Neurotoxic Syndromes Sequencially Occuring after Consumption of organophosphorus Compound -A Case Report By Peter George & NarasimhaHegde

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Abstract

Organo-phosphorus compounds (OPC) Organo-phosphorus compounds (OPC) are among the most used poisons for suicide in India, and associated toxic syndromes are well described. We report a young man who presented to us with alleged consumption of chlorpyrifos, a crystalline organophosphate insecticide. During hospitalization he developed acute organo-phosphorus toxicity (type I) and intermediate syndrome (type II), both situations were managed by assisted ventilation and supportive care. After 6 weeks of discharge he reported with features of delayed poly neuropathy (type III). It is rare for these patients to follow up at the same centre to identify and manage these toxicities. Often the type III toxicity is misdiagnosed and over investigated for other causes of neuropathy. Though OPC poisoning is commonly encountered in practice, only few reports have described all toxicities to occur in the same patient.

Index terms—

1 Introduction

ccording to the report of Accidental deaths and suicides in India, 2009, Government of India, 127151 people committed suicide in 2009 [1] . OPC poisoning is the most commonand account to half of hospital admissions due to poisoning in India. Its ready availability and easy accessibilitypossibly makes it the most used suicidal agents in India [2], [3] , [4], [5] . The neurological toxicities of OPC poisoning can be Type I syndrome or cholinergic crisis, Type II syndrome or Intermediate syndromeand Type III syndrome or organophosphate induced delayed neuropathy (OPIDN) [6], [7], [8] .A delayed organo-phosphorus compounds induced neuropsychiatric syndrome due to chronic poisoning has also been described in literature. In this report we identified all three described types of neurotoxicsyndromes due to OPC in the same individual.

2 II.

3 Case Report

We report an interesting case of OPC poisoning who developed all the described toxic syndromes. A 36 year old man was admitted to our hospital with alleged consumption of Chlorpyrifos(250 ml), an organo-phosphorus compound, with suicidal intention. He had features of type I toxicity at admission, and managed after Authors ? ?: Department of Medicine; Father Muller Medical College, Mangalore, India. e-mail: drpetergeorge2002@yahoo.com decontamination, with atropine, prali-doxime and supportive care. On day -6 of admission he developed neckand respiratory muscle weakness, followed by weakness in allhis limbs. This being typical of Type -2 syndrome (intermediate syndrome), was managed with assisted ventilation and supportive

care. On day -16 he was weaned off from assisted ventilation and on day -21 was discharged from hospital with no obvious neurological deficits.

He was readmitted to hospital after 4 weeks of discharge with history of progressive difficulty in griping objects with hand, walking and getting up from squatting position. He had distal paraesthesia in all limbs, but had no sphincter disturbances. On examination, vital signs and cranial nerves were normal, with no disturbances in autonomic or higher mental functions. There was wasting of distal muscles in all limbs; and had weak hand grip and plantar movements. Clinically, he had distal hypotonia and proximal hypertonia in the limbs. His deep tendon jerks were exaggerated, except for ankle jerks which were absent; and all modalities of sensations were normal. The routine haematology and biochemistry, including electrolytes, CPK and thyroid functions, were normal. Nerve conduction studies revealed predominantly axonal type of sensory-motor polyradiculoneuropathy in both lower limbs. He was treated with a short course of glucocorticoids, high doses of neurotropic vitamins, and physical therapy. He had little improvement even after weeks of treatment.

4 III.

5 Discussion

OPC poisoning cause inhibition of acetylcholinesterase (AChE), leading to the accumulation of acetylcholine (ACh) in the body. OPC's are being used for over 70 years and are the most used insecticides world-over, including India [2], [4], [5] . The indiscriminate use of these compounds over the decades has resulted in innumerable toxicities to humans as well animals. Suicidal and occupational OP poisoning in agricultural workers was prevalent in developing countries, whereas accidental OP poisoning was prevalent in developed countries [7] .

The Accidental deaths and suicides in India, 2009, Ministry of Home Affairs, Government of India, poisoning with pesticides contributed to 20.4 % of suicides in India, with most arising out of family problems [1] . OPC's are the most commonly used suicidal agent in India [2], [4], [5] .OPC poisoning occurs from gastrointestinal tract following suicidal consumption or absorption through skin, mucous membranes and respiratory tract following accidental exposure [5] .

These compounds after absorption are hydrolysed by esterases, and competitively bind to the esteratic site of the enzyme acetylcholinesterase (AChE), resulting in its phosphorylation. Depending on the compound involved the binding may be stable and takes hours or weeks disintegrate. The accumulation of excess acetylcholine (ACh) at the cholinergic nerve endings result in the characteristic clinical manifestations [2], [3], [6] .

The toxic syndromes after acute exposure to OPC are well described in literature. Type I and II toxicities, the cholinergic and intermediate syndrome respectively are common in the emergency department. After acute exposure of OPC, type III toxicity or organophosphate-induced delayed polyneuropathy (OPIDP) is also described. A chronic organophosphateinduced neuropsychiatric disorder (COPIND), at times described as type IV toxicity, occurs in chronic OPC exposure.

Type I or cholinergic syndrome results from excessive stimulation of muscarinic receptors, resulting in bradycardia, diarrhoea, vomiting, fasciculation, sweating, salivation and micturition [6], [7], [8] . Type 2 or Intermediate syndrome follow type I toxicity, and occurs due to excessive Ach at the neuromuscular junction causing down-regulation of nicotinic receptors resulting dysfunction of neuromuscular junction. Develop in about 20%-50% of cases depending on the ingested quantity, its duration, and the compound. Usually occur 24 to 96 hours after the recovery from the cholinergic crisis. It is marked by predominant proximal limb muscles and neck flexor weakness, with or without cranial-nerve palsies. The intermediate syndrome may last from 5 to 18 days [9], [10] .

As with other poisoning the first step in the management of these patients is gastrointestinal and skin decontamination. Atropine is used as antidote, in type I syndrome, to counter the muscarinic effects of acetylcholine. Pupillary dilation, drying up of secretions, tachycardia and fever are features of atropinisation. Once achieved, should be maintained for 3-5 days, depending upon the clinical situation. If respiratory muscule paralysis supervenes, mechanical ventilation must be instituted. Type II syndrome is supportive with mechanical ventilation and recovery is the rule, muscles of respiration being the last to recover [11], [12] . The use of oximes in cholinergic phase as rejuvenators of the enzyme cholinesterase is controversial [13] .

Our patient had features of type -I toxicity at admission, and after decontamination was managed with atropine, pralidoxime and supportive care. He did not require assisted ventilation during the type I toxicity. On day -6 of admission he developed neck and respiratory muscle weakness, followed by weakness in all his limbs; typical of Type -2 syndrome. He required assisted ventilation for 10 days along with supportive care. He responded well, and on day -21 was discharged from hospital with no neurological deficits. As described, our patient also developed the type I & II syndromes and recovered well with the supportive management.

Type III syndromes, often named as organophosphate induced delayed neuropathy (OPIDN), usually occurs about 1-3 weeks after consumption of OPC. It occurs from phosphorylation and inhibition of neuropathy target esterase (NTE) in axons causing degeneration of long axons. This is often a pure motor or axonal neuropathy [9] .

Our patient reported to hospital after 4 weeks with difficulty in griping objects with hand; walking and getting up from squatting position; distal paraesthesia of the limbs, but had no sphincter disturbances. He

was found to have a mixture of upper and lower motor neuron signs on examination, which was classical of type III toxicity. There are a few reports of type III syndromes in literature resulting from chlorpyrifos and other organo-phosphorus compounds [14][15] [16] . In addition to these neurological syndromes following acute exposure; individuals with low dose chronic exposure, develop several neuro-behavioural changes termed together as 'chronic organophosphate induced neuropsychiatric disorders' (COPIND) or type IV syndrome.

The researches with newer molecules and drugs have been inspiring in last decades. Bioscavengers, nano carriers, recombinant bacterial phosphodiesterases have been very encouraging in recent years. Alkalanisation, intravenous magnesium sulphate, hemofiltration and antoxidants have shown to reduce neurotoxicity. The recent advances in treatment of organophosphorouspoisoning must be accessible to clinicians for its morbidity, magnitude and socioeconomic implications [3], [17] .

Even though we encounter many organophosphorus compound poisoning in practice with type I & II toxicities, type III is very rare. The chances of overlooking type III syndrome are high, as it is uncommon and also due to similarity with other neuropathies. We were able to identify type III syndrome as the patient reported back for follow up. He was managed with a short course of glucocorticoids, high dose neurotropic vitamins, and physical therapy; but had little improvement after weeks of treatment [11], [12] .

IV.

6 Conclusion

Organo-phosphorus compound consumption is among the commonest poisoning, and the treatment outcome for type I & II syndromes are excellent with early identification and institution of treatment. The regular follow up of patients after discharge from hospital could possibly identify the type III and IV syndromes. No specific treatment exists to prevent occurrence of the neuropathy following exposure. [1] [2] [3]

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