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Original Article

Prognostic Significance of Various Biochemical Parameters in Acute Organophosphorus Poisoning

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ABSTRACT

Background: Organophosphorus (OP) compounds are a heterogeneous group of insecticides widely used in agricultural industry. These OP compounds are likely to have more adverse effects in developing countries like India due to its easy availability and less awareness which results in high morbidity and mortality. **Aims and objectives:** 1. To estimate plasma cholinesterase, amylase, lipase and, creatine phosphokinase (CPK) in acute OP poisoning. 2. To correlate these biochemical parameters with plasma cholinesterase levels in OP poisoning. 3. To determine the use of a biochemical marker in predicting the severity of acute OP poisoning. **Materials and Methods:** A hospital based observational study was conducted on 53 subjects who have clinically diagnosed of acute OP poisoning and admitted in emergency unit of a tertiary care rural hospital. Subjects of either gender of all age-groups were included in the study. On admission, plasma cholinesterase, serum amylase, lipase and CPK were measured. Based on plasma cholinesterase activity at the time of admission, subjects were divided into three groups. Group I-having 20-50% of plasma cholinesterase activity; Group II-10-20% of plasma cholinesterase activity; and group III-<10% of plasma cholinesterase activity. **Results:** Serum amylase, lipase and CPK were negatively correlated with plasma cholinesterase levels. Serum amylase showed statistically significant negative correlation with plasma cholinesterase. Serum amylase showed the highest diagnostic accuracy for assessing severity of poisoning followed by CPK and Lipase. **Conclusion:** OP poisoning is associated with hyperamylasemia. Serum amylase, lipase and CPK can be used as an additional prognostic indicator with plasma cholinesterase levels. Serum amylase could be considered as a better predictor of severity followed by CPK and lipase.

Key words: Amylase, CPK, lipase, organophosphorus poisoning, plasma cholinesterase

INTRODUCTION

Organophosphorus (OP) compounds are insecticides which are widely used in agriculture to control pests, weeds, or plants diseases. Because of their specific action these OP compounds are helpful in crop protection and increased productivity. The OP compounds likely to have more adverse effects in developing countries like India due to its easy availability and less awareness leading to high morbidity and mortality.[1] The OP compounds act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors. Signs and symptoms of poisoning are mainly due to muscarinic, nicotinic and central nervous system (CNS) receptor over-stimulation.[2]

In acute OP poisoning, the severity of poisoning parallels the decrease in pseudocholine esterase activity. Even though various scoring systems such as Acute Physiology And Chronic Health Evaluation (APACHE) and Simplified

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Acute Physiology Score (SAPS) are available, laboratory evaluation plays an important and crucial role for confirmation of poisoning, diagnosing the first acute organ damage and assessing the severity of poisoning. In laboratory assessment of OP poisoning, estimation of plasma cholinesterase is most specific test for OP poisoning.[3]

OP compound poisoning is associated with various biochemical abnormalities, among which hyperamylasemia is well documented and may be due to excessive cholinergic stimulation of pancreas. Studies conducted by Matsumiya N *et al.*, and Lee HC have evaluated the prognostic significance of serum amylase in OP poisoning.[4,5] Acute pancreatitis is frequent in OP poisoning and increased serum amylase is less specific and sensitive. Hence, serum lipase measurement may be useful in patients with increased amylase levels for early diagnosis of pancreatitis.[6] Hence a many research was done to evaluate a promising biochemical marker in OP poisoning. Recently, a study done by Bhattacharya K *et al.*, suggested that measurement of creatine phosphokinase (CPK) in acute OP poisoning may be useful in predicting as well as assessing prognosis of patients. It was also documented that there is rhabdomyolysis in "intermediate syndrome" and followed by a proportionate raise in CPK level.[7]

This study was undertaken to know the efficacy of newer biochemical markers like Amylase, lipase and CPK as indicators in assessing the severity of OP poisoning.

Aims and objectives

1. To estimate plasma cholinesterase, amylase, lipase and CPK in acute OP poisoning
2. To correlate these biochemical parameters with the plasma cholinesterase levels in OP poisoning
3. To determine use of a biochemical marker in prediction of severity of acute OP poisoning

MATERIALS AND METHODS

A hospital based longitudinal study was conducted among 53 subjects reported and clinically diagnosed with acute OP poisoning in the emergency unit of a tertiary care center for a period of 8 months.

Inclusion criteria

All the OP poisoning cases confirmed by history, circumstantial evidence of consumption, characteristic clinical examination and basic laboratory investigations were included in the study.

Exclusion criteria

Patients with history of consumption of OP compound mixed with any other poison or alcohol, chronic alcoholism, diseases of salivary gland, and chronic renal failure or any associated renal disorders were excluded from the study.

Sample collection

At the time of admission, after obtaining informed consent about 2 ml of blood was collected in plain tube under aseptic precautions. Blood was allowed to clot, serum was separated by centrifugation and used for the analysis of following parameters.

1) Estimation of serum amylase by chromogenic method using dyed amylopectin.[8]
2) Estimation of plasma cholinesterase activity by kinetic method based on hydrolysis of butyrylthiocholine by choline esterase.[8]
3) Estimation of serum lipase by kinetic method using 1-oleoyl-2-3-diacetyl glycerol as substrate.[8]
4) Estimation of serum creatine kinase by kinetic method.[8]

All the parameters were analyzed in Drychemisrty Vitros 250 Johnson and Johnson analyser. During the analysis, regular and routine internal quality checks using Biorad controls was carried out.

After the biochemical analysis, patient were followed up for clinical outcome like complete recovery, acute respiratory distress syndrome, circulatory failure, CNS complications, renal failure, death due any of the above mentioned complications and any other complications.

Statistical analysis

The parameters were tabulated and the mean values and standard deviation (SD) was analysed using EPI Info 7 version software. Mean and SD were compared between the groups using one way analysis of variance (ANOVA). All biochemical parameters were correlated with plasma cholinesterase using Pearson's coefficient. Chi-square test was the test of significance for qualitative variables to find the association. Diagnostic accuracy of the biochemical parameter was assessed by calculating the area under the curve in receptor operating curve (ROC).

RESULTS

Based on the plasma cholinesterase levels at the time of admission, subjects were divided into three groups.

Group I-20-50% of normal plasma cholinesterase activity; Group II-10-20%; and Group III-<10% (1). In the study it was observed that majority 49.05% (26/53) belonged to group III who had plasma cholinesterase activity <10%,

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followed by 28.3% (15/53) of cases in group II and 22.6% (12/53) in group I. Majority of the subjects were males 73.5% (39/53). Among 53 subjects, three patients died of respiratory failure all belonging to group III. Seven patients had respiratory distress but recovered after treatment.

In group I, six out of 12 patients had elevated amylase levels, three had increased lipase and five had increased CPK levels. All three patients who had elevated lipase levels also had elevated amylase and CPK. Five patients who had decreased plasma cholinesterase levels, had normal levels of amylase, lipase and CPK. Rest of the patients had isolated elevation of either amylase levels or CPK levels. In group II, seven out of 15 patients had increased amylase, three had increased lipase and 12 had increased CPK. Two patients had increased amylase and lipase levels and only one patient had elevated amylase, lipase and CPK levels. Two patients in this group with decreased plasma cholinesterase levels had normal levels of amylase, lipase and CPK. In group III, 19 out of 26 had elevated levels of amylase, six had elevated lipase and 24 had increased CPK. Elevated amlylase and lipase was observed in two patients and 12 patients had elevated amylase and CPK. Only one patient with decreased plasma cholinesterase levels had normal amylase, lipase and CPK values.

Comparison of biochemical parameters between the groups and within the groups were done by ANOVA. Plasma cholinesterase level was 1616.4 + 155.08 in group I, 906.60 + 155.08 in group II and 282.81 + 93.02 in group III. Mean values of serum amylase in group I was 90.9 ± 46.99, group II was 120.9 + 89.7 and group III was 160.42 + 84.46. Mean values of serum lipase was 82.83 ± 53.79 in group I, 72.13 + 52.64 in group II and 159.08 + 198.39 in group III. Mean values of CPK was 207.08 ± 226.60 in group I, 303.2 + 215.1 in group II and 331.46 + 207.74 in group III. There was no statistical significant difference among the groups. It can be observed from the Table 1 that when there is decrease in plasma cholinesterase level, there is increase in the mean values of amylase, lipase and CPK levels.

Correlation of various biochemical parameters with plasma cholinesterase levels show that serum amylase, lipase and CPK were negatively correlated with plasma cholinesterase levels. Whereas only serum amylase showed statistically significant negative correlation ($P = 0.029^*$) with plasma cholinesterase. [Table 2].

The association between the severity of OP (based on plasma cholinesterase) and other biochemical parameters showed that there was significant association with severity of OP poisoning with respect to amylase, lipase and CPK levels [Tables 3].

ROC to assess the predictor of severity of OP poisoning showed that the area under the curve for serum amylase was 0.714, serum CPK was 0.635 and compared to lipase was (0.571) suggesting that Amylase was the better predictor of severity among the three variables [Tables 3, 4 and Figure 1].

DISCUSSION

Acute OP poisoning often presents as a medical emergency requiring monitoring and management in intensive care unit. Management of poisoning depends on clinical severity and is assessed by clinical signs and symptoms as well as laboratory evaluation.

Inhibition of cholinesterase is a well known fact in OP poisoning. Estimation of acetylcholinesterase (AchE) and butyrylcholinesterase (BchE)/plasma cholinesterase are the screening tools for OP poisoning. Although estimation of AchE in erythrocytes is more specific, estimation of plasma cholinesterase is most widely used laboratory tool for diagnosis and prognosis of OP poisoning.[9]

In this study majority of cases belonged to Group III and mortality occurred only in group III. Similar findings were observed in the studies conducted by Amanvermez R *et al.*,[3] and Hundekari IA *et al.*,[10] demonstrating good correlation between plasma cholinesterase level and severity of poisoning. A retrospective study conducted by Manu *et al.*, have demonstrated that, patients with low plasma cholinesterase levels had poor prognosis and mortality with longer term stay in ICU and took long time to be out of mechanical ventilation.[11]. Another retrospective study by Yun HW *et al.*, demonstrated that, absence of an increase in serum cholinesterase activity is associated with high mortality and morbidity.[12]

Table 1: Comparison of biochemical parameters

Parameter Groups (% of plasma cholinesterase)	Number	Mean+SD (IU/L)			
		Plasma cholinesterase	Amylase	Lipase	CPK
Group I (20-50%)	12	1616.4±155.08	90.9±46.99	82.83±53.79	207.08±226.60
Group II (10-20%)	15	906.60±155.08	120.9±89.7	72.13±52.64	303.2±215.1
Group III (<10%)	26	282.81±93.02	160.42±84.46	159.08±198.39	331.46±207.74
Significance	*F* value	0.615	1.397	0.629	0.366
	P value	0.545	0.257	0.537	0.695

CPK = Creatine phosphokinase, SD = Standard deviation

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Table 2: Correlation of biochemical parameters with plasma cholinesterase

Parameters	Plasma cholinesterase	
	Correlation coefficient	*P* value
Amylase	−0.300*	0.029*
Lipase	−0.229	0.100
CPK	−0.263	0.058

*Significant. CPK = Creatine phosphokinase

Table 3: Association of biochemical parameters with severity of poisoning

	Plasma cholinesterase			*P* value
	<10% (*n*=26)	20-50% (*n*=15)	50% (*n*=12)	
Amylase				
25-130	9	12	7	0.018*
➢130	17	3	5	
Lipase				
23-300	21	15	12	0.057*
➢300	5	0	0	
CPK				
24-195	7	7	9	0.02*
➢195	19	8	3	

*Significant. CPK = Creatine phosphokinase

Table 4: Area under the curve

Test result variable (s)	Area
Amylase	0.714
CPK	0.635
Lipase	0.571

CPK = Creatine phosphokinase

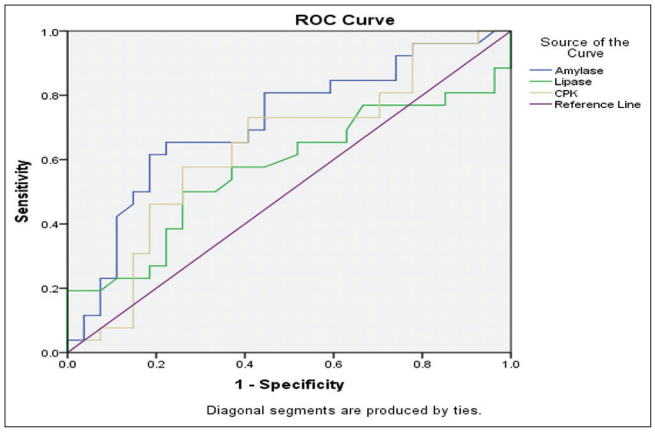


Figure 1: Diagnostic accuracies of various biochemical parameters in OP poisoning

OP poisoning is associated with many biochemical abnormalities. Among which hyperamylasemia often noted in cases of OP poisoning, may be due to the fact that acute pancreatitis is caused by excessive cholinergic stimulation of pancreas by OP compounds.[13,14] Our study results are in accordance with the study done by Lin CL *et al*., where they found that mean amylase levels were elevated in patients with respiratory support and serum amylase levels predicted ventilator support in OP poisoning.[15] In a prospective study by Singh S [16] amylase was elevated in 48.95% in patient with fenthion poisoning and serum amylase showed persistent elevation during serial estimation. An important effect of O.P or carbamate intoxication is development of acute pancreatitis. Incidence of acute pancreatitis in adults with OP poisoning is approximately 12%.[17] In our study, majority of patients who had increased amylase levels belonged to group III and showed significant negative correlation with plasma cholinesterase levels. However, lipase was elevated only in six patients, who also had associated elevated amylase levels and all of them belonged to group III. Serum lipase did not show significant correlation with plasma cholinesterase.

Another promising prognostic indicator in OP poisoning is CPK. It is shown that serum CPK is elevated due to rabdomyolysis or intermediate syndrome which is an associated complication of OP poisoning.[7] CPK was elevated in two patients who succumbed due to complications. Elevated CPK was also noticed among five cases, whom also went in to complications. A study by Battacharya *et al*., has demonstrated that CPK can be elevated in severe OP poisoning cases even in the absence of intermediate syndrome. This may be due to muscle fiber necrosis and needs to be confirmed by muscle biopsy. Study by Hassan NAM and Madboly AG[18] have also confirmed high degree of correlation between initial CPK value and severity of OP poisoning.

Diagnostic accuracy of the biochemical parameters show that serum amylase had highest diagnostic accuracy followed by serum lipase and CPK.

Limitations of this study are small sample size and biochemical parameters are estimated at the time of admission. Serial measurements of plasma cholinesterase and other biochemical parameters could help to draw better conclusions.

With this we conclude that OP poisoning is associated with hyperamylasemia. Serum amylase, lipase and CPK can also be used as an additional prognostic indicator with plasma cholinesterase levels. Among all, serum amylase could be considered as a better predictor of severity followed by CPK and Lipase. However further studies with large sample size can be useful in making conclusions.

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