ORIGINAL ARTICLE

A Study of Serum Pseudocholinesterase Levels in Acute Organophosphorus Poisoining

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Abstract:

Background and Introduction:
Acute Organophosphorus poisoning (OP) 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 cases[1,2,3].The objective of the study is to study the levels of pseudocholinesterase in serum as a diagnostic aid in patients with suspected organophosphorus poisoning and to predict the prognosis based on pseudocholinesterase activity.

Materials and Methods:
Informed consent was taken from 50 patients suspected of organophosphorus poisoning and admitted to Medical Emergency Ward. Pseudocholinesterase levels were estimated by S-butyrylthiocholine iodide method using dibucaine as inhibitor. Serum levels of pseudocholinesterase levels of patients were examined on Day 1, Day 2, Day 3 and Day 6 of admission.

Result:
Patients who survived had increasing levels of pseudocholinesterase activity 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. It was observed that the enzyme activity in patients those survived has increased on successive days indicating a better prognosis whereas 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.

Conclusion:
In early stages of poisoning, determining pseudocholinesterase activity is 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 U/L and was falling except for the Day 3. This point out that raise in enzyme levels is directly proportional to better prognosis.

Keywords:
Organophosphorus poisoning, pseudocholinesterase.

Introduction:
In parts of developing world pesticide poisoning causes more deaths than infectious diseases[4]. Organophosphate insecticides account for more than 50% of all acute poisoning in hospital practice and the majority of patients are younger than 30 years[5].In teenagers and adults the poisoning is generally due to suicidal intension though accidental poisoning occurs during spraying[2,3]. They act by irreversibly inhibiting

the enzyme cholinesterase resulting in accumulation of acetylcholine at synapses and myoneural junction and leads to cholinergic over activity[6,7,8]. Mortality ranges from 4% to 38% in Indian studies.

We have studied the levels of pseudocholinesterase in plasma as a diagnostic aid in patients with suspected organophosphorus poisoning. This helps in predicting the prognosis of OP poisoning.

Materials and Methods:

This study was undertaken at M.K.C.G. Medical College & Hospital, Berhampur, Odisha. The study was approved by institutional ethics committee. Informed consent was taken from 50 patients suspected of organophosphorus poisoning admitted to Medical Emergency Ward, M.K.C.G. Medical College Hospital, Berhampur. The present study was hospital based prospective study. In this study patient above 18 years with suspected organophosphorus poisoning cases were included.

Patients with suspected OP poisoning but below 18 years of age and those who had consumed other drugs along with OPC were excluded from the study. Also, patients who had prior hepatic dysfunction and chronic conditions which may have reduce the levels of Butyryl cholinesterase levels were also excluded. The detailed case history was taken as per the proforma and a complete physical examination was done soon after admission. The diagnosis of patients was done on the based on following criteria:

1) History or evidence of exposure to organophosphorus compound within 24 hours of admission.
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 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 Dreisbach's classification[9].

Grade (Dreisbach's)	Symptom	Symptom score
Mild	Nausea	1
	Vomiting	1
	Diarrhea	1
	Sweating	1
Moderate	Lacrimation	2
	Salivation	2
	Miosis	2
	Fasciculations	2
Severe	Coma	3
	Seizures	3
	Incontinence	3
	Apneic spells	3
	ARDS	3
	Areflexia	3

Immediately after admission, blood samples were collected and analyzed to determine the serum levels of pseudocholinesterase. Serum levels were also analyzes on Day 1, Day 2, Day 3, and Day 6 of admission. Other routine investigations such as haemoglobin, total blood count, differential count, ESR, random blood sugar was also done. The serum creatinine was done to exclude chronic conditions.

Pseudocholinesterase levels in serum were estimated by S-butyrylthiocholine iodide method using dibucaine as inhibitor. All the data collected on 50 patients was analysed using appropriate statistical test - Chi Square (x2) for detecting the p value.

Results:

In this study mean age for both sex was 25.8 years; for males 28.3 ± 10.5 and for females 22.1 ± 5.0 years. Majority of patients of both sexes were in < 20 years age group, followed by 21 - 30 years age group. Out of 50 cases 30 were males and 20 were females, Male female ratio was 1.5:1. Thirty eight percent cases were farmers and 28% of cases were students. In this study

the most common agent encountered was parathion, followed by monocrotophos. However, in 56% of the case the poison was unknown. Most of the patients were admitted within 4 hours of consumption. 24% of patients had admitted within 2 hours and 26% were brought after 6 hours. As the interval between consumption and admission increases the severity also increases. Fifty percent of the cases presented in mild stage where as 26% presented in moderate stage and 24% presented in severe stage. In this study majority of the cases had consumed between 50 –100 ml of suspected poison. The symptoms like vomiting, diarrhoea and abdominal cramps were more frequently observed. Signs of cyanosis 18%, miosis 46%, difficulty in breathing 42%, fasciculations 14%, convulsions 10% were observed.

Fifteen Patients had values below 4000 U/L and out of this 12 patients (80%) survived while 3 patients (20%) expired. 25 patients had enzyme levels between 4000 - 5000 U/L out 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 was noted that when enzyme activity was below 4000 U/L the survival rate was 80% and when enzyme levels are 5000 U/L and above the survival rate has increased to 92%.

The above finding shows that prognosis was better when patient had higher level of enzyme activity on the 1st day of admission.

The 2nd day values shows that when enzyme activity was less than 4000 U/L The survival was 81.8% whereas 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. 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 increased to 93.3%. In patients with levels less than 4000 the mortality was 100%. Out of 20 patients 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%.

It was observed that in patients who survived and had increasing levels of pseudocholinesterase activity 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.

The enzyme activity in patients who survived had increased on successive days indicating a better prognosis whereas 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.

Table No. 1: Pseudocholinesterase activity on day 1

Pseudocholinesterase levels	Survived		Expired		Total cases
	No	%	No	%	
< 4000 U/L	12	80.0	3	20.0	15
4001 - 5000 U/L	23	92.0	2	8.0	25
> 5001 U/L	9	90.0	1	10.0	10
Total	44	88.0	6	12.0	50

X2 = 1.32, DF = 2, p = 0.52

Table No. 2: Pseudocholinesterase activity on day 2

Pseudocholinesterase levels (U/L)	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

X2 = 0.53, p = 0.77, DF = 2

Table No. 3: Pseudocholinesterase activity on day 3

Pseudocholinesterase levels	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

X2 = 2.27, p = 0.32, DF = 2

Table No. 4: Pseudocholinesterase activity on day 6

Pseudocholinesterase levels	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

Table No. 5: Mean pseudocholinesterase activity in survived and expired patients

Day	Survived (Mean ± SD)	Expired (Mean ± SD)	X2	DF	t	p
1	4346 ±1098	4315 ±2630*	1.32	2	0.05	0.96
2	4501± 929	4115 ±1635*	0.53	2	0.86	0.39
3	4703 ± 837	4571±756*	2.27	2	0.36	0.72
6	5427 ± 829	4319±339#	14.5	2	2.94	< 0.05

*Not Significant - Day 1,2 &3 #Significant - Day 6

Discussion:

Organophosphorus compound (OPC) poisoning from intentional and accidental exposure is a major public health problem in the developing world[4]. Many self-poisoning cases show that it is an impulsive response to difficult or even minor situations. Because a high proportion of Indian population is involved in agriculture, the incidence of suicidal OPC poisoning is increasing as a result of easy access to highly toxic pesticides in the situations of stress[10]. For most of the youngsters self-poisoning seems to be preferred method of dealing with difficult situation. Sociologists have suggested that the young have few support system and are unable to cope up with social and cultural demands[11]. Of various agents used for suicidal purposes in India, organophosphate and carbamate form a significant group. This is peculiar to developing countries like India[12].

A study done by Twayana RS et al in 110 cases of organophosphorus compound poisoning reported the mean cholinesterase level to be 1792.90 ± 2305.9 IU/L and the duration of hospital stay was 3.99 ± 2.63 days and there was a significant correlation between low serum cholinesterase and duration of hospital stay P=0.023[13].

A study conducted by Lokesh A et al in 390 patients with OP poisoining reported that patients who survived had pseudocholinesterase values above 4300 U/L and showed increasing levels on successive days indicating better prognosis. Low values of enzymes in initial stages of poisoning as well as decreasing values on the third day indicate increased mortality[14].

Veerappa AK et al reported a positive association of SChE with hospital stay (1st day levels and serial estimation); requirement of ventilatory support (1st day levels); and outcome (serial estimation)[15].

In this study, maximum incidence of poisoning was among 20 - 30 years of age (78%), which was comparable to studies done by P.S. Shankar et al and Goel SJ et al. Incidence was more common in males with Male to Female ratio of 1.5:1.[16,17]. This is comparable to earlier workers. Parathion was the most commonly used OPC which was comparable to Goel SJ et al[17]. In this study severe degree of poisoning was 24% and comparable to APN et al study[18]. In this study instances of vomiting were 100% and convulsions was 10% which were comparable to APN Kumar et al and Goel SJ et al respectively[15,17]. In this study the common clinical signs were Miosis followed by fasciculations. Tachypnea was observed in 42% of cases which was comparable with studies by Geol SJ et al[17]. Respiratory failure was the most common complication seen in 23 patients. This is little higher than the studies by Goel SJ et al and Sangur et al[17,19]. Mortality rate in present study was 12% and is comparable to earlier studies.

In majority of patients on admission it was observed that the pseudocholinesterase enzyme activity was very low. Hence it can be inferred that low pseudocholinesterase activity can be taken as good diagnostic test for OP poisoning.

Observations from this study show that patients with higher pseudocholinesterase activity on the day of admission had 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 G et al showed that pseudocholinesterase activity below 10% of normal were associated with poor prognosis[20]. 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 are the mortality.

Conclusion:

In early stages of poisoning, determination of pseudocholinesterase activity forms a reliable diagnostic marker. 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 point out that rise in enzyme levels is directly proportional to better prognosis. The mortality rate was 12% (6 out of 50 cases). Low levels of enzymes in early stages of poisoning indicate increased mortality.

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