ORGANOPHOSPHOROUS POISONING WITH INTERMEDIATE SYNDROME

Sqn Ldr S PIPLANI^{*}, Sqn Ldr A HANDA⁺,
Sqn Ldr R AGGRAWAL[#], Sqn Ldr BK GUPTA^{**},
Wg Cdr SC MISHRA⁺⁺, Lt Col P ROY^{##},
Maj Gen ID GUPTA^{***}

MJAFI 2002; 58 : 81-83

KEY WORDS :Autonomic neuropathy; Organophosphate poisoning; Respiratory failure.

Introduction

Organophosphorous (OP) insecticides are used extensively in agriculture and horticulture. Poisoning, commonly due to deliberate ingestion, is reported to occur in 3 million individuals each year, resulting in 40,000 deaths annually [1]. They are common poisons consumed in India, being second only to Aluminium phosphide [2,3]. OP compounds are potent anticholinesterases and cause death primarily due to respiratory paralysis. We report a case of malathion poisoning complicated by respiratory paralysis and autonomic neuropathy and discuss the controversies involved in its management.

Case Report

36 year old lady ingested 15-20 ml of 50% malathion after an argument with her husband. She developed giddiness, copious oral secretions, muscle twitching and collapsed 10 minutes later. She was rushed to the hospital. On examination at admission she was cyanosed, agitated, confused, tremulous and profusely salivating. The blood pressure was 130/78 mm Hg, pulse rate was 130/min and the respiratory rate was 40/minute. Breathing was laboured and moist rales were present in the lungs. The pupils were pinpoint and nonreactive. Generalized fasciculations were visible. Examination of other systems was normal. She had incontinence of bowel and bladder. A stomach wash was performed with normal saline till the returning fluid was clear. The gastric contents had distinct kerosene oil like odour. Injection atropine was administered, 9 mg as IV bolus, followed by 3 mg every 15 minutes, till the secretions had dried and rales had disappeared. Oxygen was administered through a facemask and pharyngeal suction was done intermittently. An indwelling urinary catheter was placed. Injection Pralidoxime methiodide 2 gm, was diluted in 100 ml saline and given as intravenous infusion over 30 minutes. It was repeated thereafter every six hours. An atropine infusion was started (0.5-1mg/min) to keep pupils mid-dilated and maintain the pulse rate between 100-120/minute.

Results of the laboratory tests were as follows; haemoglobin 12

gm/dl, TLC 9200/cmm with 83% polymorphs; urine acidic, negative for protein and sugar; blood sugar 233 mg/dl (repeat blood sugar 118 mg/dl); blood urea 24 mg/dl; serum creatinine 0.8 mg/dl; serum bilirubin 0.75 mg/dl; serum sodium 140 mEq/l; and serum potassium 3.9 mEq/l. Resting electrocardiogram revealed sinus tachycardia.

The patient had a stormy course in hospital. She developed hypotension (BP 84/50 mm Hg) which was corrected by intravenous fluids and dopamine. Six hours after admission she developed respiratory paralysis. Mechanical ventilation with volume cycle ventilator was started in SIMV mode, with breath rate of 12 and tidal volume of 500 ml. Patient recovered consciousness 12 hours after admission. Artificial ventilation, atropine, PAM and other supportive measures were continued. Tracheal aspirate smear and chest radiographs were done daily. An attempt was made to wean off the ventilator on the third day but she was unable to sustain spontaneous respiration. Neck muscle weakness was noticed at this stage. On the fourth day she developed high fever (103-104°F), facial edema and purulent tracheal aspirate. Gram stain of the tracheal aspirate showed Gram-negative bacilli and the peripheral blood smear revealed toxic granules. A bedside chest radiograph revealed a non-homogenous shadow in the right middle zone. A diagnosis of ventilator associated pneumonia was made and intravenous antibiotics were started (Ceftazidime 2gm 8 hrly, Cloxacillin 2 gm IV 6 hrly and Metronidazole 500mg 8 hrly) after sending cultures. *Pseudomonas aeruginosa* was grown from tracheal aspirate but blood and urine cultures were sterile. Antibiotics were suitably modified. The facial swelling subsided in next 24h following diuresis, and fever subsided after 7 days. Atropine was gradually tapered and withdrawn by seventh day. The serial RBC cholinesterase values done starting from the seventh day onwards (Table-1) revealed progressive improvement of level with treatment. Weaning from ventilator was once again attempted on day 8. She was finally weaned off ventilator on day 10 and endotracheal tube was removed 24 hours later. Post extubation she developed features of unilateral obstructive emphysema, which subsided with nebulisation and chest physiotherapy. She thereafter developed persistent resting tachycardia (HR 120-140) and postural hypotension (BP 100/60mmHg and 80/50 mmHg). It was unresponsive to intravenous fluids. Electrocardiogram revealed sinus tachycardia and 2-D echocardiography was normal. Serum T3,

^{*}Classified Specialist (Medicine), Cancer Institute, Chennai (on study leave), ⁺Graded Specialist (Medicine), Command Hospital (Air Force), Bangalore, ⁺⁺Graded Specialist (Medicine), ^{##}Graded Specialist (Anaesthesia), ^{***}Graded Specialist (Pathology), 5 Air Force Hospital C/O 99 APO, ^{***}Commandant, Command Hospital (Central Command), Lucknow, ^{*}Classified Specialist (Anaesthesia), 7 Air Force Hospital, Kanpur.

T4 and TSH levels (ordered to exclude iodine-induced thyrotoxicosis) were also normal. Bedside tests for autonomic function, which included handgrip, valsava, deep breaths test and standing test for orthostatic hypotension, confirmed the diagnosis of autonomic neuropathy. Examination of cranial nerves, motor and sensory system was normal. She was given a high salt diet and made to sleep with head elevated at 30 degrees. Her symptom of giddiness subsided and the standing blood pressure became normal after 12 weeks. There was no evidence of delayed onset motor axonal neuropathy.

TABLE I
RBC cholinesterase values

Serial No.	Day	Value (Normal 6700-10000 IU/L)
1	7	2780
2	11	3530
3	21	4500

Discussion

Deliberate self-poisoning is the commonest form of poisoning in adults and accounts for 95% of all poisoning admissions to hospital. Hospital statistics indicate an increase in the incidence of acute poisoning in India, accounting for 6% of admissions [2]. OP poisoning has been reported to constitute 17-69% of cases of poisoning in various studies [2-5]. Organophosphates irreversibly bind to acetylcholinesterase leading to its inactivation and failure of cholinergic transmission. The clinical manifestations include the muscarinic syndrome (with rhinorrhea, bronchorrhea, bronchospasm, salivation, pulmonary edema, nausea, vomiting, miosis and blurred vision), the nicotine syndrome (fasciculations and neuromuscular paralysis) and CNS syndrome (altered sensorium and seizures). A delayed onset neuropathy has been reported to occur 2-4 weeks later due to inhibition of neuronal target esterase.

Management involves removal of soiled clothing, decontamination of skin with soap and water, gastric lavage, administration of activated charcoal to adsorb toxin, atropine to antagonize the muscarinic effects and oximes to reactivate the phosphorylated cholinesterase. Supportive measures include removal of secretions, correction of hypoxia and institution of prompt ventilatory support in the event of respiratory paralysis.

There are no clear guidelines for the dosage and duration of administration of atropine and oximes. Although the standard books recommend a dose of 0.5-2 mg of atropine every 15 minutes till secretions have dried, some studies have found highdose atropine infusion to be better [5]. The duration of atropine infusion has to be 'tailored' in individual cases to maintain a

state of mild atropinisation. Wadia et al recommend higher starting dose (3-9 mg) based on their experience in Indian patients. They have suggested that Indian patients tend to ingest higher quantity of OP. Pralidoxime was found to be useful in experimental nerve gas poisoning. Recent studies in India and abroad have however questioned its usefulness [6]. Discrepancies between the rationale for using them and failure to demonstrate their efficacy have been attributed to intermittent and inadequate doses used. It has been suggested that a continuous infusion of pralidoxime to maintain a minimum blood concentration of 4 µgm/ml is needed to derive maximum benefit [7]. Pralidoxime should be continued till the RBC cholinesterase levels return to 50% of normal. Early discontinuation of oxime may precipitate a 'second deterioration', while prolonged administration has adverse effects like iodism (with methiodide preparation commonly available). Our patient received pralidoxime for 14 days (5 days after weaning from ventilator). It resulted in extensive thrombophlebitis and allergic reactions.

Although the intermediate syndrome has been reported to occur between 24-96 hours after onset, it's development within six hours in our case indicates the severity of poisoning. In a recent study of OP poisoning, 35% of the patients needed ventilatory support [8]. Factors predictive of the requirement of ventilatory support were : delay in institution of treatment, altered sensorium, pinpoint pupils, generalized fasciculation, convulsions and presence of cyanosis at admission. Almost 50% of the patients developed ventilator associated pneumonia. Overall mortality was 8.74% but 22% of those on ventilator died. Our patient received H₂ receptor antagonist and prophylactic antibiotic while on ventilator, which seems to have predisposed her to the development of ventilator associated *Pseudomonas* pneumonia. Autonomic neuropathy, which developed in the second week, appears to be a delayed manifestation of OP poisoning. Critical illness neuropathy, which can occur under similar circumstances, is characterized by motor neuropathy without overt dysautonomic features.

This case of severe OP poisoning has been reported to highlight the importance of speedy decontamination, prompt institution of ventilatory support and prolonged administration of oximes. The complications encountered during the course of management have been discussed. Autonomic neuropathy as a delayed manifestation of OP poisoning has been reported for the first time.

References

1. Jeyratnam J. Acute Poisoning : A major health problem. *World Health Stat Q* 1990;43:139-45.
2. Singh S, Wig N, Chaudhary D, Sood NK et al. Changing pattern of acute poisoning in adults : Experience of a large north-west Indian hospital (1970-89). *J Assoc Physicians India* 1997;45:194-7.
3. Siwach SB, Gupta A. The profile of acute poisoning in Haryana-Rohtak study. *J Assoc Physicians India* 1995;11:756-9.
4. Adhlakha A, Philip PJ, Dhar KL. Organophosphate and carbamate poisoning in Punjab. *J Assoc Physicians India* 1988;36:210-12.
5. Ram JS, Kumar SS, Jayarajan A, Kuppuswamy G. Continuous infusion of high dose of atropine in management of organophosphorous compound poisoning. *J Assoc Physicians India* 1990;39:190-3.
6. De Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome of management in acute organophosphorous poisoning? *Lancet* 1992;339:1136-8.
7. Thompson DF, Thompson GD, Greenwood RB, Trammel HL. Therapeutic dosing of pralidoxime. *Drug Intell Clin Pharm* 1987; 21(7-8):590-3.
8. Goel A, Joseph S, Dutta TK. Organophosphate poisoning : predicting the need for ventilatory support. *J Assoc Physicians India* 1998;46:786-90.