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Original Research Article

Pseudo cholinesterase-diagnostic and prognostic value in organophosphorus poisoning

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ABSTRACT

Background: Organophosphorus compound poisoning is a common clinical situation encountered in emergency department. The estimation of pseudo cholinesterase levels in plasma help to identify OP poisoning. Aim of this study was the levels of pseudo cholinesterase in plasma as a diagnostic aid in patients with suspected organophosphorus poisoning and to predict the prognosis and mortality based on pseudo cholinesterase activity.
Methods: 390 cases of suspected organophosphorus compound poisoning were selected above 18 years of age. Detailed history and clinical examination were done. The serum levels of enzyme pseudo cholinesterase were estimated on 1st and 3rd and 6th day.
Results: 61% were males, 39% were females. Age range 18-55 years. Most of the patients were admitted within 4 hours of consumption. 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%), cold calmmy skin, bradycardia. Patients who survived had raising values of enzyme levels and in patients who expired did not show much increase in enzyme values.
Conclusions: In initial stages of poisoning, determining pseudo cholinesterase 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 initial stages of poisoning as well as decreasing values on the third day indicate increased mortality.

Keywords: Organophosphorus, Pseudo cholinesterase, Poisoning

INTRODUCTION

Acute poisoning is worthy cause of morbidity and mortality in India. Ina common cause medical emergency 10% of admissions are due to poisoning and organophosphorus poisoning contributes to nearly 50% of it.[1]
Apart from agricultural insecticides, pesticides, they are frequently abused for suicidal purposes because of their low cost, rapid action and easy availability. They have been imported to India since 1951, but very few knew the nature of these compounds as a virulent poison till the Kerala food poisoning tragedy in 1958. Exposure to organophosphorus compounds in the form of nerve agents and pesticides poses an ever increasing military and civilian threat.[3]
In developing countries pesticide poisoning causes more deaths than infectious diseases[4] Organophosphate

insecticides account for more than 50% of all acute poisoning in hospital practice, the majority of patients are younger than 30 years[5] mainly due to suicidal intention, though accidental poisoning occurs during spraying.[2] They act by irreversibly inhibiting the enzyme cholinesterase resulting in accumulation of acetylcholine at synapses and myoneural junction and leads to cholinergic over activity.[6-8] Mortality rate ranges from 4% to 38% in Indian studies.

The most common cause of death is due to respiratory failure. Early recognition and prompt ventilatory support may improve the survival rate.

Objectives was to study the levels of pseudo cholinesterase in plasma as a diagnostic aid in patients with suspected organophosphorus poisoning and to predict the prognosis and mortality based on pseudo cholinesterase level.

The pioneering work of De Clermant P. et al, on the synthesis of TEPP (tetra ethyl pyrophosphate) gave him the honor of conceiving the idea of OPC. Subsequently Lange and Kreuger discovered the biological activity of organophosphorus compound (OPC) esters producing a strong cholinergic effect in human beings Organophosphate (OP) esters.

German scientist Gerhard Schrader also noticed similar effect during his synthetic work and developed a method for TEPP production on a commercial scale.[10] An extensive work by Sobrader on these compounds during the world war II lead to the synthesis of around 2000 compounds like parathion, systox, tabun, sarin etc.[7,9]

OP insecticide reached Indian arena in 1948 and the incidence of human poisoning appear to be increasing in frequency.

During search for compound which can reactivate the cholinesterase inhibited by organophosphorus, Jandorf and Summerson found hydroxylamine capable of detoxifying these compounds. David and Wilson et al introduced PAM (pyridine-2- Aldoxime) as reactivator of cholinesterase enzyme. Cholinesterase exists in two forms in the body,

- Specific (acetyl) true cholinesterase which is seen in Gray matter, erythrocyte, sympathetic ganglion and motor end plates
- Nonspecific (butryl) pseudo cholinesterase seen in Plasma, white matter, intestinal mucosa, liver, pancreas.[11-12]

Mode of intoxication[6,7]

Most OP compounds are extremely lipophilic; hence they are readily absorbed by passive diffusion across lung and gastrointestinal system or skin.

METHODS

This study was undertaken from November 2015 to October 2016 at Kodagu Institute of Medical sciences, Kodagu.

390 patients of suspected organophosphorus poisoning admitted to medical emergency ward and ICU of General Hospital have formed the material for study.

Study design is a hospital based prospective study.

Inclusion criteria

In this study patients 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 patients who are having prior hepatic dysfunction and chronic conditions which may reduce the levels of Butryl cholinesterase levels are also excluded.

A detailed case history was taken as per the proforma and a complete physical examination was done soon after admission and all necessary investigations were done. Serum levels of pseudo cholinesterase on Day 1, Day 2, Day 3 and Day 6 were measured. Normal values of serum pseudo cholinesterase ranges from 4150 to 7200 U/L.

Statistical analysis

All the collected data of 390 patients was analyzed using AP Statistical method, and appropriate statistical test-Chi Square (x2) is used for detecting the p value.

RESULTS

The following observations were made after studying 390 cases of suspected OPC poisoning. All patients were in the Age group from 18-55 years. In this study mean age for both sex is 25.8 years and for males 28.3±10.5 and for females 22.1±5.0 years, majority of patients were in < 20 years age group followed by 21-30 years in both sexes. Out of 390 cases 234 patients were males and 156 were females, hence male and female ratio was 1.5:1.

In the study, major occupation of patients was farmers constitute 38 % (148 patients) followed by students 28% (108 patients), housewife constitute 20% (80 patients), labor class were 12 %.

Type of OP poisoning consumption in the study is as follows Parathion in 62 patients (16%), monocrotphos in 47 patients (12%), endosulphan in 39 patients (10%), dimethoate in 7 patients, endrine in 16 patients (4%), unknown poisoning made 56% (n-219) as most of the

patients won't bring consumed bottles with them and most were uneducated in villages.

Table 1: Time lapse between consumption and admission and its relation to severity.

Interval	No. of Cases	Percentage	Mild	Moderate	Severe
0-2	94	24	56	16	22
2-4	132	34	61	47	24
4-6	47	12	42	3	2
>6	117	30	42	33	42

Most of the patients were admitted within 4 hours of consumption. 24% of patients have admitted within 2 hours and 26% were brought after 6 hours. As per above Table as the interval between consumption of poison and admission to hospital increases the severity also increased. 195 patients of total 390 cases were of mild grade and they constitute 50% of total cases. 26% (101 cases) were of moderate grade and remaining 24% (94 patients) were of severe grade of poisoning.

Table 2: Pseudo cholinesterase activity on day 1.

Pseudo-cholinesterase levels	Survived		Expired		Total cases
	No	%	No	%	
<4000 U/L	149	82.8	31	17.2	180
4001-5000 U/L	136	92	12	8.0	148
>5001 U/L	55	88.7	07	11.3	62
Total	340	87.2	50	12.8	390

X2 (chi-square test) =1.32, DF (degree of freedom) =2, p-value=0.52.

Regarding the amount of consumption of poisoning, 48% (187 patients) consumed around 50-100ml, 26% (101 patients) consumed more than 100ml rest were consumed less than 50ml. severity of poisoning depends on quantity of consumption, age, sex and built of the person.

Clinical features of patients in this study were as follows, diarrhoea (96%), vomiting (100%), excessive sweating (68%), difficulty in breathing (42%), features of pulmonary edema (6%), cyanosis (18%), miosis (46%), fasciculations (14%), convulsions (10%).

180 Patients had values below 4000 UI and of these 149 patients (82.8%) survived while 31 patients (17.2%) expired. 148 patients had enzyme levels between 4000-5000 U/L of which 136 patients (92%) survived and 12 patients (8%) expired. Out of 62 patients who had values above 5000 UI, 55 survived (88.7%) and 7 expired (11.3%). From the above observation, it is noted that when enzyme activity was below 4000 U/L the survival rate was 82.8% and when enzyme levels are 5000 UI and above the survival rate has increased to 88.7%. The above finding is also showing that prognosis was better when patient had higher level of enzyme activity on 1st day.

Table 3: Pseudo cholinesterase activity on day 2.

Pseudo cholinesterase levels	Survived		Expired		Total cases
	No	%	No	%	
<4000U/L	70	81.4	16	18.6	86
4001-5000 UIL	195	89.4	23	10.6	218
>5001 U/L	78	90.7	8	9.3	86
Total	343	88	47	12.0	390

X2 (chi-square test) =0.53, p-value =O.77, DF (degree of freedom) =2.

Values from 2nd day shows that when enzyme activity was less than 4000 U/L, the survival was 81.4% while when the values are 5001 U/L and above the survival has improved to 90.7%. These observations were like findings on first day indicating that raising values of pseudo cholinesterase was consistent with better prognosis.

Table 4: Pseudo cholinesterase activity in day 3.

Pseudo cholinesterase levels	Survived		Expired		Total cases
	No	%	No	%	
<4000U/L	39	70.9	16	29.1	55
4001-5000 U/L	195	89.4	23	10.6	218
>5001 U/L	109	93.2	8	6.8	117
Total	343	88.0	47	12.0	390

Values of 3 day showed that when pseudo cholinesterase levels are below 4000 U/L. The survival was 70.9% and when 5001 U/L and above the survival rate has increase to 93.2%. The findings on 3rd were similar to 2nd day.

In patients with level less than 4000, the mortality was 100% Out of 156 patients with levels between 4001-5000 U/L the survival rate was 75% and 25 % of patients expired, in patients with level more than 5000 U/L survival rate was 100%.

Table 5: Pseudo cholinesterase activity on day 6.

Pseudo cholinesterase level	Survived		Expired		Total cases
	No	%	No	%	
<4000U/L	0	0	6	100	6
4001-5000U/L	117	75	41	25	158
>5001 U/L	226	100	-	0	226
Total	343	88	43	12	390

X2 (chi-square test) = 14.5 p-value <.05, significant DF (degree of freedom) =2.

Patients who survived showed raising values of pseudo cholinesterase 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 on subsequent Days i.e., 4315, 4115, 4571, 4319 U/L.

Table 6: Mean pseudo cholinesterase activity of patients who survived and those who expired.

Day	Survived	Expired
	Mean±SD	Mean±SD
1	4346±1098	4315±2630
2	4501±929	4115±1635
3	4703±837	4571±756
6	5427±829	4319±339

X2 (chi-square test) =1.32, DF (degree of freedom) =2, t=0.05, p-value =O.96 not significant-day 1
X2 (chi-square test) =0.53, DF (degree of freedom) =2, t=0.86, p-value =0.39 not significant -day 2
X2 (chi-square test) =2.27, DF (degree of freedom) =2, t=0.36, p-value =0.72 not significant-day 3
X2 (chi-square test) =14.5, DF (degree of freedom) =2, t=2.94, p-value =<O.O5 Significant-day 6.

It was observed that in patients who survived and had increasing levels of pseudo cholinesterase activity of 3.5% on 2nd day and further rise of 4.48% on 3rd day and arise 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 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.

DISCUSSION

Organophosphorus compound poisoning exposure from intentional and accidental exposure is a major public health problem in the developing world.[4] Many self-poisoning shows that it is an impulsive response to difficult or even minor situations. Majority of Indian population is involved in agriculture, hence the incidence of suicidal OPC poisoning is increasing because of easy access to highly toxic pesticides in the situations of stress.[6,8]

For most of the youngsters self-poisoning seems to be preferred method of dealing with difficult situation. Sociologists claim that most young population have no support from system and are unable to cope up with social and cultural demands.[6,7] Organophosphate and carbamate group forms the major group of poisons used in countries like India.[6,9]

In this study, maximum incidence of poisoning was among 20-30 years of age (78%), Which was comparable to studies done by Shankar PS et al and God et al.[7]

Parathion was the commonest used OPC in this study which was comparable to God A et al and Avasthi et al studies.[2,7]

Respiratory failure was the most common complication seen, this is little higher than the studies by God et al and Sangur et al.[7] Observations from this study shown that patients with higher pseudo cholinesterase activity on day of admission has a better prognosis than with lower enzyme values. Similar findings were noted on day 2' and 3.

Hence, it can be concluded that initial estimation of pseudo cholinesterase activity can be used to predict the prognosis of patients. Recent studies by Kuppuswamy G et al showed that pseudo cholinesterase activity belo* 10% of normal were associated with poor prognosis. Also observed that pseudo cholinesterase in plasma is more sensitive than acetylcholinesterase to inhibition by many compounds and is depressed well below the normal range of 60% before any symptoms due to systemic anti-cholinesterase intoxication is evident. Pseudo cholinesterase 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 2' day, 4.48% on 3rt day and 6.88% on 6 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 pseudo cholinesterase activity was consistent with better outcome.

Data from patients who died showed that out of 47 patients who expired, majority had enzyme value around 4300 U/L, which is lower limit of normal value. These observations show that lower the levels of enzyme at admission the more is the mortality.

CONCLUSION

In initial stages of poisoning determining pseudo cholinesterase activity form a reliable diagnostic test.

Mean pseudo cholinesterase 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 pseudo cholinesterase 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.

The mortality was 47 out of 390 cases. Low levels of enzymes in initial stages of poisoning indicates increased mortality.

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