liver function tests was done in both groups, it is found that serum cholinesterase levels were decreased only in liver disease patients but conventional liver function tests were abnormal in both groups of patients. Serum cholinesterase had 90% sensitivity and 100% specificity and it must be added as a routine diagnostic test beside other liver function tests for investigation of liver dysfunctions. Larger sample size study should be carried out to reconfirm the conclusion.

References

1. Sheila SH, James D; 'Diseases of the Liver and Biliary System', 11th edn: 2, p.19-35.
2. Weisinger RA; 'Cecil Textbook of Medicine', 21st edn: Laboratory tests in liver disease and approach to the patient with abnormal test, p.775-777.
3. Whicher J, Spence C. When is serum albumin worth measuring? *Annals of Clincal Biochemstry* 1987; 24(6):572-580.
4. Brimijoin S, Koenigsberger C. Cholinesterase in neural development: new findings and toxicological implications. *Environ Health Perspectives*. 1999; 107(1):59–64.
5. Moss DW, Henderson AR.; 'Tietz Textbook of Clinical Chemistry', 2nd edn: p.735-89.
6. Brown SS, Kalow W, Pilz W, Whittaker M. The plasma cholinesterases: A new perspective. *Adv Clin Chem*.1981; 22:1-123.

7. Deutsche Gesselschaft Fur, KinisclieCheMie.Proposal of standard methods for the determination of enzyme catalytic concentrations in serum and plasma at 37 degrees C. I. Alkaline phosphatase (orthophosphoric-monoester phosphohydrolase, alkaline optimum, EC 3.1.3.1).Working Group on Enzymes. *Eur J Clin Chem Clin Biochem.* 1992; 30(4):247-56.
8. Winsten S., Cehelyk B.A rapid microdiazo technique for measuring total bilirubin. *Clin Chim Acta*.1969; 25(3):441-6.
9. R.D. Stricland, M.L. Freeman, F.T. Gurule. Copper binding by proteis in alkaline solution. *Anal Chem.* 1961; 33(4):545-52.
10. Doumas BT, Watson WA, Biggs HG.Albumin standards and measurement of serum albumin with bromocresol green. *Clinical Chem Acta*.1971; 31(1):87-96.
11. Bergmeyer HU, Scheibe P, Wahlefeld AW. Optimization of methods for aspartate aminotransferase and alanine transferase. *Clin Chem*.1978; 24(1):58-78.
12. Bower GN Jr., McComb RB. Measurement of total alkaline phosphatase activity in human serum. *Clin Chem*.1975; 21 (3):1988-95.
13. McArdle B. The serum cholinesterase in jaundice and diseases of the liver. *Quart J Med*. 1940; 9(1):107-27.
14. Faber M. The relationship between serum cholinesterase and serum albumin. *Acta med Scand*. 1943; 114(1):72-91.
15. Kunkel HG, Ward SM. Plasma Esterase Activity in Patients with Liver Disease and the Nephrotic Syndrome. *J Exp Med*. 1947; 86(4):325–37.
16. Svensmark O. Enzymatic and Molecular Properties of Cholinesterases in Human Liver. *Acta Physiol Scand*. 1963; 59:378–89.
17. M.G. Khan. The evaluation of serum pseudocholinesterase as a liver function test. *Ulster Med J*. 1962; 31(2): 144–152.
18. Ogunkeye OO, Roluga AI. Serum cholinesterase activity helps to distinguish between liver disease and non-liver disease aberration inliver function tests. *Pathophysiology Journal*. 2006; 13(2): 91–93.
19. William Burnett. An assessment of the value of serum cholinesterase as a liver function test and in the diagnosis of jaundice. *Gut*. 1960; 1(4), 294-302.
20. Ramachandran, J., Sajith, K. G., Priya, S., Dutta, A. K., & Balasubramanian, K. A. Serum cholinesterase is an excellent biomarker of liver cirrhosis. *Tropical Gastroenterology*. 2014; *35*(1), 15-20.