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EVALUATION OF SERUM CHOLINESTERASE LEVELS IN PATIENTS WITH CHRONIC LIVER DISEASES

Biochemistry

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ABSTRACT

Background Serum cholinesterase is an enzyme produced mainly by hepatocytes. In chronic liver disease, serum cholinesterase activity is reduced due to decreased synthesis. Although the serum albumin may be reduced in hepatic failure, it may be decreased in nephrotic Syndrome, severe malnutrition, protein losing enteropathy. The association between serum cholinesterase level and chronic liver diseases did not seek much attention. Therefore, this study was designed to explore the serum cholinesterase levels in chronic liver diseases.

Objectives To estimate the serum cholinesterase level in chronic liver disease patients and to compare the serum cholinesterase level with liver function parameters like serum Aspartate Transaminase, serum Alanine transaminase, serum Alkaline Phosphatase, serum Bilirubin, serum protein and albumin levels in chronic liver diseases.

Materials and Methods This case-control study was conducted among 102 chronic liver disease patients. Age and sex matched apparently healthy individuals were included as controls (102 individuals). Serum cholinesterase was estimated and compared with liver function test parameters. Pearson`s correlation test was done to correlate serum cholinesterase and serum albumin.

Results The mean age group of cases and controls were 53 ± 10 and 52 ± 10. The etiology of chronic liver disease was consumption of alcohol in 72.54%. The mean of serum cholinesterase in cases and controls were 2314 ± 1413 and 7883 ± 1012 respectively. Serum cholinesterase was correlated positively with albumin ($r = 0.712$, $P = 0.00$) in the chronic liver disease patients.

Conclusion Serum cholinesterase was significantly reduced in chronic liver diseases. Hence, Serum cholinesterase can also be included to analyse the synthetic capacity of liver and in the diagnosis of liver dysfunction.

KEYWORDS

Chronic Liver Disease, Nonalcoholic Fatty Liver Disease, Serum Cholinesterase, Synthetic Function.

Introduction

Cholinesterase (ChE) is an enzyme which catalyze the hydrolysis of neurotransmitter acetyl choline into choline and acetic acid [1]. The types of ChE present in our body are acetyl cholinesterase ("true" cholinesterase) in red cells and butyryl cholinesterase (pseudo cholinesterase) in serum [2]. Albumin, blood-clotting factors and pseudo cholinesterase are synthesized in the liver and transported into the systemic circulation [1]. The commonly employed liver function tests are estimation of levels of serum Alanine transaminase (ALT), serum Aspartate Transaminase (AST) and serum Alkaline phosphatase (ALP) [3], which are increased due to the release from the cell following cell membrane damage [4]. Increased ALT level does not assimilate with the extent of liver cell damage [5]. AST is expressed in increased concentration in heart compared to liver. These enzymes usually confer hepatocyte integrity or cholestasis rather than liver function [3]. Aminotransferase levels also vary according to age and sex and may increase in strenuous exercise [3, 6]. Serum ALP is increased in physiological and pathological conditions like Paget's disease, rickets, osteomalacia, hyperparathyroidism and metastatic carcinoma of bone [7]. Some drugs and herbal remedies can also alter the levels of liver enzymes [3]. Serum bilirubin is the product of erythrocyte breakdown metabolism and it may reflect the decreased hepatic clearance [8]. Although the serum albumin may be reduced in hepatic failure, it may be decreased in nephrotic syndrome, severe malnutrition and protein losing enteropathy.

Chronic Liver diseases are one of the major causes of morbidity and mortality worldwide. A variety of laboratory tests are utilized in the evaluation of patients with chronic liver diseases such as cirrhosis of liver, chronic viral hepatitis and non-alcoholic steatohepatitis. Chronic liver disease is defined as process of progressive destruction and regeneration of the liver parenchyma, leading to fibrosis and cirrhosis [9]. Chronic liver disease is not uncommonly associated with decreased synthetic function. Serum ChE activity is reduced in liver dysfunction due to decreased synthesis [1]. Its serum level reflects the synthetic capacity of liver. Some studies hypothesized that restoration of synthesis occurs when the hepatocytes are recovered [8], this highly recommends that estimation of Serum ChE might be more specific test to detect liver dysfunction. Hence the decrease and increase in the serum ChE level clearly depicts the liver damage and recovery respectively. This illustrates that serum ChE activity considered to be more pertinent to assess hepatocyte dysfunction. Previous studies studied that serum ChE had been used to analyze the liver function, particularly to assess the progression of chronic liver disease. Most patients with chronic hepatitis are asymptomatic and develop complications such as cirrhosis and hepatocellular carcinoma. Serum transaminases like AST and ALT are elevated due to increased release from non-liver tissue sources in various disorders. To our knowledge, association between chronic liver diseases and selected biochemical parameter such as ChE level did not seek much attention. Therefore, this study was designed to estimate the serum ChE level in chronic liver disease patients and compared with healthy controls and to explore the possible association between serum ChE and other liver function tests parameters like serum AST, serum ALT, serum ALP, serum Bilirubin, serum protein and albumin levels in chronic liver diseases.

Materials and Methods

This case control study was conducted at the clinical biochemistry department in collaboration with department of medicine in the tertiary care teaching hospital, Trichy. 102 chronic liver disease patients and 102 controls with no evidence of liver disease were included as cases and controls respectively. Age group of 30-70 years of both males and females were included. The period of study was 3 months. A detailed history was elicited for Co-morbid diseases, concomitant drug intake, alcoholic intake, history of viral hepatitis. Patients with chronic liver disease like cirrhosis of liver, chronic viral hepatitis and non-alcoholic fatty liver disease were included in this study. Patients with acute liver diseases, chronic malnutrition, organophosphorus poisoning, bone diseases, known cardiac diseases, terminally ill patients, females with pregnancy and those on drugs which interfere the liver function were excluded from this study. Informed written consent was obtained from each participant before entering the study. Institutional ethical committee clearance was obtained. Liver disorders were confirmed by liver biopsy and ultrasound abdomen. Under strict aseptic precautions, 5 ml of venous blood was collected for estimation of serum ChE by DTNB (5,5′-dithiobis (2-nitrobenzoic acid) method. The reference range of serum cholinesterase is 4620-11500 U/L. ALT, AST and ALP was estimated using UV kinetic method. Serum bilirubin was estimated using photometric test using diazotized 2,4-dichloroaniline.

Serum protein and serum albumin was estimated using Biuret method and Bromocresol Green method respectively. Serum ChE and the liver function tests such as AST, ALT, ALP, Bilirubin, Total protein and albumin were assayed in MINDRAY BS 420 fully automated analyzer. Instrument were calibrated before entering the study. Quality control was maintained by internal quality control and external quality assurance scheme. Laboratory technicians were double blinded regarding the study to avoid the bias. Statistical analysis was done in SPSS version 21 (Statistical Package for Social Sciences). Continuous variables and categorical variables were represented as mean ± standard deviation and percentage respectively. Serum ChE levels in cases were compared with controls by students `t` test or Chi square test. To evaluate correlations between serum ChE levels and albumin, Pearson`s correlation test was used. A value of $p < 0.05$ was considered as statistically significant.

Results

Among 102 cases, 93 cases were males and 9 were females. Among 102 controls, 92 and 10 were males and females respectively. The mean age group of cases and controls were 53 ± 10 and 52 ± 10. The aetiology of chronic liver disease was consumption of alcohol in 72.54 %. As shown in Table 1. The mean of serum ChE in cases and controls were 2314 ± 1413 and 7883 ± 1012 respectively. In this study the level of ChE was significantly lower in chronic liver disease patients when compared to controls (Table 2). ALT, AST, ALP, Total bilirubin and direct bilirubin in blood was significantly higher in cases than the controls with significant `p` value. Serum total protein and serum albumin were significantly lower in cases than the controls. Among the 122 controls, 22 individuals had elevated serum AST and ALT levels. Serum ChE was correlated positively with albumin (r = 0.712, P = 0.00) in the chronic liver disease patients.

Table 1: Sociodemographic information of both groups

Characteristics of participants	Cases (n=102)	Control (n=102)	`p` value
Age distribution	5(4.90%)	5(4.90%)	0.07
(years)	16(15.68%)	17(16.66%)	0.13
30-40	43(42.15%)	41(40.19%)	0.15
41-50	38 (37.25%)	39(38.23%)	0.13
51-60			
61-70			
Sex	93(91.17%)	92(90.19%)	0.07
Male	9(8.82%)	10 (9.80%)	0.07
Female			
Literacy	19(18.62%)	39(38.23%)	0.04
Literate	83(81.37%)	63(61.76%)	0.04
Illiterate			
Marital status	99(97.05%)	98(96.07%)	0.10
Married	3 (2.94%)	4(3.92%)	0.09
Unmarried			
Smoking	61(59.80%)	58(56.86%)	0.07
Yes	41(40.19%)	44(43.13%)	0.07
No			
Alcohol	74(72.54%)	54(52.94%)	0.01
Yes	28(27.45%)	48(47.05%)	0.01
No			

`p`<0.05 -significant

Table 2: Comparison of serum cholinesterase and other parameters between cases and controls

Variables in Serum	Cases	Controls	`p` value
Cholinesterase	2314 ± 1413	7883 ± 1012	0.0001
Total bilirubin	5.9 ± 2.7	0.71 ± 0.4	0.0001
Direct Bilirubin	2.7 ± 1.6	0.2 ± 0.1	0.0001
Indirect Bilirubin	1.7 ± 1.5	0. 4 ± 0.2	0.0001
ALT	122 ± 57	54 ± 11	0.001
AST	108 ± 51	30 ± 9	0.001
ALP	389 ± 63	114 ± 28	0.001
Total protein	5.1 ± 0.7	6.9 ± 0.5	0.01
Albumin	2.3 ± 0.8	4.6 ± 0.2	0.01

(ALT-Alanine Transaminase; AST-Aspartate Transaminase; ALP-Alkaline Phosphatase.

`p` < 0.05-significant

Table 3 Correlation between cholinesterase and albumin in the chronic liver disease patients (pearson`s correlation)

Parameters	Correlation	`p` value
Cholinesterase: Albumin	r = 0.712	P = 0.00

Discussion

This study aimed to reveal the effectiveness of serum ChE enzyme to diagnose liver diseases precisely. The result of the study proposed that ChE activity is an indicator for liver function in patients with liver disease. Among the cases, 42.15% and 37.25% belong to the age group of 51-60 and 61-70 years respectively. In this study, the mean of serum ChE level in chronic liver diseases is 2314 ± 1413 which is significantly lower than the control group. Among the liver disease patients, 59.80 % and 72.54% of liver diseases were smokers and alcoholics respectively. Serum Cholinesterase and serum albumin was correlated with `r` value of 0.712 with $p < 0.05$.

Ramachandran et al had elucidated the median of serum ChE in cirrhosis patients was 1590 U/L (110-8143) [10]. Instead of testing the entire panel of liver function tests, this single parameter can accurately depict the chronicity of liver diseases. Serum ChE synthesized in liver and it is closely associated with the synthetic capacity of the liver. Evidence also shows that serum ChE level is improved after a successful liver transplantation [10], confirms the hepatic origin and it reflects the specificity. In our study, serum ChE activity is reduced in severe liver diseases to the level of 1123 U/L; in contrast to other enzymes in serum which is elevated from cellular sources following membrane damage. Data from study conducted by Khan et al [11] postulated that 100% patients with cirrhosis had lower serum ChE level and he also showed that there was close relationship between the severity of cirrhosis and level of serum ChE enzyme. Gokani R et al [12] found the serum cholinesterase levels were decreased in liver disease patients with significant `p` value with mean of 3424.77 U/L in cases when compared to controls with mean value of 7320.77. In the study conducted by William Burnett [13], found that serum ChE is useful both as a liver function test and in the diagnosis of jaundice. Serum ChE enables the recognition at the earliest time of onset of reduction in the synthetic capacity. Serum ChE levels below 3506 had 98.7% sensitivity and 80.3% specificity in predicting cirrhosis as mentioned in studies of Ramachandran J et al [10]. In our study, Serum ChE has the sensitivity and specificity of 86.27 (95% CI 78.04% to 92.29%) and 90.20 % (95% CI 82.71% to 95.20%) respectively which indicates serum ChE as an excellent marker for the diagnosis as well as reflects the severity of the disease. Serum Cholinesterase was well correlated with serum albumin (`r` value 0.712 with $p < 0.05$) and this implies serum ChE is decreased when the synthetic function is lost in chronic liver diseases.

Most of the conventional parameters in the Liver function test are elevated in sources other than the liver. Serum ChE is synthesized in liver. Despite all the studies, this simple biochemical test is not routinely done as a liver function test worldwide. Thus, Serum ChE might be added as a routine diagnostic test for the diagnosis of liver dysfunctions. Further research is needed to understand the roles of serum ChE in acute and chronic liver disorders. This study has its own limitations which includes, it is a single centred study and this study did not analyse the prognosis and the severity of the diseases.

Conclusion

Serum ChE was significantly reduced in chronic liver diseases. Other conventional parameters of liver function tests were elevated in chronic liver diseases and also abnormal in some individuals in control group. Serum protein and albumin were reduced in liver diseases. Thus, Serum ChE can also be included to analyse the synthetic capacity of liver and in the diagnosis of liver dysfunction.

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