Organophosphate Poisoning – Clinical Profile

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Abstract

Background: To study the clinico-demographic profile and mortality in patients with organophosphate poisoning.

Methods: In this descriptive study patients of age >13 years of either gender, who themselves or attendants gave history of intake of organophosphate (OP) containing substance, or presenting with such substance (Rat killing pills/powder, anti lice lotion, or insecticide), were included. Patients suffering from other systemic illness like diabetes mellitus, hypertension, ischemic heart disease, which could affect mortality were excluded from the study. Glasgow Coma Scale (GCS) was recorded on presentation. Mortality was determined according to GCS ≤ 13. Outcome was measured according to GCS score in terms of mortality during hospital stay. All patients were given standard treatment for OP poisoning, i.e., securing Airway, Breathing and Circulation, administering atropine at a dose of 2 mg every 10 minutes till reversal of cholinergic symptoms and administering a stat dose of pralidoxime 1 gram.

Results: A total of 62 patients with the diagnosis of acute organophosphate poisoning were registered. The gender distribution was almost equal in this study with 33 (53.2%) male patients and 29 (46.8%) females. The mean age of patients was 23.3 ± 6.1 years ranging from 14 to 40 years. The mean time since poison taken was 1.3 ± 0.7 hours ranging from 0.25 to 4.0 hours. Among these patients, majority (88.7%) took rat killing pills/powder as poison, 3.2% took insecticide spray while 8.1% of the patients took anti lice lotion. Sixteen (25.8%) patients presented with GCS ≤ 13 while 46 (74.2%) presented having GCS of > 13. Overall 9 (14.5%) of study patients required intubation and/or ventilation, while 1 (1.6%) patient died in our study due to poisoning. Nine (56.3%) out of 16 patients with GCS ≤ 13 needed intubation compared to none out of 44 patients in the group having GCS > 13.

Conclusion: GCS level is an important factor in assessing Organophosphate poisoning. Severe morbidity and mortality occurs in patients having GCS levels of < 13.

Key Words: Organophosphate poisoning, Glasgow coma scale, Morbidity, Mortality.

Introduction

Poisoning is a global issue occurring all over the world involving people of all ages and gender, from all ethnic and economic groups. It can occur in an accidental or deliberate manner.1 It is estimated that more than 700,000 deaths occur each year as a result of poisoning. About 345,000 occur from unintentional poisoning, and more than 370,000 from suicidal causes. Majority of the suicidal cases are due to pesticide poisoning.1 According to WHO estimates, more than 90% of fatal poisoning cases are seen in middle and low income countries i.e., the developing countries in general and agricultural countries in particular.2 In our neighboring countries India and Sri Lanka, pesticides and organophosphates (OP) account for more than 50% of the poisoning cases seen in hospitals.3,4 In Pakistan the incidence of Organophosphate poisoning (OPP) shown from various studies ranges from 22% up to 40%.5 Thus with passage of time OP intoxication is becoming more common a cause of poisoning with significant morbidity and mortality. A comprehensive knowledge about the nature, magnitude, morbidity and mortality of a particular poison is necessary not only for its prompt diagnosis and treatment, but also to make necessary precautions to avoid such incidents.7

Organophosphates are used worldwide as insecticide and pesticide.6,7 OPs are a heterogeneous group of chemical compounds with structural similarities and analogous biological effects on humans. The OP family comprises of more than 50,000 different chemical agents. OPs are usually esters, amides or thiol derivatives of phosphonic acid.6 It is estimated that there are over 3 million cases of OPP per year worldwide with approximately 300,000 deaths. Majority of these occur in agricultural countries, where fatality rates average about 20%.4

Intentional and unintentional pesticide poisoning has been acknowledged as a serious problem in many agricultural communities of low- and middle-income
countries, including China, India, Sri Lanka, and Viet Nam.\textsuperscript{9}

The estimated mortality rates with OPP in neighboring countries Iran and India are around 7-12\%.\textsuperscript{10} Local figures are few and variable with mortality rates from OPP ranging from 0.05\% to about 9\%.\textsuperscript{11} The main sites of entry of OP compounds are the gastrointestinal system (GIT) and the Skin. They can readily be absorbed in vapor form from the lungs especially the nerve agents.\textsuperscript{12} Absorption is rapid when taken orally. It also depends on the nature of the compound. Greater the lipophilicity more the absorption takes place. The degree of absorption depends on the contact time with the skin, the lipophilicity of the agent involved and the presence of solvents, for example xylene, and emulsifiers in the formulation which can facilitate absorption. It is probable that traumatized skin or the presence of dermatitis allows greater absorption of OP compounds.\textsuperscript{13} After absorption, OP compounds accumulate rapidly in fat, liver, kidneys and salivary glands. OP compounds generally are lipophilic and therefore cross the blood / brain barrier in most cases.\textsuperscript{13} OP compounds inhibit Acetylcholine esterase (AChE) which hydrolyses Acetyl choline (ACh). This inhibition occurs at all sites where ACh is released and is subsequently removed by AChE. These include the postganglionic parasympathetic and cholinergic sympathetic nerves, and both sympathetic and parasympathetic preganglionic fibers in addition to the Neuromuscular junction (NMJ) sites in the skeletal muscles. Inhibition of AChE also takes place in the CNS. ACh released from postganglionic parasympathetic and cholinergic sympathetic nerves acts on the muscarinic receptors present on various smooth muscles and glands. Inhibition also occurs at the nicotinic receptors which are located on postsynaptic preganglionic fibers and the NMJ. The inhibition of cholinesterase activity leads to the accumulation of ACh at synapses, causing overstimulation and subsequent disruption of transmission in both the CNS and the Peripheral Nervous Systems (PNS). Exposure to OP compounds will, therefore, interfere with synaptic transmission peripherally at muscarinic neuroeffector junctions and nicotinic receptors within sympathetic ganglia and at skeletal NMJs. This is accomplished by an overstimulation of ACh receptor sites that leads to a variety of physiologic and metabolic derangements. Disruption of transmission also will occur at the ACh receptor sites within the central nervous system.\textsuperscript{13} The clinical manifestations of OPP can be classified according to the receptor types on which ACh over stimulation occurs.

Organophosphate poisoning (OPP) can also be classified as three different phases according to the chronological appearance of a characteristic type of symptomatology, i.e., acute cholinergic phase, intermediate syndrome and OP-induced delayed polyneuropathy. These phases may or may not occur collectively in an individual with OP toxicity.\textsuperscript{14} The severity of acute OPP varies from mild to severe (Table 1).

\begin{table}
\centering
\caption{Severity of Acute Organophosphate poisoning}
\begin{tabular}{|l|l|}
\hline
\textbf{Term} & \textbf{Description} \\
\hline
Latent & • No clinical manifestations. \\
& • Serum cholinesterase activity is 50 to 90 percent of normal \\
\hline
Mild & • Fatigue, headache, dizziness, nausea and vomiting, increased salivation and sweating, lacrimation, chest tightness, abdominal cramps or diarrhea, can still walk, numbness of extremities. \\
& • Serum cholinesterase activity is 20 to 50 percent of normal. \\
\hline
Moderate & • Unable to walk, generalized weakness, difficulty talking and fasciculations, in addition to mild severity symptoms and meiosis. \\
& • Serum cholinesterase activity is 10 to 20 percent of normal. \\
\hline
Severe & • Unconsciousness, loss of pupillary light reflex, fasciculations, flaccid paralysis, moist rales in lungs, seizures, respiratory difficulties and cyanosis, secretion from mouth and nose. \\
& • Serum cholinesterase activity is less than 10 percent of normal. \\
\hline
\end{tabular}
\end{table}

Diagnosis of the cholinergic syndrome in most instances is based on history of exposure to or intake of an OP compound along with clinical features. Blood samples for cholinesterase activity should be obtained in the appropriate blood tubes as some tubes contain fluoride, which permanently inactivates cholinesterases, yielding falsely low concentrations. Specimens for RBC cholinesterase are usually drawn into tubes containing a chelating anticoagulant like ethylenediaminetetraacetic acid (EDTA) to prevent clotting.\textsuperscript{15}

The current view of specific treatment of OPP includes use of an anticholinergic drug (e.g. Atropine), cholinesterase-reactivating agents (e.g.
Pralidoxime) and anticonvulsant drugs (e.g. Benzodiazepines). Currently available antidotes include Atropine and Oximes. These do not necessarily prevent respiratory failure which is the commonest cause of death in OPP. However, early aggressive medical therapy with antidotes and intensive care management are the keys to prevention of morbidity and mortality associated with OPP.17

Patients and Methods
This descriptive study was conducted at District Headquarter Hospital Rawalpindi. Duration of study was six months, i.e., from March 2014 to August 2014. Patients of age >13 years of either gender, who themselves or attendants gave history of intake of OP containing substance, or presenting with such substance (Rat killing pills/powder, anti lice lotion, or insecticide). Patients suffering from other systemic illness like diabetes mellitus, hypertension, ischemic heart disease, which could affect mortality were excluded from the study. Glasgow Coma Scale (GCS) was recorded on presentation. Mortality was determined according to GCS ≤ 13. Outcome was measured according to GCS score in terms of mortality during hospital stay. All patients were given standard treatment for OP poisoning, i.e. securing Airway, Breathing and Circulation, administering atropine at a dose of 2 mg every 10 minutes till reversal of cholinergic symptoms and administering a stat dose of pralidoxime 1 gram.

Results
In present study a total of 62 patients with OPP were enrolled. The mean age of patients was 23.3 ± 6.1 years ranging from 14 to 40 years (Table 2). Majority of study patients were having low educational status with 12 (19.4%) patients were found to be illiterate and 43.5% from middle to matriculation qualification. The mean time was 1.3 ± 0.7 hours ranging from 0.25 to 4.0 hours. Majority (56.4%) reached hospital within an hour after poisoning (Table 3). Majority of the study patients (88.7%) took rat killing pills/powder as poison, 2 (3.2%) took insecticide spray while 5 (8.1%) of the patients took anti lice lotion (Table 4). Thirteen (21.0%) took 1 to 2 pills in case of rat killing pill and teaspoons in case of insecticide spray or others (Table 5). Sixteen (25.8%) patients presented with GCS ≤ 13 while 46 (74.2%) presented having GCS of > 13 (Table 6). One patient died in our study due to poisoning (Table 7). In majority of the patients (54.7%) dose of atropine was used up to 20 mg. In 10 (16.1%) patients 31 to 50 mg atropine was used while 4 (6.4%) patients required more than 50 mg of atropine. Nine (56.3%) out of 16 patients with GCS ≤ 13 needed intubation compared to none out of 44 patients in the group having GCS > 13. This difference in the proportions of severe morbidity was significantly associated with GCS ≤ 13 (p-value = <0.001) (Table 8). In patients with GCS level ≤ 13 the average quantity of poisoning was 5.8 ± 3.8 compared to 3.3 ± 1.5 pills and this difference in means was significantly different among GCS levels (p-value = <0.001) (Table 9).
Table 5: Quantity of poison taken

<table>
<thead>
<tr>
<th>No of patients</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 2 pills</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>21.0%</td>
</tr>
<tr>
<td>3 to 4 pills</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>50.0%</td>
</tr>
<tr>
<td>5 to 6 pills</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>24.2%</td>
</tr>
<tr>
<td>7 to 10 pills</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3.2%</td>
</tr>
<tr>
<td>More than 10 pills</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1.6%</td>
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</tbody>
</table>

Table 6: Organophosphate Poisoning - Glasgow Coma Scale

<table>
<thead>
<tr>
<th>No of patients</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 13</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>25.8%</td>
</tr>
<tr>
<td>&gt; 13</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>74.2%</td>
</tr>
</tbody>
</table>

Table 7: Morbidity and mortality

<table>
<thead>
<tr>
<th>No of patients</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for intubation</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>14.5%</td>
</tr>
<tr>
<td>Expiry</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Table 8: Association of GCS levels and mortality in the study

<table>
<thead>
<tr>
<th>GCS ≤ 13 (n = 16)</th>
<th>GCS &gt; 13 (n = 44)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need of intubation</td>
<td>9 (56.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Expiry</td>
<td>1 (6.2%)</td>
<td>1 (2.3%)</td>
</tr>
</tbody>
</table>

* Fisher’s exact values mentioned

Table 9: Organophosphate Poisoning - Comparison of GCS levels according to quantity of poisoning and time of presentation

<table>
<thead>
<tr>
<th>Quantity of poison (pills) Mean ± SD</th>
<th>GCS ≤ 13 (n = 16)</th>
<th>GCS &gt; 13 (n = 44)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.8 ± 3.8</td>
<td>3.3 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time of presentation (hours) Mean ± SD</td>
<td>2.1 ± 0.8</td>
<td>1.1 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion

Agricultural workers who are about three quarters of labour force in the developing countries use pesticides to protect crops. In this effort they expose themselves to poison.\textsuperscript{11,18} Acute poisoning occurs when toxic reactions follow shortly after exposure, however, chronic poisoning takes its time and reacts gradually after prolonged exposure.\textsuperscript{19} Easy access and low cost of these hazardous chemicals play an important role in accidental or suicidal poisoning.\textsuperscript{20} It is the commonest suicidal agent in the developing countries like Pakistan.\textsuperscript{21} OPP for suicide accounts for about 40 to 68% of all cases in many countries.\textsuperscript{22}

A study done in India on poisoning, as an unnatural cause of morbidity and mortality, reported case fatality rate of five years, 1997 – 2001, from Shri Vasantrao Naik Government Medical College, Maharashtra. The authors reported that more male poisoning deaths were observed when compared to females with a male to female ratio of 1: 0.49.\textsuperscript{2} These findings are comparable to our study results where we found out that male gender was in dominance with 53.2% incidence. A local study conducted at another medical unit of Rawalpindi Medical College, revealed contrary findings as far as gender distribution is concerned. The author reported that 58.8% of their patients with poisoning were females. However, this could be due to the target population which was self poisoning in this case.\textsuperscript{5}

In a recent study from India it was revealed that suicidal poisoning was the common cause with almost 80% incidence and majority of these cases were belonging to rural setup with low socio economic condition and low educational status.\textsuperscript{23} These reported indices of educational background are comparable to the current study findings where we found out that 20% of patients were illiterate and almost 68% were having up to 10\textsuperscript{th} grade education.

Hypoperfusion occurring in the central nervous system as a result of neuropathy and the added hemodynamic abnormalities in OPP cause dimming of GCS value and low score indicate the potential for development of respiratory insufficiency and poor prognosis.\textsuperscript{24} In a study on prediction of outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale it was concluded that GCS and IPCS PSS were similarly effective in predicting outcome.\textsuperscript{25} Case fatality rate varies from region to region.\textsuperscript{11,18} In the resource poor settings and low socioeconomic status communities the incidence of OPP is high ranging from 10 to 20% compared to developed world 0.3%.\textsuperscript{25,26}

Conclusion

1. Presenting symptoms specially GCS levels are very crucial in predicting the outcome of OPP patients.
2. Severe morbidity and mortality occurs in patients having GCS level of < 13.
References


24. Davies JO, Eddleston M, Buckley NA. Predicting outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale. QJM2008; 101:371-79.