

Management of Acute Organophosphorus Insecticide Poisoning: An Experience at a University Hospital

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ABSTRACT

OBJECTIVE: To document the management and subsequent outcome of patients with organophosphorus (OP) poisoning in intensive care unit of a university hospital.

DESIGN: Descriptive, retrospective study.

SETTING: Intensive Care Unit of Liaquat University Hospital Hyderabad, Sindh – Pakistan, from May 2004 to October 2006.

METHODS: Medical records of patients of OP poisoning admitted to intensive care unit of our hospital from May 2004 to October 2006 were reviewed. Diagnosis was confirmed from the history and clinical findings. Management, complications and subsequent outcome were noted.

RESULTS: Total 111 patients of OP poisoning were admitted in the ICU during the study period. Majority of patients i.e. 67(60.4%) were males and 44 (39.6%) were females. Mean age was 25.26±8.52 years with 85.6% within the age limit of 12-30 years. Majority of patients (89.2%) had suicidal attempt. In 94.6% patients, ingestion was the route of exposure. Mean ICU stay was 2.3±3.2 days while 20(18%) patients needed mechanical ventilatory support. Overall mortality rate was 9%.

KEY WORDS: Organophosphorus Poisoning. Atropine. Pralidoxime. ICU Management.

INTRODUCTION

Organophosphorus (OP) insecticides are widely used in agriculture, usually as pesticides. Poisoning by organophosphates frequently causes ill health and kills hundreds of thousands of people each year¹, especially in the developing countries. Worldwide number of organophosphorus intoxications is estimated at some 3,000,000 per year.² According to the estimates of World Health Organization (WHO), nearly 200,000 people die from pesticide poisoning each year.¹ However, this figure may be an underestimation as, in China alone, an estimated 175,000 deaths occur each year, mostly in farming communities.⁴ Deliberate or accidental ingestions are the commonest modes of poisoning with organophosphates.⁵ Majority of deaths occur following deliberate self-poisoning.⁶⁻¹¹ They are common suicidal agents in Pakistan¹², India¹³, Sri Lanka¹⁴, and other Asian and South Asian countries. Organophosphorus compounds irreversibly inhibit acetylcholinesterase at neuromuscular junction and in autonomic as well as central nervous system. This results in accumulation of acetylcholine and overstimulation of acetylcholine receptors leading to acute cholinergic crisis, which is characterized by bradycardia, bronchorrhoea, miosis, sweating, salivation, lacrimation, defecation, urination and hypotension. In addition, skeletal muscle weakness and fasciculations also

develop.¹⁵ After severe exposure, slurred speech, convulsions, coma and respiratory depression may also occur. Death occurs acutely due to respiratory failure or cardiovascular collapse and later as a result of peripheral respiratory failure and complications of aspiration and long-term ventilation.⁷ Current standard treatment for OP poisoning involves washing of skin and gastric lavage, administration of activated charcoal, atropine/glycopyrrolate, oximes and other newer compounds in addition to ventilatory support which they may require.¹⁶ These are only partly effective, with mortality rate of over 10% or even higher rates.¹⁰ Accident and Emergency (A&E) Department of Liaquat University Hospital Hyderabad routinely receives the victims of organophosphorus poisoning from the farming communities all around. After initial stabilization and emergency management at A&E Department, almost all the patients are shifted to the Intensive Care Unit for further management. We retrospectively reviewed the records of these patients to evaluate and document their management and subsequent outcome.

PATIENTS AND METHODS

A retrospective study of all the patients of organophosphorus poisoning, admitted and managed in the intensive care unit of Liaquat University Hospital Hy-

derabad, during May 2004 to October 2006, was conducted. Available medical records of these patients were reviewed and data entered in a proforma for further analysis. Demographic data, mode of poisoning, route of exposure, treatment, complications and mortality were recorded. Statistical analysis was done using SPSS 10.0.

RESULTS

All patients diagnosed as cases of organophosphorus poisoning were initially brought in A&E Department which is adjacent to our ICU. Diagnosis was made on the basis of history of exposure or contact and characteristic clinical picture. Treatment was started immediately at A&E Department. Clothes were removed and body washed with soap water. Nasogastric tube was passed to decompress the stomach and wash it with normal saline or tap water. Activated charcoal was not used due to its non-availability. All patients were catheterized to monitor and maintain the urine output. Patients were then shifted to ICU for further management. Oxygen was started in all patients. If patient's conscious level was depressed, could not maintain airway or had inadequate breathing, endotracheal intubation was done and oxygen was given by T-piece. Mechanical ventilatory support was given by synchronized intermittent mandatory ventilation (SIMV), pressure support (PS) and positive end expiratory pressure (PEEP), if needed. Patients did not receive any neuromuscular blocking agent to facilitate endotracheal intubation or mechanical ventilatory support. Atropine and pralidoxime sulphate were administered in all patients. Starting dose of atropine was 1- 2 mg bolus intravenously. Then 1-mg was given every 15 minutes until targets of atropine therapy were achieved (**Table I**). Dose of atropine was then progressively decreased. Pralidoxime 1-gm was given to all patients in the form of intravenous infusion, and was repeated every 8-12 hours until fasciculations disappeared or skeletal muscle weakness was relieved. Midazolam or propofol was administered as intravenous bolus or infusion for sedation. Monitoring included ECG, NIBP, SaO₂, temperature and urine output. Laboratory investigations were done on daily basis and included hematocrit, blood sugar, urea, creatinine and electrolytes. Chest X-Ray, 12-lead ECG and arterial blood gases were also done, when needed. A total of 111 patients of OP poisoning was admitted in ICU during the study period. Majority of patients (60.4%) was male. Mean age was 25.26±8.52 years. Characteristics of patients, including route as

well as mode of poisoning and severity of symptoms are given in **Table II**. Severity of poisoning was graded using modified Dreisbach's classification (**Table III**). The length of ICU stay varied from less than 24 hours to more than 7 days (**Table IV**). Complications and their frequency are given in **Table V**. Respiratory failure was observed in 18% (n=20) patients. All these patients received mechanical ventilatory support. Nine out of these patients developed ARDS (Acute Respiratory Distress Syndrome) due to aspiration of gastric contents. One patient developed delayed polyneuropathy. When discharged from the ICU, he was unable to, and could not maintain his previously erect posture due to peripheral muscle weakness. Overall mortality ratio was 9% (n=10). The mortality rate for the patients who required mechanical ventilation was 40% (n=8), but the rate was 2.2% (n=2) for the patients who were not mechanically ventilated.

**TABLE I:
TARGET END-POINTS FOR ATROPINE THERAPY**

Chest	Clear on auscultation with no wheeze
Heart rate	>100 beats/min
Pupils	No longer pinpoint
Bowel sounds	Just present

**TABLE II:
CHARACTERISTICS OF 111 PATIENTS OF OPP***

Characteristic	n (%)
Age (years)	
12-30	95 (85.6)
>30	16 (14.4)
Sex	
Male	67 (60.4)
Female	44 (39.6)
Mode of Poisoning	
Suicidal	99 (89.2)
Accidental	12 (10.8)
Route of Exposure	
Ingestion	105 (94.6)
Inhalation	4 (3.6)
Topical	2 (1.8)
Severity of Poisoning	
Mild	64 (57.7)
Moderate	30 (27.0)
Severe	17 (15.3)

*Organophosphorus Poisoning

**TABLE III:
DREISBACH'S CLASSIFICATION SHOWING
SEVERITY OF POISONING³**

Grade	Symptom
Mild	Nausea Vomiting Diarrhea Sweating
Moderate	Lacrimation Salivation Meiosis Fasciculation
Severe	Incontinence Apnoeic spells ARDS Areflexia Seizures Coma

**TABLE IV:
LENGTH OF ICU STAY**

Duration of stay	n (%)
Less than 24 hours	58 (52.3)
24 to 48 hours	30 (27.0)
2 to 4 days	12 (10.8)
5 to 7 days	6 (5.4)
More than 7 day	5 (4.5)

**TABLE V:
COMPLICATIONS DURING ICU STAY**

Complications	Number of patients (%)
Respiratory Failure	20 (18%)
ARDS	9 (8.1%)
Intermediate Syndrome	5 (4.5%)
Sepsis and MODS**	5 (4.5%)
Delayed Polyneuropathy	1 (0.9%)

**Multi Organ Dysfunction Syndrome

DISCUSSION

Organophosphorus compounds are acetylcholinesterase inhibitors. They are commonly used as pesticides in agriculture. Their easy availability has resulted in suicidal as well as accidental poisoning. OP poisoning for suicide is a major clinical problem in developing countries and is responsible for more than

90% of exposures.¹⁷ Most deaths occur in rural areas of the developing world.¹⁰ Diagnosis of OP poisoning depends mainly on history, characteristic clinical presentation and decreased levels of serum and erythrocyte cholinesterase levels. In this study, cholinesterase levels were not assessed due to non-availability of the facility. However, as a principle, treatment of OP poisoning should be started immediately and must not await the results for serum cholinesterase levels. Treatment of OP poisoning, apart from measures to decontaminate, is primarily aimed at reversing the effects of the compound by administration of atropine. Atropine is highly effective in antagonizing the actions of organophosphates at muscarinic receptor sites and is administered to adults in doses of 2-mg every 5 to 10 minutes. Pralidoxime, another compound, which regenerates and reactivates acetylcholinesterase from the OP-cholinesterase complex is used as an antidote to treat OP poisoning. Although it works at nicotinic, muscarinic, and central nervous system receptors, its main therapeutic effect is predicted to be the recovery of neuromuscular transmission at nicotinic synapses. Although pralidoxime should be given as soon as possible, a beneficial response as long as 24 hours after exposure has been reported.¹⁸ In this study, we observed that out of 111 patients, 60% were males, and 85.6% were within the age limit of 12-30 years. These observations are consistent with the results of Srinivas, et al.¹⁹ In his study, males outnumbered females (57% vs. 43%) with all types of pesticides including organophosphorus compounds and two-thirds of them were less than 30 years of age. Similarly in the studies by Safdar²⁰, Fahmi and Aziza²¹, number of male victims was higher than females. However, in some other studies^{12,22, 23}, OP poisoning was more common in females than males. Majority (89.2%) of cases was suicidal in this study. The fact that majority of cases were due to suicidal mode of poisoning was in agreement with other studies^{19, 21-24}, which showed deliberate self poisoning varying from 68% to 96%. In the study by Aziza, et al²¹, 76.92% cases were suicidal and 23.07% were accidental. Length of ICU stay in our patients was 2.3±3.2 days whereas 88 (79.2%) were discharged from ICU within 48 hours and shifted to the medical wards. One patient stayed for 28 days, who was kept on mechanical ventilatory support and ultimately expired because of ARDS and multiorgan dysfunction. Duration of ICU stay was 8.6 (range 3-15) days in the study by Aziza, et al.²¹ The reason behind this significantly longer duration of stay might be that only those patients who required mechanical ventilatory support were admitted in ICU. The duration of the intensive care stay was 5.2 ± 3.0 days in a study by Murat and Muhammed.²² The most troublesome complication in our series was res-

piratory failure, which was observed in 18% of patients. Patients with OP poisoning may have respiratory failure for many reasons, and multiple mechanisms including aspiration of gastric contents, excessive secretions, thoracic weakness, decreased respiratory drive, pneumonia and sepsis complicating ARDS.^{25,33} Intermediate syndrome is a complication which develops 1-4 days after acute organophosphorus poisoning, and is characterized by respiratory insufficiency, proximal muscle weakness and cranial nerve palsies. With the support of mechanical ventilation, it usually resolves within 4-18 days with high survival ratio. Reported frequency of intermediate syndrome varies from 8% to 49%.²⁶⁻²⁸ Frequency of intermediate syndrome in this study was 4.5% (n=5). Reported mortality following OP insecticide poisoning varies between 4% and 30%.²⁹ The overall mortality rate in this study was 9%. Mortality rate was 5.5% in a study by Malik²³ and 8% in the study by Aziza, et al.²² In some other studies^{22,30,31}, it varied from 12% to 27%. We observed that mortality rate was much higher in patients who required mechanical ventilation (40%) as compared to the patients managed on spontaneous breathing (2.2 %). In a study by Safdar, et al²⁰, 21.4% of patients who received mechanical ventilatory support ultimately expired. In another study, mortality rate for the patients who required mechanical ventilation was 50%.²² In contrast to these observations, Aziza, et al reported 8% mortality in patients who received mechanical ventilatory support. It is possible that severely poisoned patients living far away from the hospital, died before reaching there, reducing mortality among patients admitted to the ICU.

CONCLUSION

Because of widespread use of OP pesticides by farming communities of the developing world, it is very difficult to reduce mortality by primary prevention. Immediate shifting of the victim to a well-equipped and well-staffed ICU, careful resuscitation with appropriate use of antidotes and good supportive care and observation can help reduce the number of deaths in the period after admission to the hospital. Awareness and education of general practitioners in the rural areas regarding emergency management as well as prompt referral to an appropriate facility, is also recommended to reduce the mortality rate.

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