Case Report

Role of Clonidine in Organophosphate Poisoning in Children

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ABSTRACT

The most commonly used insecticides in India are either organophosphates or carbamates. Both of these classes of pesticides act by inhibiting cholinesterase enzymes. A commonly used antidote in the management of poisoning due to these compounds is atropine. While oximes are additionally used in organophosphate toxicity, they are generally not recommended for carbamate exposure. We are reporting a case of organophosphate (OP) poisoning that did not respond very well to either atropine or oximes, but improved significantly when clonidine, an alpha-adrenergic agonist was used.

Key words: Organophosphates, clonidine

The Case

A 15 year old boy was admitted in the pediatric intensive care unit of our hospital on 8th November 2004 with a history of consuming some unknown pesticide early that morning. He had a history of chronic untreated depression. The cause of depression was primarily because he was obese and faced constant ridicule from his peers.

The boy was discovered on the bathroom floor by his father. He suffered from loose stools and abrupt vomiting in the following few hours. There was no history of seizures or loss of consciousness. He was taken to a local hospital, where on examination it was found that there was increased frothing from the mouth, and he was then referred to another private hospital nearby. By this time the boy demonstrated evidence of respiratory failure, and was there subjected to mechanical ventilation. He was given atropine to reduce the respiratory secretions. The next morning, when an attempt was made to extubate the patient, it did not meet with success, and so he had to be re-intubated. Subsequently, he suffered from one episode of generalized tonic-clonic seizure, which was controlled by phenytoin. He was then referred to our hospital, by which time 4 days had elapsed since consumption of the pesticide.

On admission, the boy was found to have increased salivation, and vomited repeatedly. On examination, he was conscious, co-operative, obeyed verbal commands, and responded by gestures or through writing; he could not speak since he was brought intubated. The pupils were bilaterally normal in size, and reacted to light. The patient was started on atropine in the dose of 0.03 mg/kg/dose till the point of atropinisation, after which the dose was titred to requirement.

The hemogram, liver function tests, renal function tests, and coagulation profile were all within normal limits. Cholinesterase level done at the referring hospital was 23% of normal, while it

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was 27% of normal on admission when tested by the Analytical Toxicology Division of our hospital. This was despite the child having been treated with atropine at the referring hospital. Oximes were not administered earlier as there was suspicion that the ingested compound was a carbamate. However toxicological analysis of gastric aspirates at our hospital revealed the presence of an organophosphate, after which pralidoxime administration was begun at the rate of 50 mg /kg/dose, 8th hourly for 2 days. Other supportive measures such as maintenance of intravenous rehydration and urinary catheterization were also undertaken.

The following day, efforts were made to wean the boy off the ventilator. Nasogastric feeding was also started. The patient was extubated on the 3rd day, but had to be re-intubated after 10-11 hours due to increasing respiratory distress on account of excessive secretions, in spite of adequate atropine being given as a round the clock infusion. Artificial ventilation continued while various options were considered to reduce the respiratory secretions. As an experimental measure, clonidine was started in the dose 3μg/kg/day in 2 divided doses orally. In the next 48 hours, a remarkable decrease in the amount of oral secretions was noted. While clonidine therapy was going on, the vital parameters were under close watch. No untoward events were noted. There was no episode of bradycardia or hypotension. After 48-72 hours of the use of clonidine the process of weaning from the ventilator was re-started and the child was successfully extubated to oxygen by mask, followed by breathing of ambient air. No increase of respiratory distress or secretions were noted. The boy was then shifted to the general ward where he stayed for 5 days more, after which he was discharged. He attended the OPD for review after 2 weeks, and was found to be completely asymptomatic.

Discussion

Both organophosphates and carbamates bind to cholinesterase enzymes, preventing the degradation of acetylcholine, resulting in its accumulation at nerve synapses. Enzymes affected include acetylcholinesterase (or red blood cell cholinesterase), pseudocholinesterase (or plasma cholinesterase), and neurotoxic esterase (found in the nervous system). If left untreated, organophosphates form a permanent bond to these enzymes, inactivating them. This process, called ‘‘aging’’, occurs over 2-3 days after exposure.[1] Weeks to months are required for the body to regenerate inactivated enzymes. In contrast, carbamates form a temporary bond to the enzymes, allowing regeneration of the enzymes over several hours. Even with treatment, neurologic symptoms may occur and may persist. Atropine and oximes are traditionally used in the management of such poisonings.

Recent reports suggested the efficacy of clonidine in soman poisoning, a cholinesterase inhibitor belonging to the same group as organophosphate pesticides.[2] According to many investigators however, only pralidoxime is effective in the management of OP poisoning.[3]

A few compounds such as magnesium sulfate and clonidine have been found to be effective in OP poisoning, due to their pharmacological action of reducing the production of acetylcholine.[4] Increased survival rates, reduction in centrally mediated symptoms such as tremor and straub tail, and reduction in excessive salivation were noted when these agents were employed. The protective effects of clonidine are probably due to blockade of acetylcholine release and postmuscarinic receptors, together with transient inhibition of acetylcholinesterase. Thus, clonidine may prove very useful in the management of organophosphorus poisoning in children. Clonidine was first introduced as an antihypertensive, and is being used now in attention deficit hyperactive disorders (ADHD), and tic syndromes in children. However, since children are very sensitive to the toxic effects of clonidine, close monitoring is essential.[5]

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