Case Report

Multiple Unusual Complications in a Single Patient with Combined Organophosphate-Carbamate Pesticide Exposure

Jyothi VS[*], Shaishav S Dhage[*], Rema Pai[**], Meeval Mary Anush[*], Surjit Kamath[*], Pillay VV[***]

ABSTRACT

Poisoning with organophosphate (OP) or carbamate (CM) pesticides is very common in India. These compounds are powerful inhibitors of acetylcholinesterase, causing accumulation of acetylcholine resulting in muscarinic and nicotinic effects. In addition, there are often direct CNS effects including headache, tremor, delirium, slurred speech, ataxia, and convulsions. Coma supervenes in the later stages.

Apart from these, OP poisoning can also induce an "intermediate syndrome" (IMS) characterized by proximal muscle weakness and paralysis; a "delayed syndrome" (organophosphate-induced delayed neuropathy or OPIND) characterized by polyneuropathy and weakness of distal limb muscles; and neuropsychiatric disturbances (chronic organophosphate-induced neuropsychiatric disorder or COPIND). Other disorders have very rarely been reported, such as Guillain-Barre syndrome, Parkinsonism, transient hepatic dysfunction, pancreatitis, vocal cord paralysis, etc.

We report a case of combined organophosphate-carbamate poisoning with multiple complications, e.g., intermediate syndrome (IMS), delayed neuropathy (OPIND), and Parkinsonism. These complications are rare, and some of them to the best of our knowledge have not been reported so far.

Key Words: Organophosphorus compound/Organophosphate; Carbamate; Insecticide; Cholinergic excess; Intermediate syndrome; Organophosphate-induced delayed neuropathy; Chronic organophosphate-induced neuropsychiatric disorder; Thrombocytopenia; Parkinsonism

Introduction

Organophosphorus insecticide poisoning is the commonest poisoning encountered in all parts of India.[1] Many of these cases are suicidal in nature, while some are accidental, and a few are homicidal in nature. Organophosphates are powerful inhibitors of acetylcholinesterase. As a result, there is accumulation of acetylcholine with continued stimulation of local receptors and eventual paralysis of nerve or muscle.[2] Common muscarinic manifestations include bronchoconstriction with wheezing and dyspnoea, cough, pulmonary oedema, vomiting, diarrhoea, abdominal cramps, increased salivation, lacrimation, and sweating, bradycardia, hypotension, miosis, and urinary incontinence, and also nicotinic effects such as fasciculations, weakness, hypertension, tachycardia, and paralysis. Muscle weakness, fatiguability, and fasciculations are common. In addition, there are often direct CNS effects including restlessness, headache, tremor, drowsiness, delirium, slurred speech, ataxia, and convulsions. Coma supervenes in the later stages.

Death usually results from respiratory failure. Acute respiratory insufficiency, due to a combination of CNS depression, respiratory paralysis, bronchospasm, ARDS, or increased bronchial secretions, is the main cause of death in acute organophosphate poisonings. Metabolic acidosis

[*]Dept of Internal Medicine, Amrita Institute of Medical Sciences & Research, Cochin, Kerala
[**]*Author for correspondence*: Dept of Internal Medicine, Amrita Institute of Medical Sciences & Research, Cochin, Kerala. Email: remapai@aims.amrita.edu
[***]Poison Control Centre, Amrita Institute of Medical Sciences & Research, Cochin, Kerala

has occurred in severe poisonings. A characteristic kerosene-like odour may sometimes be perceptible in the vicinity of the patient since the solvent used in many organophosphate insecticides is some petroleum derivative such as aromax.

Apart from the classical manifestations described, OP poisoning can also induce an "Intermediate syndrome" (IMS) characterized by proximal muscle weakness and paralysis, and a "Delayed syndrome" (Organophosphate-induced Delayed Neuropathy or OPIND) characterized by polyneuropathy and weakness of distal limb muscles. Neuropsychiatric disturbances (Chronic Organophosphate-induced Neuropsychiatric Disorder or COPIND) can also occur.[3] Other disorders have rarely been reported, such as Guillain-Barre syndrome, Parkinsonism, transient hepatic dysfunction, pancreatitis, vocal cord paralysis, etc.[2]

We report a case of OP poisoning with multiple complications, including IMS, OPIND, Parkinsonism, and thrombocytopenia. So many complications in a single patient who survived have not been reported so far to the best of our knowledge.

The Case: A 20-year-old male, who was on antidepressant therapy (olanzapine and mirtazapine) for the last 2 weeks for adjustment disorder, presented to this hospital with consumption of an unknown quantity of two insecticides: an organophosphorus compound (monocrotophos) and a carbamate (carbofuran). He had been given a stomach wash at the local hospital, before being referred to this hospital. On examination, he was found to have cholinergic features (miosis, bronchospasm, bronchorrhoea, fasciculations, mental confusion), and was therefore started on the usual recommended regime of atropine and pralidoxime, along with other supportive measures. The ABG on admission revealed the following: pH 7.47, pCO_2 33.7, bicarbonate 26.1, pO_2 97, Na 137, K 4.6, phosphorus 3.8, Ca 8.7, and Mg 2.2. The severity was graded as per the modified grading method of Bardin & Van Eeden,[4] and was found to be of severe grade (secretions^{+++}, fasciculations^{+++}, and altered consciousness). Plasma cholinesterase level was moderately suppressed (4079 U/L, the lower limit of the normal reference range for adult males being 5600 U/L). It is to be noted that cholinesterase level does not serve as a useful marker of severity in OP poisoning, since it does not always show good clinical correlation.[5] On day 4, the respiratory secretions subsided, and atropine was tapered off. However since he developed respiratory distress (indicative of IMS), mechanical ventilation was begun. ABG done on day 4 revealed the following: pH 4.49, pCO_2 44, bicarbonate 26, pO_2 92. On day 6, atropine was stopped. The total dose of atropine administered was 192 mg over a period of four days, while the total dose of pralidoxime was 2 gm over two days.

On day 7, he developed fever in the range of 101-103^{0}F with confusion, generalised rigidity and tremors. Deep tendon reflexes were unaffected and the plantars were equivocal. Brain imaging and nerve conduction velocity tests were normal. Endotracheal suction tube culture revealed Klebsiella. He was therefore started on sensitive antibiotics. Neurological consultation suggested a Parkinsonian movement disorder, and dopamine agonists levodopa and bromocriptine were also added.

Repeat plasma cholinesterase levels were within normal limits. On day 16, he was extubated. Muscle rigidity was less but persistent; hence the dopa agonists were continued. On day 19, deterioration of liver function tests was noted, and therefore the dopa agonists were stopped. Over the subsequent days, rigidity gradually improved without these drugs, and the patient made a complete recovery. However, bilateral foot drop was detected on day 21, with normal power of proximal muscles. Nerve conduction velocity was repeated which showed axonal neuropathy, and a diagnosis of organophosphate-induced delayed neuropathy was made.

On day 22, the patient developed quite abrupt thrombocytopenia, with a previous platelet count of 54000 dropping to 17000 in just 2 days. There were no overt bleeding episodes. Anti nuclear antibody test (ANA) and Anti ds DNA, as well as bone marrow studies were normal. Organophosphate-induced immune dysfunction was considered, and he was treated with a short course of oral steroids, after which the platelet count improved to normal values.

Discussion

Acute organophosphate pesticide poisoning manifests as cholinergic crisis, followed by an intermediate syndrome (IMS) and delayed neuropathy (OPIND) in some patients. The diagnosis is generally based on the clinical signs and symptoms together with the measurement of erythrocyte and/or plasma cholinesterase activity. Cholinergic excess manifests as muscarinic and nicotinic symptoms due to inhibition of acetylcholinesterase. In some cases, the acute cholinergic crisis is followed by an "intermediate syndrome" (IMS) after a few days,

characterised by weakness of neck flexors, proximal limb and respiratory muscles, and paralysis of motor cranial nerves. Several investigators have proposed that IMS may develop as a result of several factors: inadequate oxime therapy, the dose and route of exposure, the chemical structure of the organophosphates, the time to initiation of therapy, and possibly efforts to decrease absorption or enhance elimination of the organophosphates.[6] Once it sets in, IMS will have to be managed by supportive measures, since it does not respond to oximes or atropine.

In a few patients, a "delayed syndrome" (OPIND) may occur 2-4 weeks after poisoning, characterized by distal motor polyneuropathy.[3] OPIND is a sensorimotor distal axonopathy that usually occurs 2-4 weeks after ingestion of an organophophorus compound. It presents as distal muscle weakness with relative sparing of the neck muscles, cranial nerves and proximal muscle groups. The weakness is said to be due to inhibition of neuropathy target esterase.[2] It does not respond to atropine or oximes. Gradual recovery may or may not occur over several months.

Other rare disorders have also been reported in association with organophosphate poisoning, such as Guillain-Barre syndrome, Parkinsonism, hepatic dysfunction, cardiac arrhythmias and cardiomyopathy.[2] Extrapyramidal symptoms resembling Parkinsonism is a recognized, though rare neurological complication. It generally occurs 4-40 days after intake of the poison, and is usually reversible within 8 weeks with or without treatment. These symptoms are often overlooked or masked by other neurological complications. Re-exposure to the organophosphorus compound may result in relapse. While neurological features akin to Parkinsonism may be the result of hypoxia, in this case, since the patient developed rigidity and other symptoms of Parkinsonism before the onset of breathlessness and mechanical ventilation, it can be concluded that hypoxia was not the cause. The MRI of brain is usually normal in cases of Parkinsonism resulting from organophosphate exposure. The condition responds to biperidin, amantadine, bromocriptine or levodopa. Spontaneous recovery can also occur. In this case, the condition lasted for only two weeks, and while dopamine agonists levodopa and bromocriptine were administerd initially, they were withdrawn when deterioration of liver function tests was noticed. In fact, all neurological deficits disappeared completely by the time the patient was discharged.

Exposure to pesticides can cause a number of effects on the immune system, varying from a slight modulation of immune function to the development of overt immune disease. Like many other toxic compounds, pesticides are substances that may possess a non-protein nature, but can combine with proteins to form complexes which are antigenic, resulting in immunological impairment. There are reports of such pesticide toxicity causing suppression of humoral immunity in animals, but information about the influence of pesticides on the human immune system is limited.[2]

Although organophosphate poisoning is quite common in India and many other developing countries, only a few case reports are available in the literature describing rare manifestations such as Parkinsonism and thrombocytopenia. This is probably the first case to document multiple abnormalities and disorders in the same patient, who went on to make a recovery over 30-35 days. It is also relevant to note that this is one of the few cases where-in an organophosphorus compound and a carbamate were ingested together. However, there are generally no specific clinical effects of carbamate which can be differentiated from those due to organophosphate compounds, and the difference lies only in the treatment, pralidoxime generally being avoided. In this case, pralidoxime was administered since there was intake of an organophosphate compound.

Conclusion

A case of combined toxicity of organophosphate and carbamate developing multiple complications, e.g., Parkinsonism, thrombocytopenia, IMS and OPIND during acute phase, and course of treatment is being reported due to rare occurrence.

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