An Investigation of Clinical Symptoms and Treatment of Organophosphate Poisoning among Patients Referred to Razi Hospital during 2006 – 2012

AZIN SAMIMI1, ALI HASSAN RAHMANI2, ROJIN ABABAF3, LEILA ZEIDOONI1

1Department of Pharmacology and Toxicology, Pharmacy School, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2Department of Clinical Toxicology, Razi Hospital, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3Medical School, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract

Background: Organophosphates are pesticides that are used widely in agriculture and industry. Because of the ease of access and abundant use of these pesticides, many cases of intentional and accidental poisoning of these compounds are reported. The aim of this comprehensive study was to evaluate the symptoms and treatment of patients referred to Razi hospital as the main center for poisoning in the South west of Iran.

Methods: In this study, patients with Organophosphate poisoning referred to Razi hospital during the years 2006 to 2012 was included. The information collected from their records includes reference data, demographic data, clinical manifestations and treatment options.

Results: Of all 173 cases, 46.2% were male. The average age of cases was 24.31 years and most of them were from rural areas. 86% of patients had deliberately consumed a toxic substance. The first clinical symptoms of more than half of the patients were nausea and vomiting. 72.8% of patients needed antidote; a combination of atropine and pralidoxime was administered in 70% of cases. 16.2% required intubation and 80% admitted to ICU. In 52% of cases a specified pesticide was found and 4% of the cases deceased.

Conclusion: Organophosphate poisoning in most cases occurred deliberately as a suicidal attempt. It was more common in rural areas. Need for admission to intensive care unit was more common in cases under the age of twenty. Treatment of patients with both antidote atropine and pralidoxime was a very suitable therapeutic model.

Keywords: Antidote; Iran; Organophosphate; Suicide


INTRODUCTION

Organophosphate (OP) are a major group of insecticides discovered more than a century ago (1). These compounds have been used as pesticides, herbicides, and chemical warfare agents in the form of nerve gases (Sarin gas) as well as therapeutic purposes, such as ecothiopate used in the treatment of glaucoma (2). OP pesticide self-poisoning is a major health concern in rural regions of developing countries, that annually kills about 200,000 people (3). Death caused by exposure to OPs usually is caused by respiratory failure. So that, some of them, even with small amounts can be lethal and lead to this dysfunction. The mechanism of OP poisoning has been determined by inhibition of acetylcholinesterase (AChE) activity, an enzyme that plays an important role in neurotransmission. OPs through AChE inhibition causing accumulation of acetylcholine at susceptible cholinergic nerve endings. The loss of activity of AChE results in continuous stimulation of cholinergic fibers throughout the nervous systems (4). Signs of organophosphate poisoning are classified into secondary effects: muscarinic, nicotinic, and central nervous system (CNS) (1). The symptoms caused by overstimulation of muscarinic receptors which lead to excessive activity of the parasympathetic system, include increased bronchial secretion, bronchoconstriction, cyanosis, excessive sweating, salivation and lachrimation, nausea, vomiting, diarrhea, abdominal cramp, urinary and faecal, bradycardia, hypotension, heart block and miosis. Nicotinic poisoning may cause muscle fasciculation, tachycardia, hypertension, hyperglycemia, cramping and weakness, while confusion, headache, restlessness, ataxia, tremor, hypotension, respiratory depression, seizures, and unconsciousness are symptoms of severe poisoning and the central nervous system effects. If neural transmission disorder caused in the central nervous system is not reversed within 24 hours, substantial amounts of acetylcholinesterase permanently disappears (5). One of the different clinical features in OP poisoning is the time of onset of symptoms. Following OPs exposure, symptoms occur acutely within minutes to hours, including salivation, lachrimation, urination, defecation, gastric cramps,
Clinical Symptoms and Treatment of Organophosphate Poisoning
A. Samimi et al.

emesis (SLUDGE); while in some patients the onset of clinical symptoms is delayed and often begins after a period of severe cholinergic symptoms (6). A decrease in plasma AChE is often used as confirmation of OP poisoning, although correlation between enzyme activity and severity of poisoning is poor (1). During the past few decades, pyridinium oximes are used as a therapeutic agent in the treatment of poisoning to organophosphates. Pyridinium oximes take action by reactivation of AChE inhibited by OP. However, Because of the differences in their activity, there is not yet, suitable oxime against all known OPs. According to studies conducted on oximes as OPs antidote, only four compounds have been identified for therapeutic use in human so far. Presently, a combination of atropine, diazepam and AChE reactivators such as pralidoxime, trimedoxime, obidoxime are used for the treatment of OP poisoning in humans (7).

In this study, we evaluated records of poisoned patients with organophosphate that referred to Razi hospital in years 2006-2012.

METHODS

We have investigated information about patients poisoned with organophosphate that were referred to Razi hospital for 6 years (2006–2012). A detailed history had been taken from the patients or their family; we collected data retrospectively from medical records.

Information including age, sex, location, onset of symptoms, first symptom of poisoning, the need to antidote, kind of antidote, duration of antidote administration, the need for intubation, admission in ICU, length of hospital stay and mortality rate were obtained from the patient records.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 18.0 (SPSS Inc., Chicago, IL, USA). For outcome analysis, Fisher's exact test was applied with the level of significance set at P < 0.05.

RESULTS

During the study period, 173 patients with OP poisoning were referred to Razi hospital. There were 80 (46.2%) male and 93 (53.8%) female; the age range was between 13-48 years. Most of the patients were 21-25 years old (Figure 1). 120 (69.4%) cases lived in rural areas and 53 (30.6%) in urban areas. Their clinical characteristics are summarized in Table 1.

The poisoning in 149 (86.1%) patients was deliberate, and in 10 (5.8%) cases was unintentional; in 14(8.1%) of patients, the reason was unclear. The time lag between exposure and hospital admission was less than 6h in 152 (87.9%) patients, between 24-48 h in 19 patients and more than 48 in 2 cases.

Length of hospital stay was 24-48 h in 23 (13.3%) patients, 48-72 h in 66 (38.2%) patients and more than 72 hours in 84 (48.6%) cases. Of all, 139 (80.3%) patients admitted in ICU, 28 (16.2%) of them needed tracheal intubation.

All patients became symptomatic in less than 6 hours after exposure. Signs and symptoms on admission included regurgitation and vomiting 50.3% (87), loss of consciousness 16.2% (28), lacrimation 8.7% (15), bronchorrhea 8.1% (14), vertigo 6.4% (11), numbness & lethargy 4.5% (8), palpitation 3.5% (6) and sweating 2.3% (4) respectively (Figure 2).

In terms of need of antidote therapy, Among 126 (72.8%) patients, 38 (30.2%) received atropine and 88 (69.8%) received a combination of atropine and pralidoxime. 47 cases did not receive atropine because muscarinic manifestations were not obvious in the initial presentations. 31.8% of patients with documented OP poisoning received atropine alone, and 46% received a combination of both antidotes. Duration of hospitalization in these cases was 24-48 hours in 9 patients, 48-72 hours in 33 patients and more than 72 hours in 49 cases. Atropine was administered in 7% of cases with unknown pesticide poisoning, and 42% of these cases received both antidotes. Duration of hospitalization in this group was 24 hours in 14 patients, 24-48 hours in 33 patients and more than 72 hours in 35 cases.

![Figure 1](image-url)

Figure 1. Distribution of 173 poisoned patients with OPs according to age
Out of all admitted cases, 7 patients died; of them, reason of poisoning in 6 cases was unclear.

OPs compounds have largely been used in agriculture in many parts of the world. The use of organophosphates to commit suicide is a major problem, particularly in developing countries. The lack of adequate regulations on the sale and easy accessibility resulted in a gradual increase in accidental and suicidal poisoning. Poisoning with OP may occur at all ages. The most commonly affected age group in our study was 13-48 year-olds.

In a study conducted by Yurumez et al in Turkey in 2007, 40.5% of patients were male and 59.5% were female, a ratio that is consistent with our study. These findings suggest that incidence of organophosphate poisoning is unrelated to gender.

Approximately 85% of patients in rural and urban areas were deliberately poisoned by OPs. Based on another study in Turkey, the majority of patients had intentionally used toxic substances in a suicidal attempt. These results are consistent with our study.

Regarding the time of referring patients to Razi hospital after the poisoning, the majority of cases were referred less than 6 hours post-exposure (87%). In 84 patients, duration of hospitalization was more than 72 hours. Also in all the cases, time lag to onset of symptoms was less than 6 hours. In Yurumez et al’s study, the average time to refer to hospital was 3 hours.

OPs, with inhibition of acetylcholinesterase lead to accumulation of acetylcholine at the synapse, overstimulating muscarinic and nicotinic receptors. Onset of symptoms, severity and duration of OP poisoning are determined by the nature of particular compounds and the type of binding with acetylcholinesterase (reversible or irreversible). OPs can also affect the CNS and causes seizures and altered consciousness.

DISCUSSION

Table 1. Clinical features of 173 poisoned patients with OPs

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male/female</td>
<td>80/93</td>
<td>46.2/53.8</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rural area/ urban</td>
<td>120/53</td>
<td>69.4/30.6</td>
</tr>
<tr>
<td>cause of poisoning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>accidently</td>
<td>10</td>
<td>5.8</td>
</tr>
<tr>
<td>intentional</td>
<td>149</td>
<td>86.1</td>
</tr>
<tr>
<td>unknown</td>
<td>14</td>
<td>8.1</td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>under 6 hours</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td>6-24 hours</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>more than 24 hours</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Need to antidote</td>
<td>126</td>
<td>72.8</td>
</tr>
<tr>
<td>Atropine</td>
<td>38</td>
<td>30.2</td>
</tr>
<tr>
<td>Atropine + Pralidoxime*</td>
<td>88</td>
<td>69.8</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>under 48 hours</td>
<td>23</td>
<td>13.3</td>
</tr>
<tr>
<td>48-72 hours</td>
<td>66</td>
<td>38.2</td>
</tr>
<tr>
<td>more than 72 hours</td>
<td>84</td>
<td>48.6</td>
</tr>
<tr>
<td>Need to Intubation</td>
<td>28</td>
<td>16.2</td>
</tr>
<tr>
<td>ICU admission**</td>
<td>139</td>
<td>80.3</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

*PAM = pralidoxime
** ICU = intensive care unit.
Clinical Symptoms and Treatment of Organophosphate Poisoning
A. Samimi et al.

The first symptoms of most cases in our study were nausea and vomiting (50%). Loss of consciousness at second place (16%), followed by tearing, drooling, dizziness, numbness and paralysis of the body, palpitations and sweating, respectively. According to Levy-Khademi’s study in 2007 which was conducted on 31 children, the most prevalent clinical symptoms were neurologic ones such as coma and convulsions (71%) (14). The different results of these two studies, represents the differences in clinical manifestations of organophosphate poisoning in children and adults.

The standard treatment for OP poisoning includes muscarinic symptoms reversal with atropine (until reduced pulmonary secretions) and regeneration of AChE using oxime compounds such as pralidoxime (2-PAM) (15, 16). 72% of patients needed antidote therapy; for the majority of them (70%), both atropine and pralidoxime were prescribed. Almost all poisoned patients were admitted in ICU and their mortality rate was low; these results are in concordance with result of our study.

CONCLUSION

It is obvious that OP poisoning is still an important health problem. By appropriate use of these agents, public education about probable risks of use and implementing adequate laws on their sale, we can reduce the incidence of poisoning by these compounds.

ACKNOWLEDGEMENTS

This work was supported by the Deputy of Research of Ahvaz Jundishapur University of Medical Sciences (Ahvaz, Iran). The authors would like to extend their thanks to the technicians of Razi hospital for their help in offering us the resources in running the program.

Conflict of interest: None to be declared.

Funding and support: This manuscript has been supported by Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

REFERENCES