

ORIGINAL RESEARCH

Pseudocholinesterase diagnostic and prognostic value in organophosphorus poisoning

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ABSTRACT

Organophosphorus compound poisoning is a common clinical situation encountered in emergency dept. The estimation of pseudocholinesterase levels in plasma help to identify the objective of the study. 50 cases of suspected organophosphorus compound poisoning were randomly selected above 18 years of age, excluding the patients who have taken other drugs with organophosphorus compound and patients with prior hepatic dysfunction. Detailed history and clinical examination were done. The serum levels of enzyme pseudocholinesterase was estimated on first, second, third and sixth day. 60% were males, 40% were females. Age range 18-55 years. Most of the patients were admitted within 4 hours. 50% cases were mild, 26% were moderate and 24% were severe cases. Commonest clinical features were vomiting, diarrhea and abdominal cramps. Common signs were miosis 46%, difficulty in breathing 42%. Patients who survived had raising values of enzyme levels and in patients who expired did not show much increase in enzyme values. In early stages of poisoning determining pseudocholinesterase activity forms a reliable test. In patients who survived had values above 4300 U/L and showed increasing levels on successive days indicating better prognosis. Low values of enzymes in early stages of poisoning indicate increased mortality.

Key words: Pseudocholinesterase, enzyme, organophosphorus

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INTRODUCTION

Acute poisoning is important cause of morbidity and mortality in India. In medical emergency 10% of admissions are due to poisoning and organophosphorus poisoning contributes to nearly 50% of it¹.

Among the new compounds emerging as poisonous substances organophosphorus compounds have also emerged due to development in the field of chemistry. Apart from use of these substances as agricultural insecticides, pesticides, they are frequently abused for suicidal purposes because of their low cost, rapid action and easy availability.

They have been imported in India since 1951, but very few knew the nature of these compounds as a virulent poison till the Kerala food poisoning tragedy in 1958. This tragedy took a toll of hundred and add due to inadvertent stocking of food stuff and

foliolpackages in the same hold where the foliol containers leaked and contaminated the gunny bags containing food stuff².

Exposure to organophosphorus compounds in the form of nerve agents and pesticides poses an ever increasing military and civilian threat³.

In parts of developing world pesticide poisoning causes more deaths than infectious diseases⁴.

Organophosphate insecticides account for more than 50% of all acute poisoning in hospital practice, the majority of patients are younger than 30 yrs. ⁵.

In teenagers and adults the poisoning is generally due to suicidal intension though accidental poisoning occurs during spraying².

They act by irreversibly inhibiting the enzyme cholinesterase resulting in stimulation of acetylcholine at synapses and myoneuronal junction and leads to cholinergic over activity^{6,7,8}.

Mortality ranges from 4% to 38% in Indian studies. The most common cause of death is respiratory failure. Earlier recognition and prompt ventilatory support may improve the survival rate.

METHODOLOGY

50 patients of suspected organophosphorus poisoning admitted to medical emergency ward, have formed the material for study.

STUDY DESIGN

Hospital based prospective study.

INCLUSION CRITERIA

In this study patient above 18 years with suspected OPC poisoning were included.

EXCLUSION CRITERIA

Patient with suspected OPC below 18 years and those who have consumed other drugs along with OPC were excluded from the study. And also patients who are having prior hepatic dysfunction and chronic conditions which may reduce the levels of Butyryl cholinesterase levels are also excluded.

All the cases satisfying inclusion and exclusion criteria were included. A detailed case history was taken as per the proforma and a complete physical examination was done soon after admission.

DIAGNOSIS BASED ON

1. History or evidence of exposure to organophosphorus compound within 24 hours.
2. Characteristic manifestations of OPC poisoning including, miosis, fasciculations, excessive salivation.
3. Improvement of signs and symptoms with administration of atropine.
4. Corroborative evidence like empty containers and

RESULTS

Table 1: Stage of severity

Stage	No. of cases	Percentage
Mild	25	50
Moderate	13	26
Severe	12	24

50% of cases presented in mild stage where as 26% presented in moderate stage and 24% presented in severe stage.

In this study vomiting, diarrhoea and abdominal

odour of gastric aspirates.

Depending on the severity of manifestations patients were classified into three grades as mild, moderate and severe depending on modified version of DrieSbach's classification.

INVESTIGATIONS

Soon after admission blood samples were collected and investigated to know the serum levels of pseudocholinesterase on Day 1, Day 2, Day 3, and Day 6.

Other routine investigations such as

- Hemoglobin percentage.
- Total blood count.
- Differential count.
- ESR.
- Random blood sugar.
- Serum creatinine.

Were done to exclude chronic conditions.

METHOD OF ESTIMATION OF PSEUDOCHOLINESTERASE

Method with S-butrylthiocholine iodide using Dibucaine as inhibitor. Cholinesterase catalyses the hydrolysis of S-butrylthiocholine Iodide to thiocholine iodide and butyrate. Thiocholine iodide reacts with 5,5-dithiobis-2-nitrobenzoate (DTNB) and forms the yellow coloured product 5-mercapto-2-nitrobenzoate. The substrate specificity prevents interference with cholinesterase liberated from erythrocytes even during slite hemolysis.

The rate of formation of 6 mercapto-2 nitro benzoate is directlyproportional to the catalytic cholinesterase activity. It is determined by measuring the increase in absorbance at 480 nm.

Normal values of serum pseudocholinesterase ranges from 4150 to 7200 U/L.

cramps were more frequently observed. Signs observed are as follows, Cyanosis 18%, miosis 46%, difficulty in breathing 42%, fasciculations 14%, convulsions 10%.

Table 2: Showing pseudocholinesterase activity on day 2

Pseudocholinesterase Level	Survived		Expired		Total Cases
	No	%	No	%	
<4000 U/L	9	81.8	2	18.2	11
4001-5000 U/L	25	89.3	3	10.7	28
>5001 U/L	10	90.9	1	9.1	11
Total	44	88.0	6	12.0	50
$X^2 = 1.32$	DF - 2	P= 0.52			

15 Patients had values below 4000 U/L and of this 12 patients (80%) survived while 3 patients (20%) expired. 25 patients had enzyme levels between 4000-5000 U/L of which 23 patients (92%) survived and 2 patients (8%) expired. Out of 10 patients who had values above 5000 U/L, 9 survived (90%) and 1 expired (10%).

From the above observation it is noted that when enzyme activity was less the survival rate was 80% and when enzyme levels are 5000 U/L and survival rate has increased to 92%.

The above findings are also showing that prognosis was better when patient had higher level of enzyme activity on 1 day.

Table 3: Showing pseudocholinesterase activity on day 2

Pseudocholinesterase Level	Survived		Expired		Total Cases
	No	%	No	%	
<4000 U/L	9	81.8	2	18.2	11
4001-5000 U/L	25	89.3	3	10.7	28
>5001 U/L	10	90.9	1	9.1	11
Total	44	88.0	6	12.0	50
$X^2 = 0.53$	p=0.77 DF=2				

Values from 2 day shows that when enzyme activity was less than 4000 U/L.

The survival was 81.8% while when the values are 5001 U/L and above the survival has improved to

90.9%. These observations were similar to findings on first day indicating that raising values of pseudocholinesterase was consistent with better prognosis.

Table 4: Showing Pseudocholinesterase Activity in Day 3

Pseudocholinesterase Level	Survived		Expired		Total Cases
	No	%	No	%	
<4000 U/L	5	71.4	2	28.6	7
4001-5000 U/L	25	89.3	3	10.7	28
>5001 U/L	14	93.3	1	6.7	15
Total	44	88.0	6	12.0	50
$X^2 = 2.27$	p=0.32 DF=2				

Values of 3rd day showed that when Pseudocholinesterase levels are below 4000 U/L. The survival was 71.4% and when 5001 U/L and above

the survival rate has increase to 93.3%. The findings 3rd day were similar to first 2 days.

Table 5: Showing pseudocholinesterase activity on day 6

Pseudocholinesterase Level	Survived		Expired		Total Cases
	No	%	No	%	
<4000 U/L	-	-	1	100.0	1
4001-5000 U/L	15	75.0	5	20.0	20
>5001 U/L	29	100.0	-	-	29
Total	44	88.0	6	12.0	50
$X^2 = 14.5$	P<.05, Significant DF=2				

In patients with levels less than 4000 the mortality was 100%.

Out of 20 patient with levels between 4000 5000 U/L the survival rate was 75% and 5 patient expired

(20%). In patient with 5001 U/L and above value the survival was 100%.

Table 6: Mean pseudocholinesterase activity of patients who survived and those who expired

Day	Survived	Expired
	Mean + SD	Mean + SD
1	4346±	4315+2630
2	4501+929	4115+1635

3	4703+837	4571+756
6	5427+820	4310+339

Patients who survived showed raising values of pseudocholinesterase activity on successive Days, i.e., 4346,4501,4703,5427 U/L. While the patients who expired has low enzyme activity and did not show much increase in subsequent Days i.e.,4315,4115,4571,4319 U/L.

It was observed that in patients who survived and had increasing levels of 3.56% on 2nd day and further rise of 4.48% on 3rd day and a rise of 6.88% on 6th day.

In patients who expired the enzyme activity had reduced by 4.6% on Day 2 and a raise of 11% on Day 3 and a fall of 5.5% on Day 6.

So it is observed that the enzyme activity in patients those survived has increased on successive days indicating a better prognosis where as the enzyme activity in patients those expired was falling except for the Day 3 where a raise of 11% was noticed. This may be probably due to the treatment given to the patients which has caused a transient raise in enzyme levels.

DISCUSSION

In majority of patients on admission it was observed that the enzyme activity was very low. Hence it can be inferred that low pseudocholinesterase activity can be taken as good diagnostic test for OP poisoning. Studies by Namba T *et al.*, and Wadia R.S *et al.*, has also shown that pseudocholinesterase activity estimation is a reliable diagnostic test in OPC poisoning^{9,10}.

Observations from this study shown that patients with higher pseudocholinesterase activity on day of admission has a better prognosis than with lower enzyme values. Similar findings were noted on day 2nd and 3rd day. Hence it can be concluded that initial estimation of pseudocholinesterase activity can be used to predict the prognosis of patients. Recent studies by Kuppuswamy *et al.* showed that pseudocholinesterase activity below 10% of normal were associated with poor prognosis. He also observed that pseudocholinesterase in plasma is more sensitive than acetylcholinesterase to inhibition by a number of compounds and is depressed well below the normal range of 60% before any symptoms due to systemic anti cholinesterase intoxication is evident.

Pseudocholinesterase activity was estimated on day 1, 2, 3 and 6 of admission and it was found that patient who survived had increase in levels of enzyme by 3.56% on 2nd day, 4.48% on 3rd day and 6.88% on 6th day. While in patients who expired the enzyme activity has reduced by 4.6% on day 2. 5.5% on day 6. These findings show that there is a greater chance of survival if the enzyme activity increases substantially on successive days, indicating a better prognosis. It can be concluded that daily increase of pseudocholinesterase activity was consistent with better outcome.

Data from patients who died showed that out of 6 patients who expired majority had enzyme value around 4300 U/L, which is lower limit of normal value. These observations shows that lower the levels of enzyme at admission the more is the mortality.

CONCLUSION

- In early stages of poisoning determining Pseudocholinesterase activity form a reliable diagnostic test.
- Mean pseudocholinesterase activity in patients who survived was above 4300 U/L and the levels had increased in the successive days above 5400 U/L which indicated better prognosis. In the patients who expired the pseudocholinesterase activity was around 4300 and was falling except for the Day 3. This points out that raise in enzyme levels is directly proportional to better prognosis.

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