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# Evaluation of Organophosphorus Poisoning: Case Series

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**Abstract**

Organophosphate insecticide compounds inhibit both acetyl cholinesterase and pseudocholinesterase activities. Acute organophosphate insecticide poisoning can manifest three different phases of toxic effects namely, acute cholinergic crisis, intermediate syndrome (IMS), and delayed polyneuropathy. Diagnosis is based on history of exposure and clinical manifestations. Management is beneficial with supportive measures along with specific antidotes. In this case reports, two patients with organophosphate insecticide poisoning are described. Both patients tried to commit suicide by ingesting an unknown amount of organophosphorus poison and both of them have developed intermediate syndrome. But one patient collapsed due to cardiac arrest and other patient was discharged with no complaints. Treatment for both patients mainly included atropine and parlidoxime.

**Keywords:** Organophosphorus poison; Intermediate syndrome; Acetylcholine receptor; Atropine; Pralidoxime

## Introduction

Pesticides comprise a wide range of compounds including insecticides, herbicides, fungicides and others. Thus, far more than 1,000 active substances have been incorporated in approximately 35,000 preparations of pesticides used in agriculture [1,2]. During the 1930s, pesticide research in Germany led to the synthesis of numerous organophosphorus compounds including parathion along with several chemical warfare agents (e.g: GA (Tabun), GB (Sarin), and GD [Soman]). Poisoning with organophosphorus (OP) compounds is a global problem. Household exposures usually do not cause a significant problem because insect sprays often contain low-potency cholinesterase inhibitors [3]. World Health Organization estimates, 3 million cases of pesticide poisoning occur every year, resulting in more than 250,000 deaths [4-6] in that one million serious unintentional poisonings occur every year and an additional two million people are hospitalized for suicide attempts with pesticides. India is a predominantly agrarian country where pesticides are routinely used for farming. According to data available from National Poison Information Centre India, suicidal poisoning with house-hold agents (OPs, carbamates, pyrethrinoids, etc.) is the most common modality of poisoning. Recent data from National crime bureau of India shows suicide by consumption of pesticides account for 19.4% and 19.7% of all cases of suicidal poisoning in the year 2006 and 2007 respectively [4]. Toxicity is usually rated low toxicity (LD50>1000 mg/kg), moderate toxicity (LD50 mg/kg to 1000 mg/kg), high toxicity (LD50<50 mg/kg) [3].

According to the oral LD50 in rats, this scale is able to roughly differentiate between very safe and very toxic pesticides-for example parathion (LD50 13 mg/kg WHO: Class IA) is highly toxic while temephos (LD50 8600 mg/kg, WHO: unlikely to cause acute hazard) has not been associated with deaths. However, large differences in human toxicity have been seen after poisoning with organophosphates with roughly the same animal toxicity, and this classification does not account for the effects of treatment [5,6].

## Mechanism of Action

Organophosphate (OP) insecticides compounds inhibit both acetylcholinesterase and pseudocholinesterase activities [7].

Acetylcholine is hydrolyzed by the enzyme cholinesterase to choline and acetate. Choline is actively taken up by the axonal membrane by a $Na^+$ [8-13]. Organophosphate inhibit the enzyme acetylcholinesterase (AChE) found in synaptic junctions, red blood cells (RBCs), and butyryl cholinesterase (also known as pseudocholinesterase or plasma cholinesterase) in the blood. Blockade of AChE leads to the accumulation of excessive acetylcholine at muscarinic receptors (cholinergic effector cells), at nicotinic receptors (skeletal neuromuscular junctions and autonomic ganglia), and in the CNS [3,6,8].

Pseudocholinesterase is a nonspecific type of enzyme occurs in the body at plasma, liver, intestine and white matter. Its main function is hydrolysis of ingested esters. Ach is slowly hydrolyzed, benzoylcholine and butyryl choline is hydrolyzed which cannot be hydrolyzed by acetyl cholinesterase [13].

Permanent inhibition of acetylcholinesterase may occur through covalent binding by the OP to the enzyme. This is known as "aging" and its rate of development is variable and depends on the specific OP. Dimethyl compounds (e.g: dimethoate) generally age more quickly than diethyl agents (e.g: chlorpyrifos). Antidotal treatment with an oxime may delay the onset of aging; early administration of oximes is therefore recommended [3].

Aging has been studied in detail using AChE as the model enzyme. The generally accepted aging mechanism for alkoxy- OP adducts invokes the catalytic participation of residues from the enzyme. Dealkylation of the OP adduct is facilitated primarily by the protonated histidine of the catalytic triad, a glutamic acid residue adjacent to the catalytic serine, and a nearby tryptophan residue [14].

## Intermediate syndrome (IMS)

IMS is well recognized as a disorder of the neuromuscular junction; however, its exact underlying mechanisms are not clearly defined. Senanayake and Karalliedde in their first report of IMS suggested that the syndrome might be caused by pathologic changes in the

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postsynaptic end-plate region of striated muscles because such lesions were described in experimental animals (hens and rats) that developed a similar pattern of paralysis after organophosphate insecticide poisoning [9].

Several researchers stated that oxidative cellular damage to muscle membranes could be another possible mechanism of muscle necrosis but not the involvement of apoptosis. A prospective study of 19 patients with organophosphate poisoning that muscle fiber necrosis was unlikely to be the etiology of IMS because muscle biopsy specimens in patients with IMS showed a few necrotic fibers only [10].

Sedgwick and Senanayake further proposed that downregulation or desensitization of postsynaptic acetylcholine receptors after prolonged acetylcholine stimulation could explain the occurrence of IMS [10].

### Peripheral neuropathy

In addition to CNS sequelae, some cholinesterase inhibitors may cause a delayed, often permanent peripheral neuropathy**.** The mechanism appears to be the result of inhibition of neuropathy target esterase (NTE). Notably, the outbreak of "Jamaican ginger paralysis" in the 1930s was due to drinking rum contaminated with triorthocresyl phosphate [3]. These organophosphates are more potent inhibitors of AChE than of neuropathy target esterase (NTE), which is thought to be the target for organophosphate-induced delayed neurotoxicity (OPIDP). Consequently, OPIDP was found both in hens (the animal of choice for OPIDP studies) and humans only at doses exceeding those which cause cholinergic toxicity [5,11]. High L-NTE inhibition measured soon after exposure is thought to herald the development of OPIDP. Other causes of neuropathy such as diabetes, alcoholism, uraemia, porphyrias, and trauma have been excluded [5].

### Respiratory failure

The pathophysiology of late respiratory failure seems to involve downregulation of nicotinic acetylcholine receptors [12].

## Clinical Manifestations

Acute organophosphate insecticide poisoning can manifest 3 different phases of toxic effects namely, acute cholinergic crisis, IMS, and delayed polyneuropathy [9,10]. Acute cholinergic crisis develops within a few minutes to several hours after exposure [9,11], IMS typically occur within 24 to 96 hours, and affect conscious patients without fasciculation or other cholinergic signs [9]. Organophosphate-related delayed neurotoxic effect, which is commonly referred to as organophosphate-induced delayed neurotoxicity (OPIDN), occurs 2 to 3 weeks after acute exposure to certain organophosphate insecticides [9,11].

### Features due to overstimulation of muscarinic acetylcholine receptors

- Respiratory: Increased bronchial secretions, bronchospasm, chest tightness, dyspnoea, cough
- Eyes: Blurred vision, conjunctival injection, dimness of vision, meiosis
- Gastrointestinal: Abdominal cramping, diarrhea, nausea, vomiting
- Urinary: Incontinence
- Cardiovascular: Bradycardia, hypotension
- Exocrine glands: Hyperamylesia, increased salivation and sweating, fluid losses can lead to systemic hypovolemia, resulting in shock.

### Features due to overstimulation of nicotinic acetylcholine receptors

- Muscle fasciculation, cramping, weakness, diaphragmatic paralysis, respiratory failure, tachycardia, hypertension and death

### Features due to overstimulation of nicotinic and muscarinic acetylcholine receptors in the CNS

- Confusion, agitation, seizures, coma, respiratory failure

### Features due to overstimulation of nicotinic acetylcholine receptors at the neuromuscular junction

- Muscle weakness, paralysis, fasciculations

## Diagnosis

- Is based on the history of exposure and the presence of characteristic muscarinic, nicotinic, and CNS manifestations of acetylcholine excess. There may be a solvent odor, and some agents have a strong garlicky odor.
- Laboratory evidence of poisoning may be obtained by measuring decreases in the plasma pseudocholinesterase (PChE) and red blood cell acetylcholinesterase (RBC AChE) activities.
- The RBC AChE activity provides a more reliable measure of the toxic effect; a 50% or greater depression in activity from baseline generally indicates a true exposure effect.
- PChE activity is a sensitive indicator of exposure but is not as specific as AChE activity (PChE may be depressed owing to genetic deficiency, medical illness, or chronic organophosphorus exposure). PChE activity usually falls before AChE and recovers faster than AChE.
- Other useful laboratory studies include electrolytes, glucose, BUN, creatinine, liver transaminases, arterial blood gases or oximetry, ECG monitoring, and chest X-ray (if pulmonary edema or aspiration of hydrocarbon solvent is suspected) [3].
- The examination of the peripheral nervous system included assessment of gait, deep tendon reflexes, muscle strength, and vibration, pin, light touch, and thermal sensitivities. Plasma butyryl cholinesterase (BuChE) was measured with commercial kits. Red blood cell, AChE, and lymphocytic neuropathy target esterase (LNTE) were determined according to Ellman et al. [11] and to Bertoncin et al. [12] respectively [5].
- Electrophysiologic study has been proposed as a specific diagnostic tool for patients with IMS [9].

## Management

- Likely to be beneficial

o Atropine, benzodiazepines to control organophosphorus induced seizures, glycopyrronium bromide (glycopyrrolate), washing the poisoned person and removing contaminated clothes

- Unknown effectiveness

o Activated charcoal (single or multiple dose), alpha2 adrenergic receptor agonists, butyryl cholinesterase replacement therapy, extracorporeal clearance, gastric lavage, magnesium sulphate, milk

or other home remedy immediately after ingestion, N-methyl-D-aspartate receptor antagonists, organophosphorus hydrolases, oximes, sodium bicarbonate

- Unlikely to be beneficial cathartics
- Likely to be ineffective or harmful *Ipecacuanha* (ipecac) [12].

## Emergency and Supportive Measures

- Maintain an open airway and assist ventilation if necessary. Pay careful attention to respiratory muscle weakness because sudden respiratory arrest may occur. This is often preceded by increasing weakness of neck flexion muscles. If intubation is required, a non-depolarizing agent should be used because the effect of succinylcholine will be extended secondary to the inhibition of PChE. Administer supplemental oxygen.
- Treat hydrocarbon pneumonitis, seizures, and coma if they occur. Seizures should be treated with benzodiazepines such as diazepam, lorazepam, and midazolam.
- Observe asymptomatic patients for at least 8 to 12 hours to rule out delayed-onset symptoms, especially after extensive skin exposure or ingestion of a highly fat-soluble agent.

## Specific Drugs and Antidotes

Specific treatment includes the anti-muscarinic agent atropine and the enzyme reactivator pralidoxime.

- Give atropine**,** 0.5 mg to 2 mg IV initially, then double the dose every 5 minutes until signs of atropinization are present (decreased secretions and wheezing, increased heart rate). The most clinically important indication for continued atropine administration is persistent wheezing or bronchorrhea. Tachycardia is not a contraindication to more atropine.
- Pralidoxime (2-PAM) is a specific antidote that acts to regenerate the enzyme activity at all affected sites prior to aging. Other oximes include obidoxime and HI-6. Oximes may be less effective against dimethyl compounds compared with diethyl agents.
- Pralidoxime should be given immediately to reverse muscular weakness and fasciculations: 1 g to 2 g initial bolus dose (20 mg/kg 40 mg/kg in children) IV over 5 to 10 minutes, followed by a continuous infusion. It is most too effective if started early, before irreversible phosphorylation of the enzyme, but may still be effective if given later, particularly after exposure to highly lipid-soluble compounds. It is unclear how long oxime therapy should be continued, but it seems reasonable to continue it for 24 h after the patient becomes asymptomatic.
- Pralidoxime generally is not recommended for carbamate intoxication, because in such cases the cholinesterase inhibition is spontaneously reversible and short-lived. However, if the exact agent is not identified and the patient has significant toxicity, pralidoxime should be given empirically.

## Decontamination

- If there is heavy liquid contamination with a solvent such as xylene or toluene, clothing removal and victim decontamination should be carried out outdoors or in a room with high-flow ventilation.
- **Skin:** Remove all contaminated clothing and wash exposed areas with soap and water, including the hair and under the nails. Irrigate exposed eyes with copious tepid water or saline.
- **Ingestion:** Administer activated charcoal orally if conditions are appropriate. Gastric lavage may be appropriate soon after moderate to large ingestions, but because of the possibility of seizures or rapidly changing mental status, lavage should be done only after intubation [3].

## Enhanced Elimination

Dialysis and hemoperfusion generally are not indicated because of the large volume of distribution of organophosphates [3].

## Aim and Objective

To know the clinical manifestation and management of op poisoning in different patients.

## Case Reports

### Case report 1

A 26-year male attempted to commit suicide by ingesting an unknown amount of an unnamed pesticide. He was found lying next to a farm field with clear consciousness and marked weakness. He was taken to the government hospital, where stomach wash was done and the patient stated that he probably had taken organophosphorus. He was then referred to tertiary care hospital for further treatment.

On arrival, his vital signs were as follows: Temperature 101°F, BP 100/60 mmHg, pulse rate 155 b/min, and RR 34/min. Physical examination revealed the presence of fasiculations, profused sweatings, increased secretions, drowsy, dyspneoa, bilateral crepts, with no response (coma). Laboratory data were remarkable for total WBC 16,000 cells/cmm (reference range: 4000 cells/cmm to 11000 cells/cmm), neutrophiles 83% (reference range: 45% to 75%), lymphocytes 12% (reference range: 20% to 45%), RBS 182 mg/dl (reference range: upto 160 mg/dl); urine examination albumin and ketone bodies were positive, pus cells and RBC's were present. Because organophosphate intoxication with impending respiratory failure was highly suspected, he was intubated with assisted ventilation. Moreover, he was treated with atropine 50 ml (1 ml/hr or 0.6 mg/hr) (1 ml=0.6 mg of atropine) and was admitted to the intensive care unit.

On day 6, plenty of oral and ET secretions, vital signs: temperature 99°F, pulse rate 104 b/min, laboratory data were remarkable for electrolytes Na 159 mEq/L (reference range:136 mEq/L to 145 mEq/L), K 2.9 mEq/L (reference range: 3.5 mEq/L to 5.0 mEq/L), Cl 123 mEq/L (reference range: 97 mEq/L to 111 mEq/L), blood urea 68 mg/dl (reference range: 10 mEq/L to 50 mg/dl); ABG analysis: Na 155.4 mmol/L, Cl 119.2 mmol/L, pH 7.7 (reference range: 7.35-7.45), $PCO_2$ 19.4 (reference range: 35 mmHg to 45 mmHg), $PO_2$ 194.5 (reference range: 75 mmHg to 100 mmHg); X-ray chest: In homogenous opacities in right paracardiac region (aspiration). Patient developed OP poisoning with respiratory failure (type 2) with intermediate syndrome with dyselectrolytenia on T piece. Patient was advised to plan for extubation after correction of electrolyte imbalance. Next day patient electrolytes were K 3.0 mEq/L (reference range 3.5 mEq/L to 5.0 mEq/L); ABG analysis pH 7.5 (reference range: 7.35-7.45), $PCO_2$ 32.2 (reference range: 35 mmHg to 45 mmHg), $PO_2$ 187.6 (reference range: 75 mmHg to 100 mmHg), advised for chest physiotherapy and abulation limb. Patient remained symptomless and was shifted to MICU. Electrolytes and ABG was corrected, on day 9, patient complained of chills and rigors, vital signs: temperature 100°F, pulse rate 140 b/min, Inj. paracetamol 2 ml (1 ml=150 mg of paracetamol) was given. All the lab parameters were corrected patient was clear without complaints, and have planned for discharge on the day 12 and have advised to follow-up after 10 days.

## Case report 2

A 36-year female attempted to commit suicide by ingesting an unknown amount of an unnamed pesticide. She was found comatose in her bedroom and was taken to a government hospital, where stomach wash was done and the patient representative stated that patient had taken organophosphorus. Patient was then referred to tertiary care hospital for further treatment. On arrival, her vital signs were as follows: Temperature 98.6°F, BP 90/70 mmHg, pulse rate 123/min, and RR 18 b/min. Physical examination revealed the presence of chills and rigors, irritable, small and constricted pinpoint pupils, bilateral crepts and rhonchi, plantar toward down. Laboratory data were remarkable for Hb 11% (reference range: 12% to 18%), total WBC 13,000 cells/cmm (reference range: 4000 cells/cmm to 11000 cells/cmm), neutrophils 80% (reference range: 45% to 75%), lymphocytes 14 (reference range: 20% to 45%); liver function test: total bilirubin 1.6 mg/dl (reference range: <1.1 mg/dl), direct bilirubin 0.7 mg/dl (reference range: <0.25 mg/dl); urine examination: albumin and ketone bodies were positive, RBC's were present; ABG analysis: $K^+$ 3.49 mmol/L, $PCO_2$ 26.4 (reference range: 35 mmHg to 45 mmHg), $HCO_3$ 13.9 mmol/L (reference range: 22 mmol/L to 26 mmol/L). Because organophosphate intoxication with impending respiratory failure was highly suspected, she was intubated with assisted ventilation. Moreover, she was treated with atropine 50 ml (4 ml/hr i.e. 2.4 mg/hr), pralidoxime 500 mg TID and was admitted to the intensive care unit.

On day 5, patient was conscious on invasive ventilation, vital signs: temperature 100°F, pulse rate 116 b/min, pupils dilated, sluggish, twitching positive, RTF 200 ml 4$^{th}$ hourly (milk+protein powder), laboratory data were remarkable for ECG showed sinus trachycardia (ST depression), ABG showed mixed metabolic and respiratory alkalosis: Na 133.3 mmol/L, $K^+$ 5.3 mmol/L, pH 5.3 (reference range: 7.35-7.45), $PCO_2$ 22.3 (reference range: 35 mmHg to 45 mmHg), $PO_2$ 140.9 (reference range: 75 mmHg to 100 mmHg), $HCO_3$ 18.9 (reference range: 22 mmol/L to 26 mmol/L). Patient has developed intermediate syndrome. The dose of Atropine made 2 ml/hr (1.2 mg/hr) and pralidoxime 500 mg TID was restared. On day 8, patient was febrile on mechanical ventilation, vital signs: temperature 106°F, BP 130/90 mmHg, pulse rate 152 b/min, laboratory data were remarkable for ECG showed sinus trachycardia, no spontaneous respiratory efforts, ABG analysis showed respiratory alkalosis patient on atropine 6 ml/hr (3.6 mg/hr), decreased ST depression, CPR was done. Patient developed hypoxia ischemic encephalopathy. Infusion Dopamine 1amp [1amp=5 ml (1 ml=40 mg of dopamine)], Inj. noradrenalin 1amp [1amp=2 ml (1 m=2 mg of noradrenalin)] was given. Very poor progress difficulty was explained to patient attenders, then patient suddenly became unconsciousness, CPR was done for 20 min Inj. adrenaline 1amp [1amp=1 ml (1 ml=1 mg of adrenaline)] with atropine was given, ECG not revealed again. CPR was done for 15 min, ECG revealed, BP was not recorded, pupils mid dilated and fixed, Inj. Noradrenalin and Inj. Dopamine was given again. Finally due to cardiac arrest patient was collapsed.

## Discussion

In these case reports two patients had taken OP poison in which both of them developed the intermediate syndrome. But one patient died due to cardiac arrest and other patent was discharged with no complaints and complications. Treatment for both patients mainly included atropine (antimuscarinic agent) and parlidoxime (enzyme reactivator). Dosing of atropine mainly depends on signs and symptoms of patient. 1 ampoule of atropine contains 0.6 mg. Dose adjustment of atropine plays a vital role in the treatment [13,14].

## Conclusion

In OP poisoning, most of the patients present with almost similar type of symptoms and some of the symptoms can be developed slowly during the progression. Laboratory parameters and symptoms were vary from person to person based on that treatment will been given, which includes atropine, pralidoxime with some of the supportive treatments based on the symptoms and patient response.

### References

1. Thunga G, Ganna Sam K, Khera K (2010) Evaluation of incidence, clinical characteristics and management in organophosphorus poisoning patients in a tertiary care hospital. J Toxicol Environ Health Sci 2: 73-76.
2. Gupta SK, Kumar S, Sheikh MI (2006) Study of Organophosphorus Poisoning in Surat, India JIAFM 28: 83-87.
3. Olson KR, Anderson IB, (2006) Text of poisoning and drug overdose. (5thedn). 519-524.
4. Banerjee I, Tripathi S, Roy AS (2012) Clinico-epidemiological characteristics of patients presenting with organophosphorus poisoning. N Am J Med Sci 4: 147-150.
5. Moretto A, Lotti M (1998) Poisoning by organophosphorus insecticides and sensory neuropathy. J Neurol Neurosurg Psychiatry 64: 463-468.
6. Eddleston M, Buckley NA, Eyer P, Dawson AH (2007) FRACP Management of acute organophosphorus pesticide poisoning 1-15.
7. Sungur M, Güven M (2001) Intensive care management of organophosphate insecticide poisoning. Crit Care 5: 211-215.
8. Timothy C. Marrs Organophosphate poisoning.
9. Senanayake N, Karalliedde L (1987) Neurotoxic effects of organophosphorus insecticides. An intermediate syndrome. N Engl J Med 316: 761-763.
10. Yang CC, Deng JF (2007) Intermediate syndrome following organophosphate insecticide poisoning. J Chin Med Assoc 70: 467-472.
11. Richardson RJ, Gupta RC (2013) Text book of Elsevier Encyclopedia vol3. Organophosphate Poisoning, Delayed Neurotoxicity, Intermediate Syndrome 302-308.
12. Eddleston M, Singh S, Buckley N (2007) clinical evidence Organophosphorus poisoning (acute) 1-16.
13. Tripati (2010) Essentials of Pharmacology, (6thedn). 93-95.
14. Shafferman A, Ordentlich A, Barak D, Stein D, Ariel N, et al. (1996) Aging of phosphylated human acetylcholinesterase: catalytic processes mediated by aromatic and polar residues of the active centre. Biochem J 318: 833-840.