Letter to the Editor

Parkinsonism Complicating Acute Organophosphate Insecticide Poisoning

Dear Editor,

Organophosphate insecticides have a triphasic effect on the central nervous system, namely acute cholinergic crisis, intermediate syndrome and delayed polyneuropathy. Although acute organophosphate poisoning is relatively common, case reports describing parkinsonism as a neurological complication following an acute intoxication are limited.[1] We report a case of parkinsonism noted on day 24 of admission following an acute severe organophosphate poisoning which was successfully treated with benzhexol and levodopa. Previously, response to levodopa was reported to be poor in 3 patients studied by Bhatt et al[1] whereas amantidine, dopamine agonist and bipiriden have been shown to be helpful.[2] To the best of our knowledge, this is the first case of parkinsonism complicating organophosphate poisoning which responded to levodopa and benzhexol therapy.

Case Report

A 26-year-old man presented to our casualty department after being found unconscious and covered with vomitus at home. Further enquiry revealed a suicide attempt in which he had ingested approximately 100mL of Malathion®. On arrival, he had cholinergic features such as sweating, bradycardia, excessive salivation, diarrhoea and pupillary constriction. Gastric lavage was performed and he was immediately started on atropine infusion. Pralidoxime was also administered. Apart from a markedly low serum cholinesterase level (293 U/L), his other routine blood investigation results were normal. Toxicology screen for other drugs (acetaminophen, benzodiazepine and salicylate) was negative.

Unfortunately, he desaturated and became drowsy the next day, thus needing intubation and care in the intensive care unit (ICU). He was kept well atropinised for a total of 18 days. His serum cholinesterase level gradually reached the normal range on day 24 of admission. However, he developed ventilator-associated pneumonia in ICU, which was treated accordingly. Due to prolonged ventilation, he had a tracheostomy on day 10 of admission. He was taken off the mechanical ventilator and transferred to the high dependency ward on day 17 of admission. However, due to persistent salivation and consecutive aspiration, he needed ventilation again for another 3 days.

Upon transfer to the ward on day 24 of admission and having been taken off ventilatory support, he was noted to have bilateral coarse resting tremors of the hands with mask-like facies and bradykinesia. His tone was increased in all limbs with cog-wheel rigidity, generalised hyper-reflexia and down going plantars. There was no family history of Parkinson's disease and he had never used any recreational or neuroleptic drugs. A diagnosis of parkinsonism secondary to organophosphate poisoning was made, after having excluded other possibilities such as drugs, Wilson's disease and hypoxic encephalopathy. A CT and MRI of the brain showed no abnormalities. Serum caeruloplasmin was also normal.

He required intensive nursing care including feeding via a nasogastric tube. His Hoehn & Yahr score was grade V at that time. The patient was treated with benzhexol (artane) 2mg tds and levodopa/benserazide (Madopar®) 125 mg tds. Five days after starting treatment, he showed marked improvement. There was less cogwheel rigidity and he was able to speak and swallow, enabling the removal of his tracheostomy and nasogastric tube prior to discharge. He was discharged well on day 38 with benzhexol and levodopa/benserazide and was asymptomatic upon review in clinic 1 month after discharge with only mild rigidity. The dosage of Madopar® and benzhexol were reduced to half until his next review.

Discussion

Extrapyramidal symptoms such as parkinsonism is an uncommon sequel following organophosphate poisoning. This typically occurs after 4 to 40 days of intoxication and is usually reversible within 8 weeks with or without treatment.[3] In our case, the features of parkinsonism were only noted on day 24 following the acute poisoning although it is possible that the signs may have developed earlier but went unnoticed as the patient was ventilated in the intensive care unit.

Organophosphate compounds exert their acute toxicity effects by inactivating acetylcholinesterase, leading to excessive acetylcholine activity. The majority of the cholinergic neurons in the human brain are localised in the striatum, the basal forebrain, and the mesoencephalic and pontine reticular formation.[4] Acetylcholinesterase is widely distributed within some subcortical areas and is especially rich in the extrapyramidal system. Therefore, it is not surprising that inhibition of acetylcholinesterase in these cholinergic neurons as a consequence of organophosphate intoxication can produce extrapyramidal manifestations.

The fact that our patient responded well with levodopa suggests that organophosphate poisoning may have an effect on the striatal dopaminergic system. There may be a transient decrease in the dopamine levels or an increase in the dopamine turnover as a short-term compensatory mechanism. Increased dopamine turnover and reduced mitochondrial function has been observed in in vivo preparations involving permethrin exposure.[5] Interestingly however,[3] patients studied by Bhatt et al[1] who received levodopa for transient parkinsonism following acute organophosphate toxicity showed little or no clinical improvement, hence the author has suggested that there may be striatal dopamine receptor dysfunction.

Our observation that organophosphate poisoning can cause parkinsonism supports previous studies and case reports implicating pesticides in the aetiology of Parkinson's disease and parkinsonism.

There is no recommended therapeutic regimen for these complications. Amantidine, dopamine agonist and bipiriden have been shown to be helpful in these conditions.[2] However, whether the disappearance of parkinsonism was due to medications or the natural progress of the disease was still uncertain. In our patient this observation was also not conclusive. The improvement could either be due to levodopa, benzhexol or even the natural progression of the illness.

In conclusion, transient parkinsonism as a sequelae of acute organophosphate poisoning should be recognised as a complication even after cholinergic symptoms have resolved. Although parkinsonian symptoms may improve spontaneously within 8 weeks, cases of prolonged parkinsonism secondary to organophosphate poisoning have been reported.[1,6] Bhatt et al[1] also reported a case of parkinsonism following organophosphate poisoning that only improved spontaneously over a period of 8 months. Therefore, the diagnosis should not be missed because complications such as aspiration pneumonia and prolonged mechanical ventilation could be prevented by appropriate treatment. Clinicians should therefore observe for signs of parkinsonism in patients with acute organophosphate poisoning and consider treatment with an anti-parkinsonism drug if these signs are present but further research is needed to identify the most appropriate medication for these complications.

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