



### Original Research Article

## A study of acute organophosphorus compound poisoning in a rural hospital with reference to pseudocholine esterase levels

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### **Abstract**

**Background & Objectives:** *India is a tropical country where agriculture forms the backbone of the nation. Majority of the population is engaged in agriculture and the most hazardous materials that the farmers are exposed to are the organophosphorus compounds which are used as pesticides. In addition to the accidental intoxication from use of these compounds as agricultural insecticides, these agents are frequently used for suicidal purposes because of their easy availability.*

*This study was done to assess the severity of symptoms of organophosphorus compound poisoning both clinically, by Peradeniya organophosphorus poisoning scoring system and by pseudocholine esterase estimations. Peradeniya scoring system could be a simple and effective system to determine the cases which would require ventilator support, early on in the course. This study will help us identify the factors, which help in the need for ventilator support in a patient with consumption of organo phosphorus compound.*

**Methods:** *This randomized cross sectional study was carried out in Sri Adichunchanagiri institute of medical science and research centre, B.G.Nagara, Mandya district on 100 patients admitted in intensive care unit of the hospital.*

*Pseudocholine esterase estimations was done at presentation. Subsequent pseudocholine esterase estimations was done at 24 hours, 48 hours and 120 hours after time of poisoning.*

*Diagnosis was made on clinical history, physical examination & investigations, which include pseudocholine esterase levels.*

**Results:** *92% of the cases were suicidal and 8% were accidental. The mortality was 4% in this study. Out of the 100 cases 68 were males and 32 were females. The male and female ratio was 2.125: 1. The maximum number of cases was seen in the age group of 18 to 30 years. Maximum number of cases were from agricultural background. In this study 52% of the cases consumed dimethoate. PChE activity in 10 control patients had values in range of 3714 – 11513 u/l, which is within the normal reference values. 79% of cases in the present study had PChE levels of less than 50% of the normal at the time of admission and out of which 94.8% required ventilatory support.*

*Pseudocholine esterase levels were significantly depressed in patients who required ventilatory support. Patients who survived showed rising values of mean pseudocholine esterase enzyme activity on successive days, while patients who expired had low pseudocholine esterase activity and did not show much increase in subsequent days.*

*This points out that better prognosis is directly proportional to higher rise in enzyme activity. Increased interval between consumption and hospitalization correlated with need for ventilatory support. Peradeniya scores of  $\geq 6$  correlated with an increased requirement of ventilatory support.*

**Interpretation & Conclusion:** *Pseudocholine esterase levels were significantly depressed in patients who required ventilatory support. Patients who survived showed rising values of mean pseudocholine esterase enzyme activity on successive days, while patients who expired had low pseudocholine esterase activity and did not show much increase in subsequent days. This points out that better prognosis is directly proportional to higher rise in enzyme activity. Signs of miosis, fasciculations, bradycardia, increased respiratory rate with cyanosis and impaired levels of consciousness all correlated with the need for ventilator support. Increased interval between consumption and hospitalization correlated with need for ventilatory support. Peradeniya scores of  $\geq 6$  correlated with an increased requirement of ventilatory support.*

**Keywords:** *Organophosphorus compound ;Pseudocholine esterase.*

## Introduction

Organophosphorus compound poisoning is a major health problem not only in developing countries but also in western countries.<sup>1</sup> Hospital based statistics suggest that nearly half of the admissions to emergency with acute poisoning are due to Organophosphorus compound poisoning.<sup>2</sup>

Organophosphorus compounds were first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control.<sup>5</sup>

Organophosphorus compound poisonings are found to be a leading cause of death in agricultural countries globally.<sup>3-4</sup> Organophosphorus compounds poisoning affects globally approximately 3 million population and causes 2,00,000 deaths annually, most of these occur in developing countries.<sup>6</sup>

Organophosphorus compounds are easily available as insecticides in shops and have resulted in a gradual increase in suicidal & accidental poisoning. Nearly 90% of the poisoning are suicidal with a fatality rate of  $>10\%$ . 8-10% accidental and  $<1\%$  Homicidal. Occupational exposure accounts for  $1/5^{\text{th}}$  of accidental poisoning with fatalities of  $<1\%$ .<sup>7</sup>

The organophosphorus compounds are the organic derivatives of phosphorous containing acids. The

phosphonate, which are organic derivatives of phosphoric acid are, not used as insecticides but are used as chemical warfare agents. Organophosphorus compounds combine with esteratic sites of acetyl cholinesterase, that is phosphorylated & phosphorylated esteratic sites undergo hydrolysis. The phosphorylated enzyme is inactive and thus unable to hydrolyze acetylcholine. The biological effects of organophosphorus compound are as a result of accumulation of endogenous acetylcholine at sites of cholinergic transmission. This causes disruption of transmission of nerve impulses in both peripheral & central nervous system. Most organophosphorus compounds are readily absorbed through respiratory, oral mucous membrane, GIT mucous and through intact skin, as they are lipid soluble. This binding is irreversible, except with early pharmacological intervention.<sup>8</sup>

The diagnosis is based on the history of exposure and features of cholinergic overactivity.<sup>9</sup> The treatment includes atropine or glycopyrrolate, which acts as a physiological antidote, PAM which help in reactivating the enzyme. Complications like respiratory failure, CNS depression & ventricular arrhythmias should be anticipated & treated.

The early causes of death in organophosphorus compound poisonings are chiefly related to ventricular arrhythmias, CNS depression, seizures

or respiratory failure due to excessive bronchial secretions, bronchospasm, pulmonary edema, aspiration of gastric contents, paralysis of respiratory muscles or apnea associated with depression of the medullary respiratory center.<sup>10</sup> Late mortality is associated with respiratory failure<sup>11,12</sup> and infections like pneumonia, septicemia or complications related to mechanical ventilator and intensive care management.<sup>13</sup> As a treatment modality for this complication ventilator is required.

This study will help us to identify the factors, which help in predicting the need for ventilatory support in a patient with consumption of organophosphorus compound.

**Aims and Objectives of the Study**

1. To estimate the level of pseudocholine esterase in organophosphorus compound poisoning.
2. To correlate pseudocholine esterase level and clinical parameters with need for ventilator support.
3. To study the level of pseudocholine esterase in plasma as a diagnostic aid in patient suspected of organophosphorus poisoning.
4. To predict the prognosis and mortality based on pseudocholinesterase activity.

**Classification**

Holmstedt proposed a classification system for organophosphorus that is of pharmacological and toxicological interest.

The compounds are divided into 5 groups with a few relevant examples.<sup>16</sup>

- Group A: (X: Halogen, Cyanide, and Thiocyanate)  
 E.g.: Disopropylphosphorofluoridate (DFP)  
 ISO propyl methyl phosphorofluoridate (SARIN)  
 Pinacolyl Methyl phosphorofluoridate (SOMAN)
- Group B: (X: Alkyl, alkoxy, aryloxy)  
 E.g.: Forstenon, DDVP, Pyrazoxon
- Group C: (X: Thiol or Thiophosphorous Compound)

E.g.: Parathion, Malathion, Azethion, Diazinon, Systox, and Demeton

Group D: (Pyrophosphates and related compounds)

E.g.; TEPP, DPDA, OMPA

Group E: (Quaternary Ammonium Compound)

E.g.: Phospholin

An older more commonly used classification divides these compounds into:

- 1) Alkyl phosphates (Eg. TEPP, HETP, OMPA, Malathion, Systox, DFP etc).
- 2) Aryl Phosphates (Eg. Demeton, Parathion, EPN, Chlorothion, Diazinon, etc).

**Clinical Features**

The clinical manifestations of organophosphorus poisoning are a result of cholinergic over activity and can be divided into the effects of over stimulation of the muscarinic, nicotinic and CNS receptors.<sup>5</sup>

Muscarinic Receptors	Nicotinic Receptors	Central Receptors
<b>CVS</b>	<b>Muscles</b>	
Bradycardia	Fasciculations	Altered Consciousness
Hypotension	Weakness	Respiratory Depression
	Paralysis	Cheyne-Stokes Respiration
<b>GIT</b>	Cramps	Dysarthria
Salivation	<b>CVS</b>	Tremors
Nausea	Tachycardia	
Vomiting	Hypertension	
Abdominal Pain		
Diarrhea		
Tenesmus		
Feecal Incontinence		
<b>RS</b>		
Bronchorrhea		
Wheezing		
Cough		
<b>Eye</b>		
Miosis		
Lacrimation		
<b>Skin- moist</b>		

The clinical diagnosis is based on:

- a. history of exposure
- b. The presence of several of the above symptoms and signs.

The time interval between the exposure and onset of symptoms and signs varies with the route and degree of exposure. The interval maybe within 5 minutes after massive ingestion and is almost always less than 12 hours. The severity of manifestation varies with the degree of poisoning.

Namba et al<sup>9</sup> have made a classification of organophosphorus poisoning insecticide which is modified from Grob et al<sup>25</sup> is as follows: -

#### **Latent poisoning**

No clinical manifestations are seen. Diagnosis based on estimation of serum cholinesterase activity, which is inhibited by 10 to 50%

#### **Mild poisoning**

The patient complains of fatigue, headache, dizziness, nausea, vomiting, excessive sweating, salivation, abdominal cramps or diarrhea. Serum cholinesterase levels are 20-50% of normal values.

#### **Moderate poisoning**

The patient complains of generalized weakness, difficulty in talking, muscular fasciculations and miosis. Serum cholinesterase levels are 10-20% of normal values.

#### **Severe poisoning**

Marked miosis, loss of pupillary reflex to light, muscular fasciculation, flaccid paralysis, and secretions from the mouth and nose, rales in the lungs, respiratory difficulty and cyanosis are seen in patients with severe poisoning. Serum cholinesterase levels are lower than 10% of normal values.

However, this proposed grading has proved unworkable in clinical practice because of many varied clinical criteria in different grades, as well as the difficulty in remembering and applying them in acute clinical situation.<sup>5, 12</sup>

The second classification was proposed by Bardin et al<sup>12</sup> and is as follows: -

Grade 0 Positive history

No signs of organophosphorus poisoning.

Grade 1 Mild secretions,

Few fasciculations,

Normal level of sensorium.

Grade 2 Copious secretions,

Generalized fasciculations,

Rhonchi, crepitations,

Hypotension (systolic BP <90mmHg)

Disturbed level of consciousness, not stuporous

Grade 3 Stupor,

PaO<sub>2</sub> < 50mmHg,

Chest roentgenogram abnormal.

This study by Bardin<sup>12</sup> et al showed that patients with grade 3 manifestations on admission were associated with increased requirement for mechanical ventilator. The presence of other complications and increased days of ICU stay have been observed in the above patients.

The Peradeniya organophosphorus poisoning scale is an effective scoring system to know the severity of OP poisoning and also for identification of those patients who might require ventilator support.

## **Materials and Methods**

### **Design of the study**

The current study is a randomized cross sectional one. The subjects of the study were taken randomly fulfilling the inclusion criteria and pseudo choline esterase estimations was done at presentation. Subsequent pseudo choline esterase estimations were done at 24 hours, 48 hours and 120 hours after time of poisoning.

### **Source of data**

Study was carried out at Sri Adichunchanagiri institute of medical science and research center B.G.Nagara, Mandya district.

The study was conducted for a proposed period 18 month of 100 patients admitted to intensive care unit of in Sri Adichunchanagiri Institute of medical sciences and research center, B.G.Nagar and fulfilling the inclusion criteria.

Diagnosis was be made on clinical history, physical examination & investigations, which include pseudo choline esterase levels.

### **Inclusion Criteria**

Those patients with history of organophosphorus poisoning or of unknown poison with characteristic symptoms of organophosphorus

compound poisoning both sexes aged above 18 years.

**Procedure**

Three milliliters of plain blood was drawn on admission and at 24, 48 and 120 hours from 100 patients with history of organophosphorus compound poisoning and sent to biochemistry laboratory for estimation of pseudo choline esterase levels. The pseudo choline esterase level was determined by Labkit Choline esterase reagent.

**Principle**

Choline esterase hydrolyses butyryl thiocholine to butyrate and thiocholine. Thiocholine reacts with 5,5'-dithio bis-2-nitrobenzoic acid (DTNB) to form 5-mercapto-2-nitrobenzoic acid (MNBA) which has an intense yellow colour.

Reference values of pseudo choline esterase by 'Lab Kit' test at 30<sup>0</sup>C 3714-11513 u/l

**Statistical tests**

Categorical variables were analysed and chi square test was used. Continuous variables were analysed using student 't' test.

Differences in sociodemographic characteristics like age, sex, type of poison consumed and quantity of poison consumed was analysed. Later patients were compared with their pseudo choline esterase levels and requirement of ventilatory support. The test of significance used between the associations of different characteristics was the Chi square test. For statistical significance, the p value was calculated and a value less than 0.05 was considered significant. SPSS 16 software was used to analyse the data.

**Ethical issues**

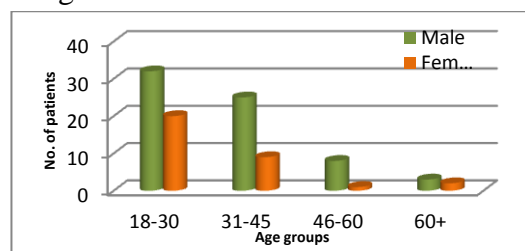
Written informed consent was taken from each patient / guardian after explaining about the study under taken. Clearance from the college ethical committee was sought and taken.

**Results**

The following observations were made after studying 100 cases of organophosphorus poisoning admitted to Sri Adichunchanagiri Institute of medical sciences and research centre,

B.G. Nagara, Mandya district, in the intensive care unit, from November 2009 to April 2011.

**Fig.1:** Age and sex distribution



Highest incidence was seen in the age group of 18 – 30 years (52%), followed by 31 – 45 years (34%). This age group corresponds to the maximum period of stressor events. Expectations exceed the reach of many and they find it difficult to adapt to these challenges. (Vyas & Ahuja, 1999). In the present study 68% of the patients were males. This correlates with the findings of the previous studies. However, in a study done by M. Vishwanathan et.al,66% of the patients who consumed organophosphorus compounds were females.

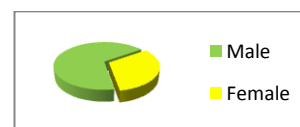
**Table – 1:** Percentage of age and sex distribution.

		SEX		Total
		Male	Female	
AGES	18-30	32	20	52
		47.1%	62.5%	52.0%
	31-45	25	9	34
		36.8%	28.1%	34.0%
	46-60	8	1	9
		11.8%	3.1%	9.0%
	60+	3	2	5
		4.4%	6.3%	5.0%
Total		68	32	100

**Table -2:** Frequency of age distribution

		Frequency	Percent
Valid	18-30	52	52.0
	31-45	34	34.0
	46-60	9	9.0
	60+	5	5.0
	Total	100	100.0

**Fig.2 :** Sex ratio.

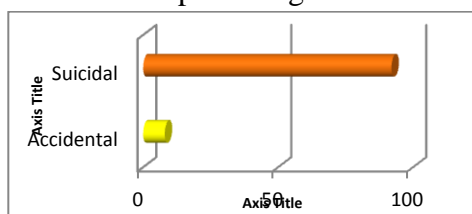


**Table- 3:** Frequency of sex distribution

		Frequency	Percent
Valid	Male	68	68.0
	Female	32	32.0
	Total	100	100.0

In this study, most of the cases was suicidal,92% & accidental was 8%.In some cases suicidal intention was denied & in some pain abdomen ,headache, burning feet ,vomiting precipitated the accidental consumption of the poison unwittingly. This corresponds to the study by Gupta et.al., (1968) when out of 60 cases,55 (91%) were due to suicidal intention & 5(8%) were due to accidental consumption.

**Fig. 3 :** Intention of poisoning.



**Table-4 :** Percentage of intention of poisoning

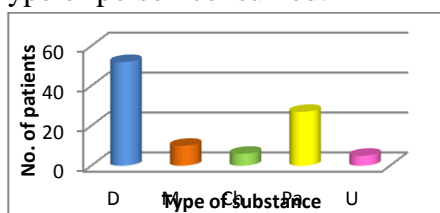
		Frequency	Percent
Valid	Accidental	8	8.0
	Suicidal	92	92.0
	Total	100	100.0

**Test Statistics**

	Intention
Chi-Square	70.560
Df	1
Asymp. Sig.	.000

**Frequencies**

**Fig.4:** Type of poison consumed.

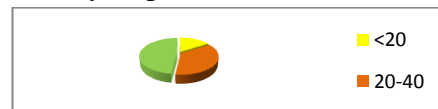


**Table-5:** Percentage of type of poison consumed

	Frequency	Percent
Dimethoate (D)	52	52.0
Monocrotophos(M)	10	10.0
Chloropyriphos(Ch)	6	6.0
Parathion(Pa)	27	27.0
Unknown(U)	5	5.0
Total	100	100.0

In this study majority of the patients took dimethoate, 52%, the next common poison was parathion, 27% & monocrotophos was seen in 10% of the cases. Chloropyriphos was taken in 6% of the cases & 5% of the cases the compound was unknown.

**Fig.5:** Quantity of poison consumed.



**Table -6:** Percentage of quantity of poison consumed

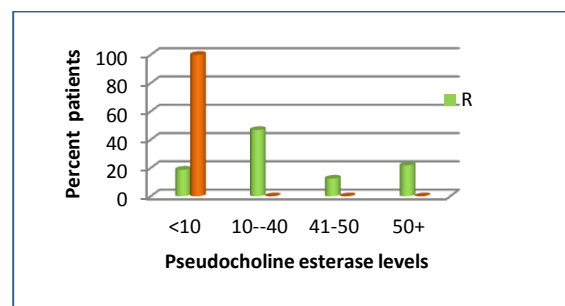
	Frequency	Percent
<20ml	16	16.0
20-40ml	36	36.0
40+ml	48	48.0
Total	100	100.0

**Test Statistics**

Chi-Square	15.680
Df	2
Asymp. Sig.	.000

The majority of the patients took more than 40 ml of the poison,48%.16% of of the patients took less than 20 ml of the poison.

**Fig.6:** Pseudocholine esterase levels at the time of admission & death



The decreased levels of pseudocholine esterase levels is highly specific for diagnosis of organophosphorus poisoning and particularly useful in suspected organophosphorus compound patients. The patients with higher pseudocholine activity on day of admission had a better prognosis than with a lower enzyme values. Similar findings were noted on 2<sup>nd</sup> & 3<sup>rd</sup> days. These observations were statistically significant. It can be concluded that initial estimation of pseudocholine esterase activity can be used to predict the prognosis of the patient.

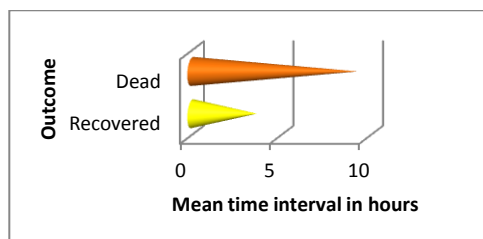
**Table-7:** Percentage of Pseudocholine esterase levels at the time of admission & death

ENZYME ACTIVITY ON ADMISSION					Total
			RECOVER	DEATH	
<10%	Count	18	4	22	
	% within DEATH	18.8%	100.0%	22.0%	
10-40%	Count	45	0	45	
	% within DEATH	46.9%	.0%	45.0%	
41-50%	Count	12	0	12	
	% within DEATH	12.5%	.0%	12.0%	
50% +	Count	21	0	21	
	% within DEATH	21.9%	.0%	21.0%	
Total		Count	96	4	100
		% within DEATH	100.0%	100.0%	100.0%

**Symmetric Measures**

			Value	Approx. Sig.
Nominal	by	Contingency	.359	.002
Nominal		Coefficient		
N of Valid Cases			100	

**Fig.7:** Mean time interval to reach the hospital & outcome.



The patients who recovered the mean time to reach the hospital was 3.63 hours & less & the patients who died the mean time to reach the hospital was 9.25 hours & more.

In this study, PChE activity was estimated on 3 successive days after admission, it was found that the mean PChE activity of patients who survived showed rising values on successive days. While patients who expired had low PChE activity on admission and did not show much increase in subsequent days, these findings show that there is greater chance of survival if the PChE activity increases substantially on successive days. It can be concluded from the study that early death was associated with low PChE activity on admission and the mortality which was 4% in this occurred within the 48 hours of admission.

**Conclusion**

One hundred cases of organophosphorus poisoning in adults aged above 18 years were studied clinically and pseudocholine esterase levels were estimated. The following observations were made.

1. The most vulnerable group was that between 18 – 30 years, next being 31 - 45 year group.
2. Male to Female ratio was 2. 125 : 1
3. Dimethoate was the commonest poison take compared to the past when diazinon was the commonest poison taken.
4. Majority of patients consumed more than 40ml of poison.
5. All the patients took the poison orally.
6. In most patients the intention of poisoning was suicidal, 92%.
7. Most patients consumed the poison after 6p.m. in the evening.
8. Majority reached the hospital within 4hrs of consumption.
9. Pseudocholine esterase levels were significantly depressed in patients who required ventilatory support. Patients who survived showed rising values of mean pseudocholine esterase enzyme activity on successive days, while patients who expired had low pseudocholine esterase activity and did not show much increase in subsequent days. This points out that better prognosis is directly proportional to higher rise in enzyme activity.
10. Signs of miosis, fasciculations, bradycardia, increased respiratory rate with cyanosis and impaired levels of consciousness all correlated with the need for ventilator support.
11. Increased interval between consumption and hospitalization correlated with need for ventilatory support.
12. Peradeniya scores of  $\geq 6$  correlated with an increased requirement of ventilatory support.
13. Estimation of pseudocholine esterase level in clinically suspected organophosphorus compound poisoning cases –

- Will assist in diagnosis of unidentified or organophosphorus compound poisoning.
- Will be a very useful parameter along with Peradeniya organophosphorus poisoning (POP) scale in predicting the need for early requirement of ventilator support.

### Summary

The study was conducted on 100 patients with history of organophosphorus compound poisoning admitted in the intensive care unit of Sri Adichunchanagiri institute of medical sciences and research centre, B.G.Nagara, Mandya district . 92% of the cases were suicidal and 8% were accidental. The mortality was 4% in this study. Out of the 100 cases 68 were males and 32 were females. The male and female ratio was 2.125: 1. The maximum number of cases was seen in the age group of 18 to 30 years. Maximum number of cases were from agricultural background.

In this study 52% of the cases consumed dimethoate. PChE activity in 10 control patients had values in range of 3714 – 11513 u/l, which is within the normal reference values. 79% of cases in the present study had PChE levels of less than 50% of the normal at the time of admission and out of which 94.8% required ventilatory support.

Pseudocholine esterase levels were significantly depressed in patients who required ventilatory support. Patients who survived showed rising values of mean pseudocholine esterase enzyme activity on successive days, while patients who expired had low pseudocholine esterase activity and did not show much increase in subsequent days. This points out that better prognosis is directly proportional to higher rise in enzyme activity.

Increased interval between consumption and hospitalization correlated with need for ventilatory support. Peradeniya scores of  $\geq 6$  correlated with an increased requirement of ventilatory support.

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#### List of Abbreviations

- PChE - Pseudocholine esterase.  
O.P.Compound - Organophosphorus compound.  
POP score - Peradeniya organophosphorus score.  
AchE- Acetylcholinesterase.