ACUTE ORGANOPHOSPHATE INSECTICIDE POISONING

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ABSTRACT

Objective *To describe the clinical course, diagnosis and outcome of acute organophosphate (OP) insecticide poisoning.*

Study design *Descriptive study.*

Place & Duration of study *At National Poisoning Control Centre (NPCC), Medical unit 1, Jinnah Post Graduate Medical Centre Karachi, from 1st January 2000 to 31st December 2007.*

Patients and Methods *A total of 6539 patients were admitted to the ICU of NPCC, out of which 2708 (41%) were of organophosphate poisoning. Lab investigations done included blood complete picture, urea, creatinine, ABG's, and serum cholinesterase levels. Data was retrieved from the files on a structured performa. Variables of the study included gender, mode of exposure, clinical course, management and complications.*

Results *There were 1391(51%) males and 1317 (48%) females. 713 (26%) had accidental exposure, while 1995 (73%) attempted suicide. The majority of patients exhibited the classic clinical features of parasympathetic over activity. 1608 patients received atropine, while pralidoxime alone was given to 399 patients and atropine along with pralidoxime to 701 patients. Complications encountered during their treatment and stay in the hospital included aspiration pneumonia in 310 patients, hyperglycemia in 982 patients. 102 patients had respiratory failure and thus required mechanical ventilation with mean ventilation duration of 2.3 ± 1.5 days. 500 patients had urinary tract infection and 789 patients developed cellulitis or phlebitis. A total of 147 patients died making a mortality rate of 0.05%.*

Conclusions *The widespread use of organophosphates as a household and agricultural pesticide, in the absence of adequate regulations and education in their use is probably the most important reason for OP poisoning in an agricultural country like Pakistan. Despite severe toxicity in most of our cases, there were very few fatalities. This reflects the necessity of early diagnosis, treatment and the implementation of advanced supportive care in ICU.*

Key words *Atropine, Organophosphate Poisoning, Pralidoxime.*

INTRODUCTION:

Organophosphates comprise a wide range of compounds including insecticides, herbicides, fungicides and others. These are used worldwide in agriculture as well as in house hold gardens. Thus far more than 1,000 active substances have been incorporated in approximately 35,000 preparations of pesticides used in agriculture.[1] Use of pesticides has increased food production in parallel with the population growth in many parts of the world. Many insect- borne diseases have been eliminated or controlled by the use of insecticides. In some countries they are used as chemical agents of warfare. OPCs may cause acute or chronic poisonings after accidental or suicidal exposure. It is the commonest suicidal agent in the developing countries like Pakistan. Worldwide, an

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estimated 3,000,000 people are exposed to insecticides each year, with up to 300,000 fatalities.[2, 3] Toxicity generally results from accidental, intentional ingestion or from exposure to agricultural pesticides. [2,4] Other potential causes of organophosphate toxicity include ingestion of contaminated fruit, flour, or cooking oil, and wearing contaminated clothing.[4,5] Hundreds of patients of organophosphate poisoning are admitted to the ICU of NPCC each year. Early diagnosis and appropriate treatment is often life saving. The clinical course of OP poisoning may be quite severe and may need intensive care management. The current study was aimed to evaluate clinical features, characteristics, and management modalities and compare them to other studies.

PATIENTS AND METHODS:

This was a descriptive study conduced at National Poisoning Control Centre, Medical Unit 1, Jinnah Postgraduate Medical Centre Karachi, from 1st January 2000 to 31st December 2007. All the patients of organophosphate poisoning were included in the study. The diagnosis of OP poisoning was based on history of exposure, clinical manifestations of OP poisoning and low serum pseudocholinesterase activity. The more sensitive acetylcholinesterase is not available in our laboratory.

Data was retrieved from the files on the structured performa including demographic characteristics, clinical presentation, history of previous diseases, coexisting medical conditions, drug history, physical examination findings, electro-cardiography, radiography results, and laboratory findings, response to drugs, complications occurred during their stay in the ICU and mortality rate. Data was analyzed using SPSS-10. Frequencies and percentages were computed to present all categorical variables.

RESULTS:

A total of 6539 patients of poisoning were admitted to the ICU of National Poisoning Control Centre during the study period of 8 years. Out of this 2708 (41%) patients were of organophosphate poisoning. 1391(51%) were males and 1317 (48%) females. Most patients ingested the compond (n=2468 - 91%).142 patients (5%) had dermal exposure, 91 patients (3%) had inhalation while 7 patients(0.2%) had parenteral exposure. 73% (n=1995) were suicidal cases while only 26% (713 patients) had accidental exposure. The majority of patients exhibited the classic clinical features of parasympathetic over activity. Almost all the patients had muscle fasicultion. Increased salivation was observed in 97% (2627) cases, 96% (2608) had constricted pupils, increased gut sounds were heard in 94% (2562) cases. The least frequent clinical manifestation was lung crepitations which were observed in only29% (801) cases.

Out of 2708 patients, 1527 (56%) had serum cholinesterase level <4500IU that is below the normal range. In 1604 (59%) cases it was between 4,500-10,000 IU while levels above 10,000 IU were found in only 303 (11%) cases. 1608 patients received atropine. Pralidoxime alone was given to 399 patients and atropine along with pralidoxime was used in 701 patients. Complications encountered during treatment and stay in the hospital included aspiration pneumonia in 310 patients, hyperglycaemia in 982 patients. 102 patients had respiratory failure and required mechanical ventilation with mean ventilation duration of 2.3 ± 1.5 days. 500 patients had urinary tract infection and 789 patients developed cellulitis or phlebitis. The outcome of the organophophate poisoning showed complete recovery in 2531 (93%) patients while 30 (1.1%) patients left the ICU without the medical advice. 147 (5%) patients in this study died.

DISCUSSION:

Organophosphates are widely used in agriculture worldwide and are common cause of poisoning that continue to result in significant fatalities. This is because of free availability of pesticides and it's over the counter sale. The study conducted in Multan from 1996-2000 showed 370 patients of organophoshate poisoning with a mortality rate of 15 %. [6] In California 950 cases were reported within 4 years. Our study showed 2708 (41%) patients of organophsphate poisoning. Easy availability of the compounds has resulted in a gradual increase in accidental and suicidal poisoning, mainly in developing countries. [7] Ingestion of OP in an attempt at suicide is a major problem, especially for developing countries including Pakistan, 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. [8] OP poisoning due to suicidal attempt accounts for at least 40-68% of all cases in some countries [9,10] including some African countries. [7]

Worldwide, the main route of intoxication reported was the oral route possibly due to the high frequency of accidental exposure, especially in children. [11, 12] This study showed the similar results according to which the most common route of exposure was ingestion (91%). Dermal exposure was noted in 5 % cases. Public perception of toxicity of OP is low and many are unaware that even minute quantities of OP are readily absorbed through the skin and can be lethal. Many people who work in farms are simple people who lack experience in dealing with these products. This has been reflected in this study where 3 % cases inhaled the poison due to lack of the appropriate protection and safety measures. In agreement with other reports the insecticide agent was unknown in almost half the patients in our study, and the diagnosis was based on a history of exposure to an unknown agent, clinical findings and low pseudocholinesterase levels.[13,14] This may be due to the fact that those agents are unknown or not licensed for use in the country. In the remaining half, diazinon and malathion were the cause of toxicity.

The primary mechanism of action of OPCs is inhibition of acetylcholinesterase (AChE). OPCs inactivate AChE by phosphorylating the serine hydroxyl group located at the active site of AChE. They inhibit both cholinesterase (known as red blood cell acetylcholinesterase) and pseudocholinesterase (known as plasma cholinesterase) activity. The inhibition of acetylcholinesterase causes accumulation of acetylcholine at synapses with resultant

overstimulation and disruption of neurotransmission in both central and peripheral nervous systems. [15] After some period of time (dependent on the chemical structure of the organophosphorous agent), the acetylcholinesterase-organophosphorous compound undergoes a conformational change, known as "aging," which renders the enzyme irreversibly resistant to reactivation by an antidotal oxime. [16] The clinical features of OP poisoning are due to excess acetylcholine at the muscarinic and nicotinic receptors which leads to initial stimulation and eventual exhaustion of cholinergic synapses.[10] Symptoms of cholinergic crisis are due to stimulation of the muscarinic and nicotinic receptors: Nicotinic manifestations include increased or decreased muscle power and skeletal muscle fasciculations. Muscarinic manifestations include excessive salivation, miosis, diarrhea, bronchorrhoea, bronchospasm, bradycardia and urination. Other signs include vomiting, respiratory distress, abdominal pain and depressed level of consciousness. In agreement with other reports [11] the most frequent symptoms in our study were excessive salivation, agitation, disturbance of consciousness, abdominal pain and abdominal cramps, while the most common physical findings were miosis, weakness, bradycardia and fasciculation. The cholinergic phase is a medical emergency that requires treatment in an ICU. Death is likely during this initial cholinergic phase due to the effects on the heart (bradycardia and other arrhythmias), respiration (central or peripheral ventilatory failure) and on the brain (depression of vital centers). The cholinergic phase usually passes off within 48-72 hours but complete clinical recovery from all the effects may take up to a week. Treatment is supportive with oximes, atropine and mechanical ventilation, in addition to gastric lavage and decontamination. Oximes (effective in the early phase) are clinically important reactivators of acetylcholinesterase, which can prevent degenerative effects of insecticide intoxication.

It is a policy in our center to admit all patients with OP poisoning to ICU regardless of the severity of the clinical signs and symptoms. The cholinergic phase is treated as soon as the diagnosis of OP insecticide poisoning is suspected. Atropine and/or pralidoxime sulfate are the standard treatments administered. Atropine competes with acetylcholine at muscarinic receptors, preventing cholinergic activation. Muscarinic signs such as miosis, diarrhea, vomiting, sweating, bronchial secretions are usually first to appear, and are treated with atropine. Nicotinic signs usually appear later, and do not respond to atropine. A gastric lavage is required, which was done in all patients included in the study, and this may profitably be repeated after 2-3 hours as the drug is secreted back into the stomach and to remove any residue not fully removed. Atropine is given as a continuous infusion started as 0.02-0.08 mg/kg per hour, [17] dosing should be titrated to the therapeutic end point of the clearing of respiratory secretions and the cessation of bronchoconstriction.[18] Atropinization is assessed by a combination of signs including pupils, pulse rate, pulmonary secretions and mental state. It is not desirable to use any one criterion alone, because cases are seen where the pupils do not dilate or pulse does not become fast inspite of adequate doses. Atropinisation, once achieved, should be maintained for 1-3 days, depending upon the compound involved. When muscular paralysis supervenes, mechanical ventilation is required. The maximum dose of atropine in two reports was 1300 mg and 19590 mg respectively.[17,19] There has been only one placebo-controlled trial regarding oxime treatment for OP poisonings, which showed that pralidoxime + atropine does not have any benefit over atropine alone in OP poisonings. [20]

In the present study, we observed that mortality is not significantly different whether or not the patients are treated with pralidoxime sulfate. This observation is also confirmed by the study of De Silva et al [20] but, since the data is still limited, we strongly suggest using pralidoxime. This issue needs further controlled studies The duration of hospitalization ranged as expected from only 3 days for the mild cases to 9 days for the severe cases, but prolonged durations also have been reported.[21] Mortality rate in different studies ranged from 12 - 27.6 %.[22]

No mortalities were reported in our patients which may be attributed to the early diagnosis and treatment, in the presence of facilities for advanced supportive care like mechanical ventilation. The most troublesome complication was respiratory failure, which was observed in 102 patients that required mechanical ventilation. Eight of them died due to delay in endotracheal intubation. 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. The most common complication that was encountered was cellulites/phlebitis. Mortality rate in different studies ranged from 12 - 27.6 % .[22-23] Our mortality rate 5 % (147 deaths) is much lesser compared with series reported.

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