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Research Article

Toxicity Indicator Value of Plasma Pseudocholine Esterase in Hepatic Patients

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Abstract

A small proportion of the healthy population is lacking in plasma cholinesterase enzyme (ChE) due to a genotype aberration. Plasma (ChE) activity is reduced in liver dysfunction due to reduced synthesis. A prospective cross-sectional study was carried out at Dammam Regional Poison Control Center in cooperation with Dammam Medical Complex Hospital to measure ChE and establish its relationship with hepatic condition status in the studied cases. The studied cases were divided into the following groups: Group I comprised fifty age-matched male and female subjects, not exposed to pesticides, who were recruited randomly as a control group. All participants were from the same geographical setting. Group II comprised seventy-five patients with chronic liver diseases of different etiologies. Fibroscan and biochemical enzyme assays had been done including a ChE assay. From the current study, the researchers found that the activity of the ChE enzyme was significantly lower in the hepatic patients as compared to the control group (120.1 ± 69.3 and 167.1 ± 30.6 Ukat/l respectively). There was a significant decrease in plasma ChE as the fibroscan score increased. There was also a significant decrease in ChE level in Wilson & intrahepatic cholestasis regarding hepatitis B & C cases. There was a significant decrease in plasma (ChE) level with increase in age; a significant inverse relationship with variables hepatic profiles Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and Gamma Glutamyl Transferase (GGT). Plasma (ChE) level had a significant negative correlation with plasma prothrombin time and INR ratio. In conclusion, the present study clarifies the non-interpretable plasma choline esterase enzyme in cases of suspected insecticide toxicity of hepatic patients.

INTRODUCTION

A small proportion of the healthy population is lacking in plasma (ChE) enzyme, due to a genotype aberration. Studies carried out in Europe indicate a 3-4%prevalence of congenital serum B ChE deficiency [1]. ChE is synthesized in the liver, and a hepatocellular impairment will lead to decreased enzyme activity. In fact, plasma levels fall in acute and chronic liver damage, cirrhosis, and liver metastases, and this fall is a biochemical marker of organ damage. Low plasma (ChE) levels have also been found in protein-energy malnutrition, during stress and (chronic and acute) inflammation, and in other clinical conditions [2].

Cholinesterase is synthesized mainly in hepatocytes and is released into the blood [3]. Plasma (ChE) 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 as a result of enhanced release from their cellular sources following cell membrane damage [4].

Plasma (ChE) 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 succinyl choline [5].

The current study aimed to evaluate the usefulness of interpretation of ChE enzyme level as an indicator of insecticide toxicity in hepatic patients.

SUBJECTS AND METHODS

Study setting

A prospective cross-sectional study was carried out at Dammam Regional Poison Control Center in cooperation with Dammam Medical Complex Hospital. The Human Subjects Review Committee of the Dammam poison control center approved the study protocol.

Inclusion criteria: For group (I): healthy male and female subjects around 30 years old from the same geographical setting. For group (II): chronic liver disease patients with different etiologies (Chronic hepatitis B and C, Wilson disease, NASH, auto-immune disease and obstructive jaundice, in Dammam Medical Complex, Gastroenterology department).

Exclusion criteria: Dystrophy, motor neuron disease, pregnancy, dermatomyositis, recent surgery and patients on neostigmine and tetra-methyl ammonium chloride treatment were excluded from the study to exclude the inherited decrease in plasma (CE) Enzyme.

Grouping of the studied Cases

Group I: Fifty age-matched male and female subjects, not exposed to pesticides were recruited as a control group. In order to avoid differences in environmental exposure to pesticide residues, all participants were from the same geographical setting, thus their socio-economic and nutrition status were comparable.

Group II: Seventy five patients with chronic liver diseases of different etiologies.

Assay procedure

Ten milliliters (mls) of venous blood samples were collected from each subject while in the supine position, without application of a tourniquet. Then, 5 mls of the sample were placed in non-heparinized vacutainers to get serum and 5mls in heparinized vacutainers. The blood was centrifuged at 3000 rpm for 15 minutes to separate the serum. The serum was kept at -20ºC for further biochemical assays.

Biochemical assays: Plasma (ChE) assayed was intended for kinetic colorimetric determination of Plasma (ChE) according to Deutsche Gesellshaft fur Klinische chemie (DGKC) recommendations on serum on the ARCHITECT system using ARCHITECT c4000, model i1000 SR by ABBOTT LABORATORIES, Abbott Park, IL60064 USA

Markers for liver damage, Gamma Glutamyl Transferase (GGT), Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) Prothrombin time (PT) and International Normalized Ratio (INR) were determined using the commercial diagnostic kit (Stanbio Co., Spain).)

Fibroscan evaluation: Fibroscan is a medical device using propriety Vibration Controlled Transient Elastography (VCTE™) at 50 HZ. Fibroscan provides a liver stiffness measurement, expressed in KPa, as well as a Controlled Attenuation Parameter (CAP ™),expressed in dB/m. A Fibroscan ™ 502 touch device was used in the study, manufactured by Echosens, Paris, France.

Statistical analysis

Database management and the statistical analysis were performed using the SPSS software for Windows (ver. 19.0; SPSS, Chicago, IL, USA).Descriptive results were expressed as the mean ± standard deviation (SD) or number (percentage) of patients with a condition. A Students T-test and multiple comparisons in an ANOVA test were used to compare the mean data and the Pearson correction test. The tests were two-tailed and $P<0.05$ was considered to indicate a statistically significant difference.

RESULTS

The demographic features and smoking habits of both groups of subjects are shown in (table 1). The age, sex, nationality, and smoking habits of both groups (I) and (II) were comparable.

Table 2 demonstrates the variable hepatic pathological condition and fibroscan scores of the hepatic patients. Hepatitis (B & C) represents the majority of hepatic pathological conditions (62.7%). On the same side the fibroscan score 4 represented the top incidence (44%) of overall fibroscan score degrees.

The activity of the ChE enzyme was significantly lower in the hepatic patients as compared to the control group (167.1 ± 30.6 and 120.1 ± 69.3 Ukat/l in control and chronic hepatic patients groups respectively) (Figure 1).

There was a significant decrease in plasma (ChE) level by increasing the degree of fibroscan score, and there was also a significant decrease in plasma (ChE) level in Wilson & Obstructive jaundice cases regarding hepatitis B & C cases. There were no significant differences in plasma (ChE) level regarding sex and smoking habits (Table 3).

Table (4) shows the variable hepatic indicator measurements in relation to different fibroscan scores in the studied cases

Table 1: Demographic features of the study subjects.

Parameters	Control cases (n = 50)	Studied cases (n = 75)
Age (years)		
Mean ±SD	39.7±112.2	43.9±14.2
Sex		
Male	34(68 %)	61 (81.3%)
Female	16 (32 %)	14 (18.7%)
Smoking		
Non-smoker	26 (52%)	61 (81.3%)
Mild	14 (28%)	5 (6.7%)
Moderate	6 (12%)	7 (9.3%)
Severe	4 (8%)	2 (2.7%)
Nationality		
Saudi	30 (60%)	63 (84%)
Egyptian	7 (14%)	4 (5.3%)
Filibino	3 (6%)	2 (2.7%)
Indian	5 (10%)	2 (2.7%)
Syrian	5 (10%)	2 (2.7%)

*p value < 0.05

There was a significant decrease in plasma (ChE) level as age increased. Also there was a significant inverse relationship between plasma (ChE) level and different hepatic profiles such as AST, ALT, GGT, while there was a significant positive relationship between plasma (ChE) level and total Bilirubin, as shown in (Table 5). Also, plasma (ChE) level was negatively correlated with plasma prothrombin time and increased INR ratio.

DISCUSSION

In the current study the activity of the ChE enzyme was significantly decreased in the hepatic patients as compared to the control group. In agreement with our findings, Flanna et al, [6] stated that, plasma (ChE) activity may drop by up to 50% in acute hepatitis, hepatic cirrhosis and chronic hepatic malignancies.

On the opposite side of the current results, McQueen [7] found that normal levels of ChE activity vary widely. Each individual retains his/her own level of serum ChE under normal circumstances. They also showed that the half-life of plasma (ChE) is approximately 10 to 14 days, and it is considered an unreliable source for tracking liver disease. The reasons for the previously mentioned results may be the relationship between the acute hepatic condition and plasma (ChE) level and not involving the chronic hepatic impairment conditions.

Table 2: Variable hepatic pathological conditions and fibroscan score in group (II).

Parameters	Number	Percentage (%)
Liver Disease		
HepatitisB	30	40.0%
Hepatitis C	17	22.7%
Wilson Disease	12	16.0%
NASH	1	1.3%
Auto Immune Disease	1	1.3%
Obstructive jaundice	14	18.7%
Total	75	100.0%
Fibroscan score		
0	11	14.7
1	15	20.0
2	10	13.3
3	6	8.0
4	33	44.0
Total	75	100.0%

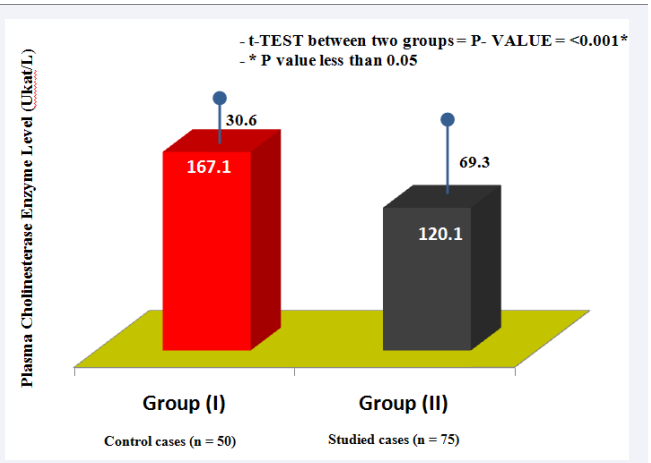

Figure 1 Statistical relationship between control and hepatic patients regarding the level of plasma cholinesterase level.

Table 3: Plasma cholinesterase level in relation to sex, smoking habits, variable hepatic pathological conditions and fibroscan score in group (II) hepatic patients.

Parameter	Pseudo Choline Esterase (ukat/l)	P value
Sex		
Male	124.18±72.21	P value: 0.17
Female	102.36±53.23	
Fibroscan score		
0	171.5± 63.54	P value: 0.000*
1	156.9 ± 45.05	
2	180.2 ± 41.54	
3	100.1 ± 63.81	
4	71.7 ± 51.61	
Smoking habits		
Non-smoker	121.2 ± 71.27	P value: 0.541
Mild	121.2 ± 88.98	
Moderate	138.4± 36.88	
Severe	61.2 ± .02	
Liver Disease		
Hepatitis B	160.1± 67.85	P value: 0.000*
Hepatitis C	124.9± 57.3	
Wilson Disease	55.3±41.1	
NASH	206.3	
AutoImmune Disease	145.50	
Obstructive jaundice	76.07±35.7	

*p value < 0.05

There was a significant decrease in plasma ChE as the fibroscan score increased, severity of Wilson disease and obstructive jaundice cases regarding hepatitis B and C cases. The same results were revealed by Shinya [8] and Ziol [9] ,who stated the overall investigation of the hepatitis C cases significantly correlated with plasma ChE, fibrosis markers and fibroscan score.

The present study revealed a significant inverse relationship between plasma ChE level and different hepatic profiles such as AST, ALT, GGT, PT and INR while there was a significant positive relationship between plasma ChE level and total Bilirubin level. Several studies have reached the same conclusions as the current presentation: Jeyamaniet, [10] Meltter, [11] LI Q, [12] Fanping [13]. The authors of the discussed study attributed the negatively correlated ChE level to total bilirubin level and to plasma prothrombin time, as those substances are synthesized in the liver and reduced in liver dysfunction.

CONCLUSION

In conclusion, the current results clarify the non-interpretable plasma choline esterase enzyme in cases of suspected toxicity of hepatic patients. So in a clinical situation with a patient suffering from exacerbated hepatic condition it is recommended to exclude

Table 4: Measurable variable hepatic indicator according to different degree of Fibroscan score in group (II) hepatic patients.

Parameters Mean ± SD	Fibroscan Score				
	0	1	2	3	4
GGT (IU/L)	100.18±131.63	81.40 ±108.74	83.30±158.81	197.67±201.17	279.79±180.72
ALT (IU/L)	49.91±40.98	39.07±15.14	49.23±30.51	72.33±46.39	84.00±51.92
AST (IU/L)	38.09 ± 22.61	25.85 ± 7.50	37.10±13.77	59.00±41.83	95.33±96.87
Total Bilirubin (mg/dl)	1.65 ±1.31	0.67 ±0.27	2.75±4.20	0.75±0.13	5.55±9.14
INR (%)	1.15 ±.12	1.08±0.09	0.97±0.07	1.25±0.16	1.38±.33
WBCs (K/mm cubed)	8134.6±3959.6	5922.7±2382.57	6936.0±3213.	7138.3±2040.6	9588.3±7894.4
Creatinine (mg/dl)	0.87± 0.23	1.94±2.86	0.84±0.24	1.09±0.08	1.51±2.54
Haemoglobin (gm/dl)	13.75 ±1.23	13.53 ±2.04	12.69±4.43	12.90±0.98	11.75±2.26

*p value < 0.05

Table 5: Statistical relationship between plasma cholinesterase level and variable hepatic profile parameters in group (II) hepatic patients.

Statistical relationship	Correlation Coefficient	P value
PChE level (Ukat/L) &Age	- 0.353	0.037*
PChE level & GGT	- 0.316	0.064
PChE level & ALT	- 0.019	0.914
PChE level &- AST	- 0.043	0.806
PChE level &Total Bilirubin	- 0.448	0.007*
PChE level &Prothrombin time	- 0.073	0.677
PChE level &INR	- 0.319	0.062

*p value < 0.05

the toxicological elements in order to decrease the level of the plasma pseudocholine esterase enzyme.

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