ORIGINAL PROF-757

ORGANOPHOSPHOROUS POISONING;
EMERGENCY MANAGEMENT IN INTENSIVE CARE UNIT

DR. SAFDAR ABBAS, MBBS, MCPS, FCPS
Classified Anaesthetist
CMH Pano Aqil Cantt

DR. SAEED AKRAM, FCPS
CMH Pano Aqil Cantt

DR. MOHAMMAD NASIM RIAZ,, MCPS, DA (UK), FCPS
CMH Pano Aqil Cantt

A B S T R A C T

Objective: To evaluate the clinical presentation, management and outcome of organophosphorous pesticides poisoning in intensive care unit. Design: A retrospective study. Place & Duration: Intensive Care Unit of Combined Military Hospital Pano Aqil from January 2002 to August 2003. Subjects & Methods: 26 patients of organophosphorous(OP) poisoning admitted to intensive care unit during this period were included. Diagnosis was based upon history and clinical findings. Decontamination of skin, gastric lavage with activated charcoal and intravenous administration of atropine were the mainstays of therapy, pralidoxime could not be given to any patient due to its non-availability. Endotracheal intubation and mechanical ventilation was performed in case of altered conscious state, respiratory insufficiency and circulatory collapse. Ventilatory support was provided on synchronized intermittent mandatory ventilation with pressure support and positive end expiratory pressure (Bennet-7200 ventilator). Data is presented as $\pm$ standard deviation. Results: There were 16 male and 10 female patients. Mean age was 35 $\pm$ 15 yrs. 14 were suicidal and 12 were accidental exposures. 21 patients were affected through gastrointestinal route, 4 persons through inhalation and 1 patient through abraded skin. Diagnosis was delayed in 3 patients. Excessive salivation, altered mental state and miosis were the most frequent signs at the time of presentation. Initially, 17 patients presented with gastrointestinal symptoms, 7 with neuromuscular weakness and 2 patients had chest pain with syncope. 14 patients required ventilatory support. Overall complications were observed in 16 patients, 7 patients developed respiratory, (aspiration, pulmonary oedema, pneumonia, sepsis), 3 had neurological problems (convulsions, coma, polyneuropathy), 2 had cardiac arrhythmias, and 1 had renal failure. 3 patients developed intermediate syndrome. 5 patients died. Average duration of stay in intensive care unit was 6.2 $\pm$ 2.8 days. Conclusion: Organophosphorous insecticide poisoning is a common, rapidly progressive and potentially fatal clinical entity. Such patients need careful thorough assessment, early diagnosis, vigilant monitoring and aggressive supportive management in the intensive care setting. Mechanical ventilation is life saving in many of such cases.

Key Words: Organophosphorous, anticholinergic, oximes, mechanical ventilation, pesticides

INTRODUCTION

Organophosphorous (OP) compounds constitute the main class of organic insecticides used globally for the pest control[1]. World Health Organization has estimated that more than three million cases of acute serious pesticides poisoning occur worldwide annually mainly by organophosphates and is a major cause of morbidity and

mortality especially in the third world countries [2]. In Pakistan it accounts for 39.7% of cases admitted with poisoning and 16% of total admissions to the intensive care unit (ICU)[3], whereas in India, 12% of all ICU admissions are due to such cases[4]. Rural areas are worst affected. Poisoning results either from suicidal, or accidental over exposure during farming mainly through the gastrointestinal, inhalational or the dermal routes[5]. Males (<30 years) are usually affected more than females and a large number of cases present following a suicidal attempt [6]. Parathion is the most common cause of human poisoning. OP insecticides inhibit both true and pseudocholinesterase irreversibly resulting in accumulation of acetylcholine at nicotinic, muscarinic and central cholinergic synapsis, causing their over stimulation and disruption of neurotransmission in the central and peripheral nervous system.

Clinical features are variable and usually occur within 24 hours after exposure with multi-system manifestations involving the gastrointestinal, respiratory, nervous, and cardiovascular systems. Skeletal muscles and metabolic disturbances are also seen in some cases (table 1). The mortality rate of OP poisoning is high and related to a delayed diagnosis and inappropriate treatment. The stormy clinical course often necesscitates ICU admission, vigilant monitoring and aggressive management of such cases. We present our experience of management of serious OP poisoning cases in ICU.

METHODS

A retrospective study was carried out in our intensive care unit between January 2002 to August 2003. 26 patients of OP poisoning were admitted during this period. Diagnosis was based on history and clinical findings. Laboratory values of cholinesterase could not be measured due to its non-availability. Management in the ICU included skin decontamination, gastric lavage, administration of activated charcoal through nasogastric tube (1g/kg body weight) and intravenous atropine boluses (2mg every 20min) followed by infusion (0.02-0.06 mg/kg/hour) till secretions were reduced (main reliance therapeutic point), heart rate around 110-140 beats/min and pupils were mid-dilated (heart rate and pupil size were not the absolute points to stop atropine therapy). Pralidoxime could not be given to any patient as it was not available. Intavenous fluid resuscitation was carried out in patients with circulatory collapse. Patients with deteriorating levels of consciousness, impending respiratory failure (tachypnoea with respiratory rate > 35 breaths/min, oxygen saturation < 90% on oxygen mask) and persistently poor circulatory status (blood pressure <70mmHg) were intubated and placed on ventilatory support with synchronized intermittent mandatory ventilation (SIMV) mode and pressure support of 10cm of water. Positive end expiratory pressure (PEEP) 4-6cm of water was added to keep oxygen saturation > 95% on fraction inspired oxygen concentration (FIO_2) of 0.4-0.5. Weaning from ventilatory support was carried out by gradual withdrawl of PEEP, decrease in SIMV rate and intermittent disconnection from the ventilator. Monitoring included electrocardiography, non-invasive blood pressure, oxygen saturation (SPO_2) urine output and body temperature (core and peripheral). Routine biochemistry was performed on daily basis, however facilities for monitoring arterial blood gases and acid-base status were not available. Data being presented as mean $\pm$ standard deviation.

RESULTS

26 patients with OP poisoning were included, there were 16 male (61.5%) and 10 female (38.4 %) patients. Mean age was 35 $\pm$12 years. Fourteen patients (53.8%) made suicidal attempt while twelve patients (46.1%) had accidental / occupational exposure.

Eighteen patients (69.2%) were with medium severity and eight patients (30.6%) were with high severity of illness. Twenty-one patients (80.7%) were poisoned through the gastrointestinal tract whereas in four patients (15.3%) inhalation route was involved, one patient (3.8%) had absorption through the abraded skin of back (while carrying the pesticide drum).

Average time to reach hospital after poisoning was 10.4 hours (range 4 - 68 hours). Seventeen patients (65.3%) presented with gastrointestinal symptoms (excessive salivation,abdominal cramps,vomiting and diarrhoea), seven patients (26.9%) predominantly had neurological disturbances (drowsiness, restlessness, agitation, stupor muscular weakness, tremor and convulsions) and two patients (7.6%) presented with syncope and severe hypotension (blood pressure < 70mmHg).

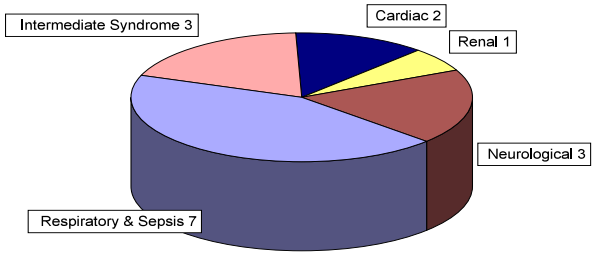
Table-I Signs & Symptoms of OP poisoning		
Muscarinic	Nicotinic	Central Receptors
CARDIOVASCULAR	CARDIOVASCULAR	Anxiety
Bardycardia	Tachycardia	Ataxia
Hypotension	Hypertension	Restlessness
		Convulsions
RESPIRATORY	MUSCULOSKELETAL	Trremors
Rinorrhea	Weakness	Coma
Bronchorrhea	Fasciculation	Respiratory
Bronchospasm	Cramps	Depression
Cough	Paralysis	Circulatory
		Collapse
GASTROIMTESTINAL		
Increased salivation		
Nausea and vomiting		
Abdominal pain		
Diarrhoea		
Faecal incontinence		
GENITOURINARY		
Urinary incontinence		
OCULAR		
Blurred vision		
Increased lacrimation		
OTHER		
Excessive sweating		

Miosis was observed in all patients. Atropine was the main line of therapy for all the patients, 3 - 4 bolus doses (2mg at 20min interval) were followed by infusion which was continued for 3.7 $\pm$ 2.1 days with a total average dose of 88.6 $\pm$ 33.4mg. None of the patients could get pralidoxime therapy due to its non-availability.

Complications were noted in sixteen patients (61.5%) (Fig-1). Fourteen patients (53.8%) were mechanically ventilated for a duration of 5.4 $\pm$ 2.1 days. Mortality rate for the mechanically ventilated patients was 21.4% (3 patients) whereas it was 16.6% (2 patients) for those who were not mechanically ventilated. Overall mortality was 19.2%, (five patients died); two of them had aspiration pneumonia later developed respiratory distress syndrome, pulmonary oedema and septicaemia culminating in multiple organ failure, one patients had acute renal failure secondary to prolonged hypotension also developed bilateral pneumonia,

the other two who were not being ventilated died – one had sudden severe convulsions followed by cardiac arrest and could not be revived, the other one died of intermediate syndrome. Total stay in intensive care unit was 6.2 ± 2.8 days.

Fig-1. Complications in 16 patients



- Respiratory & Sepsis (7) (aspiration pneumonia, pulmonary oedema, ARDS)
- Neurological (3) (convulsions, nerve palsies, dysarthria)
- Renal (1) (renal failure)
- Cardiac (2) Ventricular fibrillation, heart block)
- Intermediate Syndrome (3) (developed after cholinergic crisis)

DISCUSSION

Tetra-ethyl pyrophosphate (TEPP) was the first organophosphorous compound synthesized in 1854. It remained in agricultural use and as a nerve gas in chemical warfare [7]. The rampant use of OP compounds in agriculture, easy accessibility, and ignorance about their potential toxicity especially in the developing countries has led to increased human fatalities in recent years. A significant proportion of young patients present after suicidal attempt [8]. Fourteen of our patients (53.8%) presented following a suicidal attempt which is comparatively less than in some of the African countries (68%) and Sri Lanka[9]. These compounds bind irreversibly with the cholinesterase at the cholinergic nerve endings and interfere with the neuronal transmission in the central and peripheral nervous system thereby acting as neurotoxins[10]. Initially, most of the patients presented with symptoms and signs of acute gastroenteritis, vomiting, diarrhoea and abdominal pain usually within 24 hours of exposure. In our study, 65.3% of the patients presented with gastrointestinal symptoms (21 patients). ECG changes (prolonged PR interval, ST elevation) were observed in 5 patients. Metabolic disturbances are also common in these patients depending upon the dose, duration, type of compound ingested and organ system involved (perhaps due to circulatory collapse, respiratory paralysis, vomiting, metabolic or respiratory acidosis and hyperglycemia)[11].

In our study, raised aspartate aminotransferase and hyperglycemia were noted in 10 and 18 patients respectively. We had some limitations during the course of management as oximes (pralidoxime, obidoxime) could not be used due to non- availability but literature points to their efficacy especially if administered early in the course of disease and in low – moderate dosages[12], however, more experience is still required in this regard. We relied entirely upon atropine therapy (boluses and infusion) which is also supported by the experiences of Ram and Kumar that atropine infusion reduces the chances of toxicity and overall mortality[13]. With infusion therapy, uncontrolled tachyarrhythmias are avoided which are likely to occur in a hypoxic heart with dangerous consequences. Atropine blocks acetylcholine receptors and halts cholinergic stimulation. Clearing of bronchial secretions is the end point of atropine stimulation and not the pupil size or the absolute dose of atropine. Although bronchorrhoea and bronchospasm is encountered in many of such cases but theophylline is contraindicated[14].

Similarly we did not have the facility to monitor cholinesterase levels though literature points that true cholinesterase (but not pseudocholinesterase) levels correlate with the severity of illness[15].

Mechanical ventilation is life saving in patients with deteriorating levels of consciousness, neuromuscular weakness/paralysis and poor haemodynamics (an early priority is to prevent gastric aspiration and its sequelae-severe protracted hypoxaemia). Tachypnoea was the earliest sign in patients who developed respiratory failure. Mortality rate was more in patients who were mechanically ventilated. Fourteen patients (53.8%) with impending respiratory failure were mechanically ventilated, only three

of them died (21.4%). On the other hand, twelve patients (46.1%) did not require ventilatory support and two (16.6%) of them died. Intermediate syndrome developed in three patients (11.5%). It is a distinct clinical entity that develops after acute cholinergic crisis and before the expected onset of delayed polyneuropathy (24-96 hours after poisoning). Synanyake in his series of 10 patients observed that it developed as respiratory insufficiency after initial cholinergic crisis (Type II respiratory failure) and 70% of such patients required ventilatory support[16-18].

One of the earliest signs is inability of the patient to lift the neck from pillow and weakness of proximal muscles. Cranial nerve palsies (involving extraocular muscles, 7th & 10th cranial nerves) are also seen in some patients[19]. Overall our16 patients (61.5%) developed various complications.

Respiratory support in ICU consisted of synchronized intermittent mandatory ventilation plus pressure support and positive end expiratory pressure to achieve adequate lung expansion and oxygenation on moderate concentration of inspired oxygen (40-50%). Other measures include humidification, nebulization, removal of secretions, nutritional support and appropriate antibiotics coverage. Respiratory failure due to aspiration pneumonia and acute respiratory distress syndrome was the most difficult complication to manage as 21.4% (3 patients) of our mechanically ventilated patients died.

CONCLUSION

OP poisoning is a common, rapidly progressive and potentially fatal clinical entity. Careful, thorough clinical assessment with early diagnosis, aggressive therapeutic interventions (including mechanical ventilation), vigilant monitoring and overall good supportive nursing care with special emphasis to prevention and treatment of respiratory complications all are necessary to achieve a favourable outcome.

REFERENCES

1. Bardin, PG, Van Eeden, SF, Moolman, et al. Organophosphate and Carbamate Poisoning. Arch Intern Med 1994, 154:143-144.

2. Jeyaratnam J. Acute Pesticide Poisoning a major health problem. World Health Stat Q 1990; 43:139-145.

3. Jamil H. Organophosphorous Insecticide Poisoning. JPMA 1989; 39:27-31.

4. Cherian AM, Jeyaseelan L, Peter JV, et al. Pralidoxime in the treatment of organophosphorus poisoning-a randomized, double blind, placebo-controlled clinical trial. INCLEN Monograph series on Critical International Health Issues No.7, Dec 1997.

5. Shah AC, Trivedi AM Vishwanath N et al Intensive respiratory care service. Organisation, orientation, system and future. Our experience of management of 288 cases. J Assoc Physicians India 1990;38:140-143.

6. Hayes, WJ: organophophate insecticides. In pesticides studied in Man. Edi by Hayes WJ. Baltimore, MD Williams and Wilkins; 1982:285-315.

7. Haddad LM. Organophosphates and other insecticides. In: Haddad LM, Winchester J,eds. Clinical management of Poisoning and Drug over dose, W.B. Saunders Company 1990;1076-1087.

8. Agarwal SB. A clinical, biochemical, neurobehavioral and sociopsychological study of 190 patients admitted to hospital as a result of acute organophosphorous poisoning. Environ Res 1993;62:63-70.

9. Wadia RS, Sadagopan C, Amin RB, Sardesai HV. Neurological manifestations of organophosphorous insecticide poisoning. J Neurol Neurosurg Pshychiatry 1974;37:841-847.

10. Bardin PG, van Eeden SF. Organophosphate poisoning: grading the severity and comparing treatment between atropine and glycopyrolate. Crit Care Med 1990;18:956-960.

11. Kamal AA, Elgarhy, MT, Maklady, F, et al. a serum choline esterase and liver function among a group of organophophorous pesticides sprayers in Egypt. J Toxical Clin Exp1990, 10:427-435.

12. De Silva, HJ, Wijewickrema, R, & Senanyake, N: Does pralidoxime affect outcome in acute organophophorous poisoning? Lancet 1992, 339:1136-1138.

13. Ram JS, Kumar SS, Jayarajan A, Continuous infusion of high doses of atropamine in the management of organophosphorous compound poisoning. J Assoc Physicians India 1991;39:190-193.

14. Tafuri J, Roberts J< organophosphate poisoning. Ann Emerg Med 1987;16:193-202.

15. Bobba R, Venkataraman BV, Pais P, Joseph T. correlation between the severity of symptoms in organophosphorous poisoning and cholinesterase activity (RBC and Plasma) in humans. Ind J Physiol Pharm 1996;40;249-252.

16. Tsao TC, Juang Y, Lan R, Respiratory failure of acute organophosphate and carbamate. Chest 1990;98:631-636.

17. De Bleecker J, Van Den Neuker K, Colardyn F. intermediate syndrome in organophosphorous poisoning: a prospective study, Crit Care Med 1993;21:1706-1711.

18. He F, Xu H, Qin F, et al. intermediate myasthenia syndrome following acute organophosphate poisoning-an analysis of 21 cases. Hum Exp Toxicol 1998;17:40-45.

19. Moretto A, Lotti M. poisoning by organophosphorous insecticides and sensory neuropathy. J Neurol Neurosurg Psychiatry 1998;64:463-468.