

## PRESENTATION AND MANAGEMENT OF ORGANOPHOSPHATE POISONING IN AN INTENSIVE CARE UNIT

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### ABSTRACT

**Objective:** To determine the various demographic factors, clinical features, management and outcome of organophosphate poisoning in an intensive care unit (ICU) setting.

**Study Design:** Descriptive, quantitative study.

**Place and Duration of Study:** ICU of PNS Shifa hospital, Karachi. From February 2008-February 2010.

**Patients and Methods:** Total of 40 patients were admitted in the ICU of PNS Shifa hospital, Karachi from Feb 2008- Feb 2010 with the history of organophosphate (OP) ingestion. A complete history was taken from the patients and relatives. Baseline laboratory investigations were done. All the data was tabulated on a structured proforma after taking consent from the relatives. Variables of the study were demographic factors as gender, age, cause and mode of poisoning, clinical course, ICU management and its outcome.

**Results:** Out of 40 patients 32 (80%) were females and 8 (20%) were males. The age varied from 12-56 years. Twenty eight (70%) were in the 14-28 years age group. Twenty nine (72%) had poison for suicidal purpose and rest had the insecticide accidentally. Twenty six (62%) of them were unmarried. In 38 (95%) patients the clinical features of parasympathetic overactivity was observed. All these patients were given atropine and pralidoxime. Fifteen (37%) patients required mechanical ventilation. Five (12%) out of these patients developed ventilator associated pneumonia. The time duration of mechanical ventilation was 1-3 weeks. All the patients were successfully recovered. Total duration of hospital stay in our patients was 2-4 weeks.

**Conclusion:** Early and aggressive management of organophosphate poisoning in an ICU setting reduces not only the mortality but also decreases the duration of hospital stay.

**Keywords:** Intensive care unit, Organophosphate, Pralidoxime.

### INTRODUCTION

To determine the various demographic factors, clinical features, management and outcome of organophosphate poisoning in an intensive care unit (ICU) setting. Organophosphate compounds are widely used in both rural and urban areas as agricultural products, pesticides, insecticides, ophthalmic agents, nerve gases and defoliants. All apparently share a common mechanism, exposure to the same organophosphate by multiple routes or to multiple organophosphates by various routes may result in serious additive toxicity. These are widely used in both domestic as well as industrial settings. Thus there are far more than 1000 active substances that are used in approximately 35,000 preparations of pesticides,

used only in agriculture<sup>1</sup>. Pesticides are among the most common ways of poisoning fatalities.

In countries such as Pakistan and India organophosphate compounds in the form of insecticides and pesticides are easily accessible and therefore a source of both intentional and unintentional poisoning. The incidence of international organophosphate related human exposures appear to be underestimated<sup>2</sup>. According to world health organization approximately 200,000 people die each year by organophosphate poisoning<sup>3</sup>. Organophosphates cause irreversible inhibition of the enzyme acetyl cholinesterase resulting in sustained depolarization of the post- synaptic neurons. This leads to unwanted muscarinic and nicotinic effects. Early and intense management in an ICU setting with atropine and early oxime administration is clinically important for the favorable outcome of these poisoned patients.

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## PATIENTS AND METHODS

It was a descriptive and quantitative study conducted at PNS Shifa hospital Karachi from Feb 2008 - Feb 2010. All the patients with the history of organophosphate ingestion and with the clinical features, who were admitted in ICU were included in the study. Patients presented with the poisoning other than organophosphate, mixed poisoning and snake bite were excluded from the study. Consent was taken from the institutional ethical committee and from individual patient or the relative. A complete history from the relatives and the patients was taken with the particular emphasis on demographic factors (as gender, age, marital status), mode of poisoning, type of organophosphate, reason of poisoning. A complete examination was carried out specially taking into account the clinical features of organophosphate ingestion such as conscious level, pupil size, fasciculation, bronchorrhoea and increased salivation, after the assessment of airways, breathing and circulation. All the patients had gastric lavage done. The baseline investigations like blood complete picture (CP), liver function tests (LFT's), urea creatine electrolytes (UCE), urine detailed report (DR), x-ray chest along with the arterial blood gases (ABG,s). Serum cholinesterase was not done because of unavailability of the kit. Treatment was started as soon as the organophosphate poisoning was suspected at the time of admission. All the patients were atropinized till the full atropinization was achieved indicated by decreased secretions and tachycardia along with pralidoxime in a dose of 30 ml/kg stat and then 15 ml/kg/hour infusion. All the data variables were noted on a structured proforma and was analyzed using SPSS software (version 16). Frequencies and percentages were computed to present all categorical variables. Variables that were analyzed included: age, gender, mode of poisoning, type of poisoning, cause of poisoning, clinical presentation, mechanical ventilation, duration of mechanical ventilation and mortality rate.

## RESULTS

Total of 72 patients with various types of poisonings were admitted in the ICU in the study time duration. Out of these 40 patients (55%) had organophosphate poisoning as indicated by history and clinical features. Eight (20%) were males and 38 (80%) were females. The age varied from 12-56 years. Twenty eight (70%) were in the 14-28 years age group, 25 (62%) patients were married. Regarding the mode of poisoning, there was a history of ingestion in 28 (70%) patients, 7 (20%) patients had dermal exposure and 5 (12%) patients had a history of inhalation. Cause of poisoning was suicidal attempt in 26 (65%) patients, accidental in 8 (20%) patients and occupational in 6 (15%) patients. Thirty eight (95%) patients came within 4 hours of exposure. Except 2 (5%) patients, all showed the classical clinical features of organophosphate poisoning<sup>2</sup> which included muscle fasciculation, constricted pupil, salivation, bronchorrhoea and increased gut sounds. Two (5%) patients didn't show any sign or symptom even after 48 hours of admission. No treatment was given to these patients and was discharged with the diagnosis of malingering. Gastric lavage of all the patients was done. Fifteen (37%) patients required mechanical ventilation. Ten (25%) of these developed acute respiratory failure and 5 (12%) developed intermediate syndrome. The total duration of mechanical ventilation required was 2-3 weeks. Five (12%) out of these 15 patients developed ventilator associated pneumonia which was treated. All the patients were recovered making the recovery rate of 100%. The total duration of hospital stay noted in our patients was 2-4 weeks.

## DISCUSSION

Organophosphate compounds have been used worldwide, for pest control for more than 100 years. These are the pesticides of choice in the agricultural world and are the most common type of poisoning among the organic pesticides. It is the most important cause of poisoning in Pakistan<sup>4,5</sup>, Srilanka<sup>6</sup> and other countries of

southeast Asia. This has been seen in various studies that it accounts for majority of deaths occurring as a result of deliberate self-harm in developed countries as well<sup>7</sup>. As these compounds are readily available over counter and are easily accessible, they are commonly used for deliberate self harm<sup>5</sup>. In Pakistan, particularly, most of the areas of southern Punjab and northern Sindh are major cotton growing areas where more than 76% of total consumption of pesticides is used. Such an intense and extreme use raises a concern about public health and necessitates surveillance of public health in cotton belt<sup>4</sup>.

Our study showed the majority of the cases were males (60%). Other studies showed M : F = 3:18<sup>9</sup>. As evident from the results most of the patients belonged to a younger age group (14-28 years). That is also supported by various studies<sup>10,11</sup>. The provocative risk factors in this age group are socioeconomic status, joint family system, peer pressure, competition and expectations in school and at home, excessive pressure of studies, unemployment, depression and most importantly easy access to these compounds<sup>4,12</sup>. Most cases were due to suicidal attempt and it was specially seen in females of younger age group as evident in our study. This is also reinforced by other studies conducted in our country and other countries<sup>13</sup>. In one study conducted in Turkey, the suicidal attempt rate was 70%<sup>14</sup>. Suicidal behavior is one of the most important reasons for hospitalization in adolescents and young adults<sup>5</sup> it has been seen not only in our society but globally that hopelessness, unemployment and severity of depression emerge as the most important predictors of suicidal behavior in both adults and adolescents<sup>15</sup>. The most common route of poisoning was ingestion according to our study and evident by other studies as well<sup>9</sup>.

The mechanism of action of organophosphates is inhibition of acetylcholinesterase leading to excessive acetylcholine accumulation resulting in overstimulation of cholinergic nerves. Early oxime administration that is within 48

hours, is useful in patients poisoned with these agents. In addition to reaction with a acetylcholinesterase, organophosphates also react with serum cholinesterase, which is a circulating plasma glycoprotein, synthesized in the liver<sup>16</sup>. Clinical features of acute poisoning occur within 24 hours of ingestion of organophosphate compounds. Its effects consist of muscarinic, nicotinic and may affect the central nervous system. Muscarinic features include bronchorrhoea, bronchoconstriction, constricted pupils, abdominal cramps, involuntary defecation and urination, tachycardia, QT prolongation and hypotension. Nicotinic features include twitching of fine muscles, fasciculation and hyper reflexia which may progressively lead to flaccid paralysis. The most prominent CNS symptoms include headache, dizziness, drowsiness, confusion, anxiety, slurred speech, ataxia, tremor psychosis, convulsions, coma and respiratory depression<sup>16,17</sup>. The most common clinical signs of poisoning observed in our patients were constricted pupils, muscle fasciculation, bronchorrhea, diarrhea and increased salivation. Acute respiratory failure was seen only in 15 patients that is in 37% patients. It is consistent with another study conducted by Senance Yakeetal, which showed respiratory failure in 33% patients<sup>18</sup>. Management in an intensive care unit with gastric lavage, decontamination, administration of atropine, oximes and mechanical ventilation whenever required. Gastric lavage was done in all patients and according to few studies this may be repeated after 2-3 hours as the drug is secreted back into the stomach and also to remove any residual drug<sup>19</sup>. The goal of ICU protocol is the reversal of muscarinic signs with atropine and enzyme reactivation by pralidoxime. Frequent atropine doses or continuous infusion are used to achieve drying of secretions and the resolution of bradycardia<sup>20,21</sup>. In our ICU the atropine was given as a continuous infusion started as 0.02-0.08 mg/kg/hour dosage was titrated to the therapeutic end point of the clearing respiratory secretions and the cessation of broncho-

constriction<sup>22</sup>. The pupillary dilation is not considered as a therapeutic end point of atropine as miosis may persist for weeks after significant exposure<sup>20</sup>. In our patients pupils got dilated within 24-48 hours after atropinization. This is also seen in another study conducted by Willemijin et al<sup>21</sup>. Atropine should be continued for 1-3 days after successful atropinization. All our patients received pralidoxime 30 ml/kg stat then 15 ml/kg/hour infusion. Pralidoxime is used as an antidote of organophosphate poisoning. Its main therapeutic effect is the recovery of neuromuscular transmission at nicotinic synapsis. Pralidoxime should be given as soon as the diagnosis is suspected, within 48 hours of ingestion, for the early recovery and better outcome of the patients<sup>23</sup>. The result of other studies suggest that oximes significantly reduce atropine consumption in OP poisoning, and signs of atropinization might occur earlier when oximes were given<sup>16,24</sup>. Another study conducted in Serbia showed that the length of hospitalization was the lowest in the group on atropine and oxime therapy ( $p < 0.001$ ) and when bicarbonate was added to oximes and atropine the duration of mechanical ventilation was significantly reduced ( $p < 0.001$ )<sup>25</sup>. Pralidoxime should be used as early as possible before irreversible inhibition of acetylcholine occurs<sup>26</sup>. Total duration of hospital stay in our patients was 2-4 weeks. It was more in those patients who required mechanical ventilation. Fifteen patients were intubated and required mechanical ventilation. Ten of these patients developed respiratory failure and in 5 intermediate syndrome was observed. Intermediate syndrome is a muscle paralysis that occurs after recovery from cholinergic crisis, 24-96 hours after the poisoning probably result from post-synaptic neuromuscular junction dysfunction<sup>27</sup>. In these patients respiratory insufficiency signifies the onset of syndrome. Proximal muscle weakness was also observed. The reported incidence varies between 8% and 49%<sup>28,29</sup>. The patients were weaned off successfully in 2-3 weeks. It has been reported previously that prolonged respiratory

support and difficult weaning may be a result of intermediate syndrome<sup>27</sup>. Five out of 15 patients who required mechanical ventilation developed ventilator associated pneumonia which was then treated.

The most important and noteworthy aspect of this study was the mortality rate, which was nil. A comparatively low mortality rate was also seen in another study conducted in a military hospital Pano Aqil Pakistan, where the patients were timely managed in an ICU setting and the mortality rate was only 12.5%. All the patients were successfully treated and every patient at the time of discharge received psychotherapy.

## CONCLUSION

Organophosphate poisoning is a medical emergency 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 significantly reduce the mortality. This could be achieved by improving ICU management and appropriate timely supportive care. Immediate shifting of victims of poisoning to well-equipped ICU, early use of antidote and careful timely resuscitation help to reduce the mortality in these patients.

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