

# Study on Plasma Pseudocholine Esterase Levels in Organophosphate Poisoning and it's Outcome

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## ABSTRACT

Published on 27<sup>th</sup> September 2017

**Background and Objective:** DSH is a major problem in the developing world.<sup>1</sup> Poisoning is one of most common methods employed for the act of DSH. The delay in attaining medical care and the lack of facilities in the rural areas have resulted in increased number of deaths due to OP poisoning. In this study, we aim to find out the most common OP compound used for DSH and the variation in the level of PCE with respect to various compounds. Also the prognosis and outcome of each patient are assessed in relation to the PCE values.

**Methods:** 100 patients admitted to this hospital were enrolled into this study. After getting informed consent, investigations were carried out especially PCE levels. Serial monitoring of PCE levels was done in each case. The incidence of complications and other measures of outcome were compared with respect to the PCE levels.

**Results:** 66 males and 34 females were studied. 74% of the patients survived following poisoning while 26% expired. Chlorpyriphos was the compound consumed by most of the patients, followed by Quinalphos.<sup>5</sup> 50% death is due to Chlorpyriphos poisoning. The most common symptom was vomiting followed by frothing. 12% of patients had history of psychiatric illness. Crackles were the most common clinical sign which was seen in 66% of the study population.

**Interpretation and Conclusions:** From this study it was revealed that lower the PCE, higher the mortality. Majority of the ventilated patients had PCE levels below 200. The incidence of intermediate syndrome seemed to be a very important factor in the survival of the patient. In this study, all patients who developed IMS expired. PCE levels, ventilator assistance and IMS were all high in the Chlorpyriphos group.

**Keywords:** Organophosphate compounds, IMS, PCE, Chlorpyriphos, Quinalphos

\*See End Note for complete author details

Organophosphate (OP) compounds have been used worldwide for pest control for over 100 years. They are the insecticides of choice in the agricultural world. Organophosphates are cholinesterase inhibiting chemicals used predominately as pesticides. They are also used as chemical warfare agents. They are ubiquitous in the environment. Organophosphates are of significant importance due to their practical usefulness and chemical instability. They do not persist in the body or environment as do organochlorides and have replaced DDT; an organochloride compound.<sup>2</sup> It is becoming apparent that inhibition of choline esterases plays a key role in the toxicology of organophosphates.

## AIM OF THE STUDY

- To assess the variations in plasma pseudocholine

esterase levels in acute OP poisoning.

- To know the difference in plasma pseudocholine esterase levels in different OP compounds
- To assess the clinical outcome according to the levels of pseudocholine esterase.

## REVIEW OF LITERATURE

### Chemistry of Organophosphates

Most Organophosphates are polar, water – soluble chemical but a few lipophilic compounds exist. These organophosphate compounds are inhibitors of serine esterases and serine proteases, and have a high affinity for AChE. During the phosphorylation reaction, the OP molecule is destroyed through stoichiometric reaction with the enzyme.

*Cite this article as:* Baburaj P, George EJ, Harikrishnan BL. Study on Plasma Pseudocholine Esterase Levels in Organophosphate Poisoning and it's Outcome. Kerala Medical Journal. 2017 Sep 27;10(3):110-3.

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## Classifications

1. Highly toxic organophosphates: (e.g. tetra – ethyl pyrophosphates, parathion). These are mainly used as agricultural insecticides.
2. Intermediately toxic organophosphates: (e.g. coumaphos, chlorpyriphos, trichlorofos). These are used as animal insecticides.
3. Low toxicity: (e.g. diazinon, Malathion, dichlorvos). These are used for household application and as field sprays.

## MECHANISM OF ACTION

Acetylcholine (ACh) is the neurotransmitter released at all postganglionic parasympathetic nerve endings and at the synapses of both sympathetic and parasympathetic ganglia. It is also released at the skeletal muscle myoneural junction, and serves as a neurotransmitter in the central nervous system.<sup>3</sup> ACh is hydrolyzed by acetyl cholinesterase into two fragments: acetic acid and choline.

Acetyl cholinesterase



Acetyl cholinesterase (AChE) is present in two forms:

1. True acetyl cholinesterase (AChE)/ erythrocyte cholinesterase which is found primarily in the tissues and erythrocytes
2. Pseudocholine esterase/ butyrylcholine esterase (BuChE) which is found in the serum and liver.

The amount of AChE activity in red blood cells reflects the state of neuronal and muscular AChE activity. The role of BuChE has not been established. However, it is easy to assay and its activity mirrors AChE closely enough to provide a good marker for cholinesterase function.

## Pharmacokinetics

The signs and symptoms of cholinesterase – inhibitor poisoning are related to their effects on three separate areas of the cholinergic nervous system:

1. Postganglionic parasympathetic hollow end- organ (muscarinic) effects - what have been commonly called the “wet findings” – “SLUDGE”. These are characterized by excessive salivation, lacrimation, bronchorrhoea, urinary and fecal incontinence,

and vomiting.<sup>4</sup> Bronchoconstriction is a muscarinic finding, as is miosis

2. Sympathetic and parasympathetic ganglionic and somatic neuromuscular junction (nicotinic) effects - Nicotinic stimulation impairs muscular activity at the level of the neuromuscular junction. Neuromuscular findings include muscular fasciculations, muscle cramping, weakness, and paralysis of muscles including diaphragm.
3. CNS effects - anxiety, restlessness, headache, tremor, confusion, slurred speech, delirium, psychosis, seizures, and death. Ataxia, absent reflexes, insomnia, tremors, coma, hyperreflexia and Cheyne Stocks breathing are all described.

## Laboratory Studies

Organophosphate (OP) toxicity is a clinical diagnosis. Confirmation of organophosphate poisoning is based on the measurement of cholinesterase activity. Although RBC and plasma (pseudo) cholinesterase levels can both be used, RBC cholinesterase correlates better with CNS acetyl cholinesterase (AChE) and is, therefore, a more useful marker of OP poisoning.

## MATERIALS AND METHODS

Type of study : Descriptive Study

Duration of study : 18 months from 01.01.2012 to 31.6.2013.

## METHODOLOGY

**Study setting:** Jubilee Mission Medical College & Research Institute

**Study Objects:** All acute Organophosphate poisoning

**Inclusion Criteria:** Acute poisoning cases with evidence of OP compound.

**Exclusion Criteria:**

1. All cases of OP poisoning brought dead or dying within hours following hospitalization.
2. Those cases which could not be investigated fully.
3. Patients below 12 years of age.

The diagnosis of OP poisoning was based on the compound brought to the hospital. We could not confirm the diagnosis by sending the molecule for toxicology assessment since these are not done in our

hospital and due to financial constraints, it could not be done from outside as well.

**Investigations & Treatment:** Routine investigations and plasma Pseudocholine esterase level estimation were done. All the patients were given atropine as per protocol in the form of repeated double doses starting from 0.6mg of atropine till the chest became clear followed by infusion. 80% of the patients were given PAM 30mg/kg over 15 minutes bolus dose and then 2mg/hr infusion for the next 2 days. It was tried in cases where patients reached the hospital soon after the consumption of the poison. PAM was not tried in those reaching the hospital after 36 hours after the ingestion of the OP compound.<sup>2</sup>

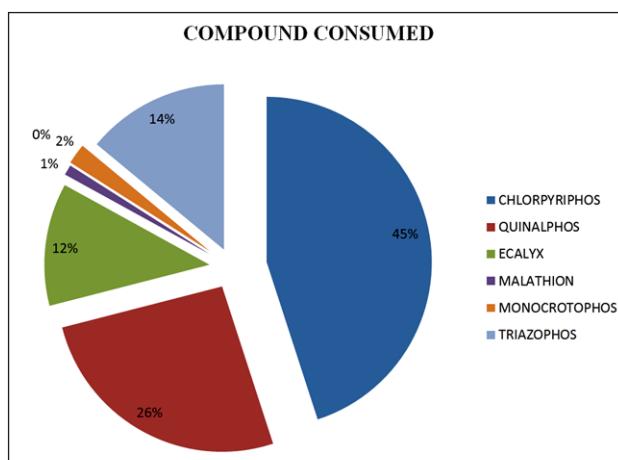
## RESULTS

The mean age of the patients was 34 with standard deviation of 13.3. The minimum age was 12 years and maximum age was 74 years (**table 1**).

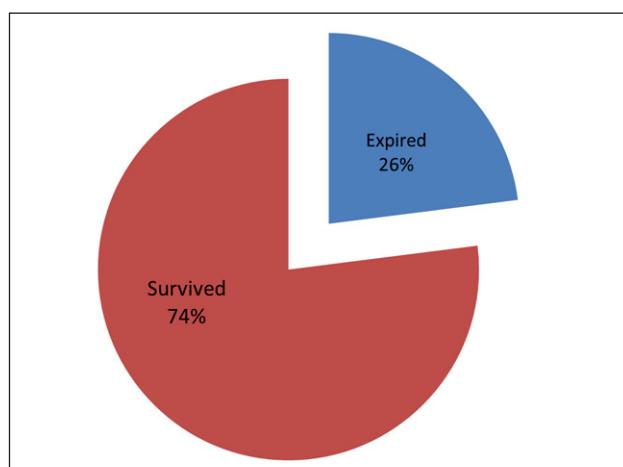
Chlorpyriphos was the compound consumed by most of the patients, followed by Quinalphos (**figure 1**).

**Table 1.** Table showing Age and Sex wise distribution percentage of patients admitted with OP poisoning

Age group	Number of Patients (Male/Female)	Percentage
10 to 20 years	10 (3,7)	10
20 to 30 years	36 (22,14)	36
30 to 40 years	30 (20,10)	30
40 to 50 years	10 (7,3)	10
50 to 60 years	07 (4,3)	7
60 to 70 years	05 (2,3)	5
70 to 80 years	02 (2,0)	2
80 to 90 years	0	0
<b>TOTAL</b>	<b>100</b>	<b>100</b>



**Figure 1.** Pie Chart showing percentage of OP Compounds consumed by patients



**Figure 2.** 74% of the patients survived following poisoning while 26% expired

**Table 2.** Table showing outcome of patients according to Pseudocholine esterase levels

Parameter	Response	Survived	Expired
	<200	3	21
Pseudocholine esterase levels	200-1000	17	4
	>1000	54	1

## Poisoning and Outcome

### Pseudocholine Esterase Levels and Outcome of the Patients

From this study it is revealed that lower the level of PCE (**table 2**), higher the mortality is. Higher the value of plasma PCE levels, there is more chance of recovery. The decreased PCE level is useful in suspected OP compound patients. Those with higher PCE levels had a better prognosis than others. These observations were statistically significant and hence concluded that estimation of plasma PCE activity can be used for the prediction of prognosis of the patient. It was also found that patients who survived had rising values of PCE on subsequent days.

### Pseudo Choline Esterase Levels & Ventilatory Support

Majority of the ventilated patients had pseudo choline esterase levels below 200 which mean that lower the value of plasma pseudo choline esterase, higher the chance of respiratory failure and other complications which require ventilator assistance (**table 3**).

**Table 3.** Table showing requirement of ventilatory support according to Pseudocholine esterase levels

Treatment	Response	Survived
	PCE <200	14
Ventilator	PCE <1000	2
	PCE >1000	1

Compound	PCE levels <200	Total
Chlorpyriphos	9	9
Quinalphos	9	9
Rest	6	6

In this study, it is noted that 9 patients each who consumed Chlorpyriphos and Quinalphos had PCE levels below 200 (table 4).

## CONCLUSION

1. Of the 100 consecutive patients, majority belonged to 20-30 years age-group with male predominance
2. Chlorpyriphos was the most common compound to be consumed by most of the patients.
3. Patients with low pseudo choline esterase levels fared badly and they have increased chance of ventilator assistance, intermediate syndrome and death.
4. 21 out of 24 patients who had low PCE levels expired despite our best efforts.
5. The most common clinical sign was crackles (66%) followed by constricted pupil & fasciculations (60% each). Tachycardia was more common than bradycardia. Similarly hypertension was seen in more patients than hypotension. Extensor plantar response was elicited in 32% of the patients, Coma defined as GCS<8 were seen in 9% of the patients.

6. The total mortality rate during the study period was 26% (figure 2)

## END NOTE

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**Conflict of Interest:** None declared

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