

# Organophosphate Induced Delayed Neuropathy: A Case Report

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## ABSTRACT

**Introduction:** Acute organophosphorous poisoning is one of the most common poisonings that we come across in emergency medicine producing significant mortality and morbidity. The sinister spectrum of organophosphorous poisoning is not only related to an initial life threatening acute cholinergic crisis but also to the delayed neurological symptoms which can be potentially debilitating. Accidental or suicidal exposure with these anticholinesterase compounds results in three well defined syndromes i.e. initial acute cholinergic crisis, intermediate syndrome (12-96 hours after exposure) and a organophosphorous induced delayed neuropathy (3-4 weeks after initial exposure).

**Case report:** Herein we describe a 22 year old male patient who after ingestion of large amount of (250 ml) Chlorpyrifos based insecticide had an acute cholinergic crisis and intermediate syndrome followed by development of paraesthesia and lower limb weakness 3 weeks after initial exposure to organophosphorous. Pyramidal tract involvement was also observed as the patient developed spastic paraparesis in lower limbs. Electrophysiological study was characterized by motor axonal polyneuropathy.

**Conclusion:** This was a case of organophosphate induced delayed polyneuropathy with Corticospinal tract involvement leading to spastic paraparesis. Hence all patients with organophosphorous poisoning should be under regular follow up and examined for neurological involvement.

**Keywords:** Organophosphorous, Intermediate syndrome, organophosphorous induced delayed neuropathy, Spastic paraparesis, motor axonal polyneuropathy.

## INTRODUCTION

Organophosphorous poisoning is the most common poisoning in an agriculture based country like India, where the easy availability of several organophosphorous based insecticides account for its rampant misuse. In India organophosphorous (OP) compounds are among the most commonly used agents for suicidal poisoning accounting for half of hospital admissions due to poisoning.<sup>1</sup> The pathophysiological basis of for the clinical manifestation of OP poisoning is inactivation of the enzyme, acetylcholinesterase at the peripheral muscarinic and nicotinic nerve terminals and junctions. Additionally these agents also inhibit the enzyme neuropathy target esterase (NTE) which is responsible for the delayed polyneuropathy in some of the patients.

## CASE REPORT

A 22 year old previously healthy male student consumed a large amount of organophosphorous insecticide (Chlorpyrifos 200 ml) with a suicidal intent around three weeks before being admitted to this hospital. At the time of that admission he was having frothing, nausea, vomiting, and respiratory distress. He was having miosis, bronchorrhoea, bradycardia and was in altered sensorium. He was having signs of cholinergic crisis and was managed vigorously by gastric lavage, inj Atropine, and

pralidoxime yet the symptoms persisted for the whole day. In the next two days the patient improved and the dose of atropine was gradually tapered when he started showing signs of atropinization.

On the third day of his hospital stay the patient suddenly complained of weakness of neck flexors and he also had bilateral ptosis. Fasciculations were observed in the thigh and calf muscles. Injection Atropine was being continued at 1 ml/ hour at this time. The next day the patient complained of breathing difficulty and was shifted to Medical ICU. The patient had developed flaccid paralysis and respiratory muscle weakness (Intermediate syndrome).

He was given proper oxygenation and his airway was secured. Injection Atropine and other symptomatic treatment were continued with close monitoring of his oxygen saturation and pulse rate. He symptomatically improved in a period of 8-10 days. Power in the lower limb gradually improved and he started walking. The patient was discharged with proper medical advice.

After remaining asymptomatic for three weeks he started having tingling sensation in his right foot specifically on the lateral border of right foot and little toe. Two days after this the patient complained of weakness in right lower limb and he started having difficulty in walking. Gradually he also developed weakness of left lower limb in subsequent two to three days. He then started walking with support. Tingling and numbness which was his initial complaint resolved during this period but weakness in both lower limbs persisted.

There was no history of fever, back ache, joint pain, and swelling of joints prior to this event. There was no history of root pain, girdle like sensation or bowel and bladder involvement. On neurological examination the patient had normal higher mental function and cranial nerves functions were intact. Motor system examination revealed weakness of both lower limbs however the power in upper limb was normal. Tone of the lower limb muscles was increased. There was clasp knife spasticity. Ankle jerk and knee jerk were exaggerated but biceps, triceps and supinator jerks were normal. Babinski sign was present, abdominal, cremastic and anal reflexes were present. Ankle and patellar clonus was present. Touch, temperature, pain and proprioception was preserved there was no sensory impairment. Investigations of this patient revealed normal blood investigations (table-1). CSF analysis was normal (table-1). MRI spine was

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normal however nerve conduction velocity studies showed features suggestive of Motor Axonal Polyneuropathy (table-2). Sensory Nerve studies were within normal range. Both peroneal and tibial CMAP'S show delayed latency. CMAPs were smaller in both peroneal and left tibial nerves. Other parameters were within normal limits. Sensory nerve action potentials were within normal limits. 'F' wave study showed delayed response in tested nerves.

**Impression:** Suggests Motor Axonal Polyneuropathy.

**MRI of whole spine:** Loss of lumbar lordosis.

## DISCUSSION

Organophosphates are a large group of compounds which exerts its toxicity due to inhibition of the enzymes cholinesterase, acetylcholinesterase and neuropathy target esterase. The organophosphorous compounds are rampantly used as insecticides, pesticides, industrial plasticizers and petroleum additives. Poisoning with organophosphorous compounds is serious problem worldwide. According to WHO one million serious unintentional poisonings occur every year and an additional two million people are hospitalized for suicidal attempts with pesticides.<sup>2</sup> Other common modes of OP poisoning include ingestion of contaminated fruits and vegetables, exposure to skin as well as inhalational routes. Organophosphorous associated with neuropathy are Tri-o-cresyl phosphate (TOCP), chlorpyrifos, trichlorophos, malathion, parathion, metrifonate and metamidophos. The most dangerous OP ester is TOCP.<sup>3</sup>

The clinical syndromes following an acute organophosphorous poisoning is divided into three types:

First is the acute cholinergic crisis which occurs due to excessive stimulation of muscarinic receptors by Acetylcholine due to blockade of acetylcholinesterase by an organophosphorous. The symptoms usually manifest within hours heralded by the onset of nausea, vomiting, fasciculations, increased sweating, lacrimation and salivation. Clinical examination reveals bradycardia, miosis and bronchorrhea proportionate to the amount of poison ingested. Excessive exposure may sometimes causes irritability, altered sensorium, convulsions and coma.

Second is the Intermediate syndrome which usually appears after 24-96 hours after poisoning on the recovery of cholinergic crisis. This is caused by the dysfunction of the neuromuscular junction caused by the down regulation of presynaptic and postsynaptic nicotinic receptors due to the release of excessive Acetylcholine and Calcium.<sup>4</sup> The main features comprise of muscle weakness affecting the proximal muscles and neck flexors. Cranial nerve involvement is common during this phase. Intermediate syndrome may also involve the respiratory muscles and patients may require ventilatory assistance. The clinical course usually lasts from about 5 to 18 days. Recovery from intermediate syndrome is usually complete though intermediate syndrome does carry death risk due to Type 2 respiratory failure.<sup>5</sup>

Third is the Organophosphorous induced delayed neuropathy (OPIDN) which usually develops two to three weeks after the initial symptoms. It is characterized by a distal motor axonal neuropathy with minimal or no sensory loss. The earliest symptoms to be seen are paraesthesia and calf pain. Weakness initially develops in the distal leg muscles causing foot drop, later it may extend proximally. Cranial nerve and autonomic involvement are absent. OPIDN is pathophysiologically related

Parameters	Normal level	Value
Total leucocyte count	4000–11000/ cumm	4240 Cells/ cumm
Neutrophils	40–70%	46.5%
Lymphocytes	20–40%	39.4%
Monocytes	1–8%	8.7%
Eosionophils	1–4%	5.2%
Basophils	0–1%	0.2%
Haemoglobin	13–18g/dl	10.8 g/dl
MCV	77–95 fL	63.5 fl
Blood urea	7–20 mg/dl	16 mg/dl
Serum creatinine	0.6–1.2 mg/dl	0.7 mg/dl
Serum bilirubin total	0.3–1.9 mg/dl	1.52 mg/dl
SGPT	7–56 IU/L	92 IU/L
SGOT	5–40 IU/L	59 IU/L
Serum cholinesterase level	5320-12920 U/L	
On second day of poisoning		140.7 U/L
After 3 weeks of poisoning		4670.2 U/L
HIV		Non-Reactive
HbSAg		Non-Reactive
Serum sodium	135–145 mmol/l	143 mmol/l
Serum potassium	3.5–5 mmol/l	4.2 mmol/l
Serum calcium	2.2–2.7 mmol/l	1.21 mmol/l
Vit. B12 Level		>2000 pg/ml
Blood glucose (Fasting)	>125mg/dl	80 mg/dl
CSF Glucose	45-80 mg/dl	37 mg/dl
CSF Protein	40-80 mg/dl	70 mg/dl
Cells	0-5	03/cumm

**Table-1:** Investigation reports

Nerve	Normal NCV value (m/s)	Result
Right median	>52	54.59
Left median	>52	70.62
Right ulnar	>57	53.74
Left ulnar	>57	52.62
Right peroneal	>44	43.64
Left peroneal	>44	46.7
Right tibial	>48	47.39
Left tibial	>48	45.14
Ulnar cmap	>4	61
Median cmap	>4	37.4
Peroneal cmap	>2	2.4
Tibial cmap	>2	4.6

**Table-2:** Nerve conduction velocity study.

to inhibition of a carboxyesterase called neuropathy target esterase. OP compounds that do not inhibit this enzyme do not induce OPIDN. NTE is present in brain, spinal cord and peripheral nerves as well as some non neural cells. The natural history of this neuropathy has revealed that it is subacute in onset with slow progression. Clinical involvement of the corticospinal tract and the dorsal column becomes apparent when the peripheral neuropathy improves.<sup>6</sup> The prognosis of the patients with mild neuropathy is generally good but majority of patients with severe neuropathy and pyramidal tract involvement are left with residual disabilities like spasticity and ataxia.

After ingesting chlorpyrifos our patient presents with all these three syndromes i.e., an initial cholinergic crisis, intermediate syndrome and finally after a symptom free interval of three weeks he developed organophosphorous induced delayed

neuropathy.

Luiz Felipe R Vasconcellos et al in their case report described a 39 year old female with Dichlorvos based insecticide poisoning who later on developed organophosphorous induced delayed neuropathy.<sup>7</sup> However she developed flaccid paralysis of both upper and lower limbs. The striking dissimilarity in our case was the development of spastic paralysis with increased tone, exaggerated deep tendon reflexes and well sustained ankle clonus.

Nand et al in their case report described a 19 year old man who developed OPIDN following Dichlorvos ingestion. He later on developed spastic weakness of lower limbs.<sup>8</sup>

Pyramidal tract involvement in OPIDN is quite rare in itself and very few cases have been reported in India. Thiamine and methylprednisolone have been used in these cases but with variable success.

## CONCLUSION

Neurological manifestations in organophosphorous poisoning is an uncommon finding. Our patient presented with all three syndromes of acute organophosphosphate poisoning. In addition to the classical symptoms and sign our patient also demonstrated pyramidal tract involvement which is quite rare. Hence regular follow up of patients of organophosphorous poisoning is important for detection of organophosphate induced delayed polyneuropathy. This particular patient was managed symptomatically as there is no definite treatment for this condition.

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