Respiratory failure in organophosphate insecticide poisoning

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ABSTRACT

Objectives: Organophosphate compounds (OP) are usual insecticides and may poison human beings in a suicide attempt or accidental exposure. They inhibit activity of cholinesterase. Poisoning may be enough sever for intensive care support. In this paper, we study the prevalence and management of sever cases as well.

Methods: We studied patients with OP poisoning, from November 2002 to November 2005 in Sina Hospital, Tabriz, Iran, retrospectively and found patients who needed intensive care. During 4 years study, we documented 80 patients who were hospitalized due to OP poisoning and used drugs. Treatment with intravenous atropine and pralidoxime was started as soon as possible. We did not administer pralidoxim for 20 patients due to late admission (5 patients) and unavailability of the medicine (15 patients).

Results: Forty-five male and 35 female patients were enrolled in our study. The majority of the patients used OP for suicide attempt and 4 patients had accidental exposure. The mortality rate was 18% in patients who were treated with pralidoxim and patients without pralidoxim had a mortality rate of 21%. Ten patients were mechanically ventilated and the mortality rate was 50%. In patients without MV the mortality rate was 11.7%. The duration of intensive care stay was 7.1±2 days.

Conclusion: Organophosphate compounds poisoning is a serious and lethal condition and needs early diagnosis and appropriate treatment. In patients with respiratory failure the mortality is very high; therefore we recommended early diagnosis, careful monitoring and appropriate management of complications in reducing the mortality rate.

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Organophosphates are used worldwidely as agricultural insecticide and in Iran too, and also they are important agents which lead to serious poisonings.[1] These drugs inhibit the activity of cholinesterase,[2] irreversibly. Inhibition of cholinesterase activity leads to accumulation of acetylcholine in synapses and overestimates neurotransmitters in nervous system,[2] so nicotinic and muscarinic manifestation appear.[3] Organophosphates enter the body space from different routs like skin, gastrointestinal and respiratory tract.[4] In majority of cases, the most important way is via gastrointestinal tract for suicide attempt.[5] In most case, the mortality rate of OP poisoning is high due to delay in diagnosis and treatment. Early diagnosis and appropriate treatment may save the patients life. In sever cases, proper intensive care will be necessary. Majority of patients who need intensive care have respiratory failure and the mortality rate is high.[6]

Methods. We retrospectively studied patients with OP poisoning during 4 years in Sina Hospital, Tabriz, Iran from 2002 to 2005. We had 80 cases. Information was taken from patients or their relatives. We cannot measure cholinesterase blood level. Treatment was initiated as soon as the diagnosis of OP poisoning was suspected. Criteria for inclusion were patients with documented OP poisoning only, without previous respiratory problems, without aspiration pneumonia and septic problems, without previous history of heart failure or diabetes mellitus and without previous liver problems history. Criteria for exclusion were patients without documented OP poisoning, poisoned with OP and other drugs simultaneously, with aspiration pneumonia or septic problems, with previous history of heart failure or diabetes mellitus and with positive liver problems history.

Atropine and/or pralidoxime was administered intravenously. Continuous infusion of atropine with initial dose of 0.01-0.1 mg/kg/hour was used until we controlled the hypersecretion. When

heart rate was above 130 beats/min, oral or intravenous propranolol was administered in the absence of hypotension. Atropine was discontinued 24 hours after atropinization or drying of secretions. Pralidoxime was administered in initial dose of 4 g in 4 divided doses as long as the medicine is available. Twenty patients did not received Pralidoxime due to unavailability of the drugs and late admission. Daily biochemical and arterial blood gas examinations were performed. Gastric lavage followed by administration of activated charcoal via nasogastric tube and washing of the whole body was started. Based on severity of poisoning, patients were admitted to the intensive care unit. If patients had excessive secretion, depressed consciousness, gas exchange impairment, cardiopulmonary arrest, sever acidosis or homodynamic instability with hypotension (<90 mm Hg), they were transferred to the intensive care unit. Mechanically ventilated patients were on synchronized intermittent mandatory ventilation or pressure support mode. Positive end expiratory pressure was initiated with 5 cm H_2O and titrated to keep oxygen saturation of above 90% with 30% Fio2. Weaning from MV was carried out with pressure support or T-tube trial. We used chi-square test for statistical analysis.

Results. The mean age was 35±18 years (45 males and 35 females). Seventy-six patients had suicide attempts and 4 accidental exposures. Approximately 94% (75 patients) poisoned by gastrointestinal route. Estimated average time before admission in the emergency room was 8.2 hours (range, 1-72 hours). The most common clinical signs were meiosis, change in mental state, hypersalivation, agitation and fasciculation (**Table 1**). All patients received atropine. It was administered for 3.8 ± 1.1 days with a total dose of 87.2 ± 51.1 mg. We used pralidoxime for 60 patients. It was administered for 3 ± 1 day with a dose of 3.3 ± 1.0 g. The mortality rate in patients with pralidoxime were 18% but without pralidoxime was 21%. Mechanical ventilation was applied for 10 patients. Mean arterial blood values are summarized in **Table 2**. Duration of MV was 5.2-4.3 days. The mortality rate of mechanically ventilated patients was 50% (5 patients). But the total mortality rate of all patients was 11.7% (7 patients). The mortality rate of mechanically ventilated patients was due to cardiopulmonary arrest, pneumonia and ARDS. Mortality of patients without MV was due to cardiac complications like cardiac arrest. Abnormal laboratory values in these patients were elevated serum LDH; and liver enzymes, leukocytosis and hypokalemia (**Table 3**).

Table 1 - Clinical signs and symptoms.

Sign or symptoms	n	(%)
Meiosis	66	(82)
Hypersalivation	56	(70)
Agitation	46	(58)
Depressed level of consciousness	56	(70)
Fasciculation	34	(42)
Tachycardia	20	(25)
Muscle weakness	18	(22)

Discussion. Organophosphate compounds are used in Iran for agriculture. These drugs are easily available over the counter, that could commonly used for suicide attempt but accidental exposure is also seen.[6] Twenty-five percents of all drug poisonings in our center is due to OP compounds. Inhibition of cholinesterase activity leads to accumulation of acetylcholine in synapses and over stimulation of nervous system. Nicotinic manifestations are increasing or decreasing muscle power and fasciculation. Muscarinic manifestations are excessive salivation, meiosis and diarrhea. The most frequent signs are meiosis, hypersalivation, respiratory distress, loss of consciousness and abdominal pain.[7] In our study, the most common sign was meiosis, hypersalivation, agitation and depressed level of consciousness. We found leukocytosis in 60 patients and Elevated liver enzymes in 15 patients as described in previous studies.[8,9] Elevated liver enzymes were seen in 15 patients that support previous study.[15] Elevation of LDH level occurred in 40 patients and it may be due to oxidative injury.[10] The most important pharmacologic effect of pralidoxime is

Table 2 - Mean arterial blood values.

Value	Mean in patients	Normal range
pH	7.21	6.97-7.45
Carbon dioxide partial pressure (mm Hg)	40.2	22-52
Oxygen partial pressure (mm Hg)	65.1	54-90
Bicarbonate (mmol/L	14.2	11-23
Saturation of oxygen (%)	86.2	72-92

Table 3 - Abnormal laboratory findings.

Laboratory findings	Patients values	Normal values
Aspartate aminotransferase	50.7 ± 84.3	0 - 45
Lactate dehydrogenase	592 ± 40	220 - 400
White blood cell count	14221 ± 6540	4000 - 10,000
Potassium level	4 ±1.5	4 - 5.5

the reactivation of acetylcholinestrase due to the removal of phosphate groups from esteratic site.[11] Pralidoxime must be prescribed before the "aging phenomenon".[12] This drug reserves the effects of OP on the nervous system.[13] In a previous study, it was emphasized that pralidoxime+atropine were not effective in the treatment of poisoning than atropine alone; and the combination therapy had no useful effects on respiratory failure, cardiac or nervous system complications of OP.[14] We observed that pralidoxime did not reduce mortality rate but this issue needs further controlled studies. Therefore, in spite on the observed results, we strongly recommended pralidoxime utilization in these patients. We should implement a well-programmed emergency medical system that we currently do not have. Implement an educational program for professional persons in the field of internal medicine regarding intoxication. After recovery from cholinergic crisis muscle weakness may be occurred[15] and this problem may lead to respiratory failure. An obvious observed finding of respiratory failure is increasing of respiratory rate. Mean respiratory rate increased to 39±4 breaths/min. In this case, patients need respiratory support; and weaning from MV may be more difficult.[16] Patients need oxygen and intubations for MV may be necessary. Signs such as hypoxia, tachypnea, paradoxical respiration and vigorous use of accessory respiratory muscles should be followed closely. These problems must be managed with an intensivist. The mortality rate of mechanically ventilated patients is very high (60%). But it is approximately 11.7 % in other studies. Respiratory failure is one of the most important complications in OP poisoning.[17] It may be due to respiratory muscle weakness, aspiration, hypersecretion, pneumonia, sepsis or ARDS.[18] Aspiration pneumonia is a troublesome complication and we can easily prevent it with careful monitoring.[19] Early diagnosis of respiratory failure and prompt endothracheal incubation and MV may save the patients life.[20,21]

In conclusion, respiratory failure is a life threatening condition in OP poisoning with a very high mortality. Appropriate monitoring and treatment of this problem may diminish mortality.

References

1. Mortensen ML. Management of acute childhood poisoning caused by selected insecticides and herbicides. ***Pediatr Clin North Am*** 1986; 33: 421-445.
2. Bardin PG, Van Eeden SF, Moolman JA, Foden AP, Joubert JR. Organophosphate and carbamate poisoning. ***Arch Intern Med*** 1994; 154: 1433-1441.
3. Öztürk MA, Kelestimur F, Kurtoglu S, Güven K, Arslan D. Anticholinesterase poisonings in Turkey, clinical, laboratory and radiologic evaluation of 269 cases. ***Hum Exp Toxicol*** 1990; 9: 273-279.
4. Guven M, Unluhizarci K, Goktas Z, Kurtoglu S. Intravenous organophosphate injection: an unusual way of intoxication. ***Hum Exp Toxicol*** 1997; 16: 279-280.
5. Midtling J, Barnet P, Coye M, Velasco AR, Romero P, Clements CL, et al. Clinical management of field worker organophosphate poisoning. ***West J Med*** 1985; 142: 514-518.
6. Namba T, Nolte CT, Jackrel J, Grob D. Poisoning due to organophosphate insecticides. Acute and chronic manifestations. ***Am J Med*** 1971; 50: 475-492.
7. Bardin PG, Van Eden SF. Organophosphate poisoning: grading the severity and comparing treatment between atropine and glycopyrolate. ***Crit Care Med*** 1990; 18: 956-960.
8. Hayes, WJ. Organophosphate insecticides. In Pesticides Studied in Man Edited by Hayes WJ. Baltimore (MD): Williams & Wilkins; 1982. pp. 285-315.
9. Bagchi D, Bagchi M, Hassound EA, Stohs SJ. In vitro and in vivo generation of reactive oxygen species, DNA damage and lactate dehydrogenase leakage by selected pesticides. ***Toxicology*** 1995; 104: 129-140.
10. Meller D, Frasier I, Kruger M. Hyperglycemia in anticholinesterase poisoning. ***Can Med Assoc J*** 1981; 124: 745-747.
11. Durham WF, Hayes WJ. Organic phosphorus poisoning and its therapy. ***Arch Environ Health*** 1962; 5: 21-33.
12. Du Toit PW, Muller FO, Van Tonder WM, Ungerer MJ. Experience with the intensive care management of organophosphate insecticide poisoning. ***S Afr Med J*** 1998; 60: 227-229.
13. Mack R. Toxic encounters of the dangerous kind. ***N Carolina Med J*** 1983; 44: 103-105.
14. Kamal AA, Elgarhy MT, Maklady F, Mostafa MA, Massound A. Serum choline esterase and liver function among a group of organophosphorus pesticides sprayers in Egypt. ***J Toxicol Clin Exp*** 1990; 10: 427-435.
15. Hui K. Metabolic disturbances in oranophosphate insecticide poisoning [letter]. ***Arch Pathol Lab Med*** 1983; 107: 154.
16. Haddad L, Winchester J. Clinical Management of Poisoning and Overdose. Philadelphia (PA): WB Saunders, 1983.
17. Namba T. Diagnosis and treatment of organophosphate poisoning. ***Med Times*** 1972; 100: 100-126.
18. Hodgson M, Parkinson D. Diagnosis of organophosphate intoxication [letter]. ***N Engl J Med*** 1985; 313: 329.
19. Hayes MM, Van der Westhuizen NG, Gelfand M. Organophosphate poisoning in Rhodesia. ***S Afr Med J*** 1978; 54: 230-234.
20. De Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome in acute organophosphorus poisoning? ***Lancet*** 1992; 339: 1136-1138.
21. Karalliedde L, Senanayake N. Organophosphorus insecticide poisoning. ***Br J Anaesth*** 1989; 63: 736-750.