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Study of Organophosphorus Poisoning at a Tertiary Care Teaching Hospital

Rumaisa Ayoub[1*], Gulnar Fatima[2], Yawar Nazir[3]

[1]Post Graduate Scholar, Department of Anesthesiology and Critical Care, GMC Srinagar, 3QPX+9GP, Bemina, Srinagar, Jammu and Kashmir 190010, India

[2]Post Graduate, Department of Anesthesiology and Critical Care, GMC Srinagar, 3QPX+9GP, Bemina, Srinagar, Jammu and Kashmir 190010, India

[3]Senior Resident, Department of Surgery, SKIMS, Soura, SKIMS Main Rd, Soura, Srinagar, Jammu and Kashmir 190011, India

Abstract: ***Introduction*:** Organophosphate (OP) insecticides inhibit both cholinesterase and pseudo-cholinesterase activities. The inhibition of acetylcholinesterase causes accumulation of acetylcholine at synapses, and overstimulation of neurotransmission occurs as a result of this accumulation. The mortality rate of OP poisoning is high. Early diagnosis and appropriate treatment is often life saving. Treatment of OP poisoning consists of intravenous atropine and oximes. The clinical course of OP poisoning may be quite severe and may need intensive care management. ***Methods:*** A retrospective study was performed on the patients with OP poisoning. Fifty patients were included. Diagnosis was performed from the history taken either from the patient or from the patient's relatives about the agent involved in the exposure. Diagnosis could was confirmed with serum and red blood cell anticholinesterase levels. Intravenous atropine and pralidoxime was administered as soon as possible. Other measures for the treatment were gastric lavage and administration of activated charcoal via nasogastric tube, and cleansing the patient's body with soap and water. The patients were intubated and mechanically ventilated if the patients had respiratory failure, a depressed level of consciousness, which causes an inability to protect the airway, and hemodynamic instability. Mechanical ventilation was performed as synchronized intermittent mandatory ventilation + pressure support mode, either as volume or pressure control. Positive end expiratory pressure was titrated to keep SaO_2 above 94% with 40% FIO_2. Weaning was performed using either T-tube trials or pressure support weaning. The chi-square test was used for statistical analysis. Data are presented as mean ± standard deviation. ***Results:*** There were 26 female and 24 male patients. Thirty-five were suicide attempts and 15 were accidental exposure. The gastrointestinal route was the main route in 44 patients. The most frequent signs were meiosis, change in mental status, hypersalivation and fasciculations. Ten patients (20.0%) required mechanical ventilation. Complications were observed in 35 patients. These complications were respiratory failure (14 patients), aspiration pneumonia (10 patients), urinary system infection (6 patients), convulsion (4 patients) and septic shock (1 patient). The duration of the intensive care stay was 5.2 ± 3.0 days. Discussion**:** Ingestion of OP compounds for suicidal purposes is a major problem, especially in developing countries. Thirty-five of our patients used the OP insecticide for suicide. The average respiratory rate of these patients increased from 22 to 38 breaths/min, which is an important sign of respiratory distress. The nurse to patient ratio was increased after these events. Early recognition of respiratory failure resulting in intubation and mechanical ventilation is a life-saving intervention for patients with OP poisoning. Respiratory failure is the most troublesome complication, which was observed in 35 patients. Patients with OP poisoning may have respiratory failure for many reasons, including aspiration of the gastric content, excessive secretions, pneumonia and septicemia complicating acute respiratory distress syndrome. ***Conclusions:*** OP insecticide poisoning is a serious condition that needs rapid diagnosis and treatment. Since respiratory failure is the major reason for mortality, careful monitoring, appropriate management and early recognition of this complication may decrease the mortality rate among these patients.

Keywords: Anticholinesterase, atropine, organophosphate pesticides, poisoning, pralidoxime.

Research Paper

***Corresponding Author:**
Rumaisa Ayoub
Post Graduate Scholar, Department of Anesthesiology and Critical Care, GMC Srinagar, 3QPX+9GP, Bemina, Srinagar, Jammu and Kashmir 190010, India

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INTRODUCTION

Hundreds of OP compounds are currently available to use as insecticides [1]. OP insecticides inhibit both cholinesterase and pseudocholinesterase activities [2], as they are irreversible cholinesterase inhibitors. The inhibition of cholinesterase activity leads to accumulation of acetylcholine at synapses, causing overstimulation and disruption of neurotransmission in both central and peripheral nervous systems [2]. Exaggerated manifestations of nicotinic and muscarinic receptors appear as a result of these actions [3]. OP insecticides are one of the most important causes of poisoning in Turkey, as in many developing countries [4]. The mode of exposure to OP insecticides varies, including dermal, gastrointestinal, inhalational and

intravenous routes [2, 5, 6]. Poisoning occurs as a result of agricultural use, accidental exposure, suicide and, rarely, homicide [2, 7, 8]. The mortality rate of OP poisoning is high: fatal issue is often related to a delay in diagnosis or an improper management. Early diagnosis and appropriate treatment, conversely, are often life saving, although the clinical course of OP poisonings might be quite severe and necessitate intensive care management. In this article, we report our experience with the intensive care management of serious OP insecticide poisonings.

METHODS

A retrospective study was conducted on patients with OP poisoning 1990. The diagnosis was based on information taken either from the patient or from the patient's family about the agent involved in the exposure. Treatment was implemented as soon as the diagnosis of OP insecticide poisoning was suspected. Atropine and/or pralidoxime sulfate was administered. Atropine is given either as a continuous infusion or intermittent dosing. Continuous infusion was started as 0.02-0.08 mg/kg per hour until control of hypersecretion occurred. Heart rates exceeding 130 beats/min were avoided using intravenous diltiazem or propranolol for myocardial protection. Intermittent dosing was performed using 2 mg atropine every 15 min until secretions were controlled. Heart rate and pupil size were not used as indices as long as the heart rate was above 60 beats/min. Atropine was discontinued 24 hours after all signs of atropinisation occurred and drying of secretions was achieved. Pralidoxime sulfate was administered as 4 g daily divided to four doses for every patient as long as available.

Blood gas and routine biochemistry were performed daily. Gastric lavage followed by administration of activated charcoal via nasogastric tube, and cleansing of the patient's body with soap and water was started. The patients were admitted to the intensive care unit based on the severity of the clinical signs and symptoms. The indications for endotracheal intubation and mechanical ventilation were as follows: excessive secretions; a depressed level of consciousness, which causes an inability to protect the airway; poor gas exchange, which was unresponsive to oxygen treatment; cardiorespiratory arrest; and severe metabolic acidosis with hemodynamic instability (systolic blood pressure <90 mmHg). Synchronized intermittent mandatory ventilation + pressure support mode in either pressure-controlled or volume-controlled form was started. The positive end expiratory pressure was initially applied as 5 cmH_2O and then titrated to keep SaO_2 above 94% with 40% FIO_2. Weaning from mechanical ventilation was carried out with pressure support weaning and T-tube trials. The chi-square test was used for statistical analysis. Data are presented as mean ± standard deviation.

RESULTS

During the study period, 50 patients who had OP poisoning with a known agent were admitted. There were 26 female and 24 male patients. The mean age was 30 ± 15 years when admitted to hospital. Thirty-five (70%) patients were suicide attempts and 15 (30%) were accidental exposure. Forty-four (88.0%) of the patients were poisoned through the gastrointestinal route. One (2.1%) patient had inhalational poisoning and two (4.2%) patients had intravenous injection for suicidal purposes. The estimated average time for the admission to the emergency department after the exposure was 9.4 hours (range, 1-96 hours). The most frequent clinical signs were meiosis, change in mental status, hypersalivation, agitation and fasciculations

Table 1: Clinical signs and symptoms of the patients

Meiosis	37 (74%)
Depressed mental status	36 (72%)
Hypersalivation	31 (62%)
Agitation	26 (52%)
Fasciculation	23 (46%)
Tachycardia	12 (24%)
Nausea	12 (24%)
Bradicardia	11 (22%)
Muscle weakness	9 (18%)
Vomiting	7 (14%)
Diarrhea	5 (10%)
Midriasis	3 (6%)

Table 2: Abnormal laboratory findings of the patients

Aspartate aminotransferase (U/l)	0-50	53.7 ± 84.3
Lactate dehydrogenase (U/l)	225-450	548.8 ± 45.5
White blood cell count	4000-10,000	13,857 ± 7040
Blood glucose (mg/dl)	70-110	131 ± 61.9

Abnormal laboratory values were elevated liver enzymes, elevated lactate dehyrogenase, elevated blood glucose and leukocytosis. Complications were observed in 35 (74.4%) patients: respiratory failure (14 patients), aspiration pneumonia (10 patients), urinary system infection (6 patients), convulsion (4 patients) and septic shock (1 patient). The duration of the intensive care stay was 5.2 ± 3.0 days.

DISCUSSION

OP compounds are used worldwide in agriculture as well as in household gardens [9]. This easy availability of the compounds has resulted in a gradual increase in accidental and suicidal poisoning, mainly in developing countries [10]. Ingestion of OP in an attempt at suicide is a major problem, especially for developing countries, probably because of the wide availability of pesticides as result of extensive use in agriculture and because of sale of these items over the counter in these countries [1]. OP poisoning due to suicidal attempt accounts for at least 40-60% of all cases in some African countries [10, 11]. In this study, our rate of suicidal poisoning is 70%, probably because of the uncontrolled sale and use of these agents all over the country.

The inhibition of cholinesterase activity leads to the accumulation of acetylcholine at synapses, causing overstimulation of both central and peripheral nervous systems. Exposure to OP will interfere with synaptic transmission peripherally at muscarinic receptors and nicotinic receptors. Nicotinic manifestations include increased or decreased muscle power and skeletal muscle fasciculations. Muscarinic manifestations include excessive salivation, meiosis and diarrhea. The most frequent signs are reported to be meiosis, vomiting, hypersalivation, respiratory distress, abdominal pain, and depressed level of consciousness and muscle fasciculation [10]. In the present case series, the most frequent signs were meiosis, a depressed level of consciousness, hypersalivation, agitation and fasciculations.

Hyperglycemia has been reported many times in the literature [10, 12, 13], and we also observed mild hyperglycemia in 15 patients. The increase in serum glucose is believed to be due to secondary release of catecholamines from the adrenal medulla [14]. We observed 11 patients that had abnormal aspartate aminotransferase levels, which is reported very rarely [15]. OP compounds contain many solvents that may cause this effect. High lactate dehydrogenase levels may be associated with oxidative tissue damage induced by OP insecticides [16], and this level was high in 15 of our patients. Leukocytosis, which we observed in 34 patients, both with and without a left shift has been reported many times [10, 14, 17].

Intermediate syndrome is a state of muscle paralysis that occurs after recovery from cholinergic crisis but before the expected onset of the delayed polyneuropath, and probably results from post-synaptic neuromuscular junction dysfunction [20]. Patients with intermediate syndrome require optimal respiratory management, atropine and pralidoxime. Three patients with intermediate syndrome did not receive pralidoxime and two of these patients eventually died. The rate of intermediate syndrome of our cases was 19.1%, with 4 of the patients intubated and mechanically ventilated, but 3 patients could not be weaned from the mechanical ventilator and died. Three of the cases with intermediate syndrome died due to delay for endotracheal intubation. After these events, we increased the nurse to patient ratio and the number of the residents in the unit because it was obvious that these cases had severe respiratory distress requiring endotracheal intubation before they died.

The mean respiratory rate increased from 22 ± 6 breaths/min to 38 ± 8 breaths/min, which is an obvious sign of respiratory failure, during the last 6 hours of hospitalisation. It has been reported previously that prolonged respiratory support and difficult weaning may be a consequence of intermediate syndrome [11]. Patients with intermediate syndrome may be followed with oxygen support without intubation and mechanical ventilation, but hypoxia and signs of respiratory failure such as tachypnea, paradoxical respiration and vigorous use of accessory respiratory muscles should be followed closely. Observation of any of these signs by an intensive care physician must lead to an assessment of the patient for endotracheal intubation and mechanical ventilation. Aspiration pneumonia is another troublesome complication, and careful monitoring during transport and early recognition of an absent gag reflex may reduce the incidence of aspiration pneumonia. Early recognition of respiratory failure, prompt endotracheal intubation and mechanical ventilation are life-saving measures in severe OP poisoning.

In conclusion, OP insecticide poisoning is a serious condition that needs rapid diagnosis and treatment. Since respiratory failure is the major reason for mortality, careful monitoring, appropriate management and early recognition of this complication may decrease the mortality rate among these patients.

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