Association of Organophosphate Poisoning with Kidney Injury: A Mini Review

Ali Kemal Erenler1,* , Barış Eser2, Tuba Sariydın1, Mehmet Oğuzhan Ay1, Güvenç Doğan3 and Ahmet Baydın4

1Department of Emergency Medicine, Hitit University School of Medicine, Çorum, Turkey
2Department of Nephrology, Hitit University, School of Medicine, Çorum, Turkey
3Department of Anesthesiology, Hitit University, School of Medicine, Çorum, Turkey
4Department of Emergency Medicine, Ondokuzmayıs University, School of Medicine, Samsun, Turkey

Abstract: Poisoning by Organophosphates is a public health problem particularly in developing countries. Although they are commonly used in agriculture as pesticides, unfortunately, their use as weapons in chemical warfare is not rare. Due to lack of control, they are usually available in stores. Individuals may be effected by these compounds either by accidents or suicidal attempts. Poisoning may occur following peroral, inhalational or dermal intake. Due to structure of the compound (highly soluble), exposure by each route causes high morbidity and mortality. Organophosphates inhibit both acetylcholinesterase (AChE) and pseudocholinesterase. Inhibition of AChE results in accumulation of acetylcholine. This mechanism is the main reason for toxic effects. Toxic effects may present as muscarinic, nicotinic and central nervous system (CNS). Progression of the poisoning may be seen in three stages: cholinergic phase, intermediate syndrome and delayed neuropathy. Although cardiovascular, gastrointestinal, respiratory, ocular, musculoskeletal and CNS manifestations of the poisoning are well-described in the literature, its effects on renal system remains as a neglected field due to its scarcity. In this mini-review, our aim was to determine hazardous effects of OP poisoning on renal system and emphasize the importance of monitorization and early intervention.

Keywords: Kidney injury, organophosphate poisoning, toxicology.

INTRODUCTION

Organophosphates (OPs) are highly toxic substances that are lipid soluble [1]. They are commonly used as pesticides in crop protection [2]. When exposed to OPs intentionally or accidentally, regardless of route (via gastrointestinal, respiratory or skin), they cause severe toxic effects by inhibiting acetylcholinesterase (AChE) enzyme after entering the body. The continued stimulation and eventual paralysis of the acetylcholine receptors exposes the clinical signs and symptoms of OP poisoning [1,3]. Many of the patients present at the cholinergic phase. Then, the disease progreses into the intermediate phase. Both phases are associated with high rates of morbidity and mortality [4]. For cholinergic effects, atropine is used but for nicotinergic effects, oximes are needed in treatment [5]. Kidney injury is an underestimated complication of OP poisoning particularly when combined with other intoxications [6]. When kidney injury occurs, hemodyalisis must be kept in mind [7]. In this review, we aimed to underline the importance of renal injury; a rare complication of OP poisoning.

MATERIALS AND METHODS

Search items “organophosphate” and “renal injury” were entered into the scientific database Pubmed. Original articles, reviews, case series and case reports with full texts and explanatory abstracts were reviewed. After initial review, all material was re-evaluated by a nephrologist and toxicologist for accuracy. A total of 30 articles were included into the study. Those without full texts and explanatory abstracts were excluded. Data, then, was discussed between authors and the review was composed.

DISCUSSION

Organophosphates are popular pesticides commonly used in the world, particularly in the Third World Countries [4]. Clinical manifestations of OP poisoning are related to accumulation of acetylcholine at the cholinergic synapses as a result of inhibition of AChE activity [8]. Symptoms can be divided into subgroups as nicotinic, muscarinic and the CNS [2]. After exposure, OPs irreversibly bind to AChE enzyme and inhibit its activity. This inhibition results in accumulation and prolonged activity of acetylcholine. Thus, muscarinic and nicotinergic effects of poisoning occur [4]. Table 1 summarizes the clinical manifestations of OP poisoning. Following poisoning,
cholinergic crisis, respiratory failure, intermediate syndrome or delayed neuropathy may develop. Additionally, involvement of other systems such as kidneys, although rare, may worsen the clinical presentation and prognosis [5]. It is well-known that OP poisoning is associated with acute tubular necrosis [9]. It was reported in a study that OP poisoning was associated with 6.17-fold increase in acute kidney injury [6]. One of the target organs of oxidative stress following poisoning is kidney [9,10]. High concentrations of OPs may be detected in kidney [11-13]. Also in some reports, it was stated that, after ingestion of OPs, higher concentration of the poison in kidney when compared to gastric content and blood was determined [14,15]. In a study with 23 patients by Shobha et al., glucosuria observed in patients with OP poisoning was reported to be a possible evidence for oxidative stress followed by renal tubular damage [16]. For determination of kidney injury as a result of OP poisoning, creatinine level and urine output monitorization are most commonly used parameters. Serum cystatin C level may also be helpful but need for a more specific marker for kidney injury in OP poisoning still continues [17].

In the literature, kidney injury due to OP poisoning is mainly based on case reports, case series and animal studies. See Table 2 for details of researches involved in this review. Specific antidotes in OP poisoning are atropine and pralidoxime. Atropine inhibits muscarinic receptors and causes a decrease in acetylcholine-induced cholinergic effects. It was reported that pralidoxime, in contrast to atropine, does not affect any specific receptors; rather it acts to regenerate AchE, which has been rendered non-functional by the OPs [5]. However, in a case series, it was stated that obidoxime itself which is an oxime used as an antidote, may cause renal damage and should be adjusted according to renal function [18]. Cavari et al. reported a young patient who developed renal failure following OP poisoning. The patients were treated by replacement therapy and continuous veno-venous hemofiltration [19]. Similarly, continuous venous-venous haemofiltration, in addition to conventional atropin and oxime regime, was successfully performed in another case [20]. Recovery was obtained in both patients. In rats, it was proven that bladder damage accompanies renal injury which reveals that damage that OPs cause in the renal system may not be limited to kidneys [21]. Organophosphate poisoning not only causes renal injury itself but also increases the risk for intermediate syndrome development in patients with underlying renal disease [22]. Despite those potential hazards of OPs to the kidneys, in the literature, there is a case of OP poisoned patient whose liver and kidneys were transplanted to recipients successfully [23]. Additionally, in a study in rats, acute organophosphate poisoning and antidotal treatment were not found to be associated with histopathological changes in the rat kidney [24]. In postmortem analysis, it was revealed that in kidney and fat tissue, higher concentrations of OPs were determined when compared to blood [15]. These findings emphasize the importance of redistribution of OPs following acute poisoning which may, consequently, cause secondary damage to certain systems. Renal elimination half-life for OPs was found to be 3.3 hours and physicians must be aware of secondary rise in plasma level of the compound [25].

**CONCLUSION**

There is a strong evidence that OP poisoning causes renal damage via oxidative stress. Kidney functions must be monitored and supported in every

<table>
<thead>
<tr>
<th>Table 1: Muscarinic, Nicotinic and Central Effects of Organophosphate Poisoning [2, 4]</th>
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<tbody>
<tr>
<td><strong>Muscarinic effects</strong></td>
</tr>
<tr>
<td>Cardiovascular: <strong>Bradycardia, hypotension</strong></td>
</tr>
<tr>
<td>Respiratory: <strong>Rhinorrhea, bronchorrhea, bronchospasm, cough</strong></td>
</tr>
<tr>
<td>Gastrointestinal: <strong>Increased salivation, nausea and vomiting, abdominal pain, diarrhea, faecal incontinence</strong></td>
</tr>
<tr>
<td>Genitourinary: <strong>Urinary incontinence</strong></td>
</tr>
<tr>
<td>Ocular: <strong>Blurred vision, increased lacrimation, miosis</strong></td>
</tr>
<tr>
<td>Others: <strong>Excessive sweating</strong></td>
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<tr>
<td><strong>Nicotinic Effects</strong></td>
</tr>
<tr>
<td>Cardiovascular: <strong>Tachycardia, hypertension</strong></td>
</tr>
<tr>
<td>Musculoskeletal: <strong>Weakness, fasciculations, cramps, paralysis</strong></td>
</tr>
<tr>
<td><strong>Central Nervous System Effects</strong></td>
</tr>
<tr>
<td>Anxiety, ataxia, absence of reflexes, depression, headache, giddiness, agitation, restlessness, tremor, insomnia, confusion, dysarthria, delirium, coma, seizures, Cheyne-Stokes respiration, respiratory depression, circulatory collapse**</td>
</tr>
</tbody>
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stage of patient care. Despite the fact that main mechanism of injury needs to be clarified, patients with OP poisoning must be considered as candidates of renal failure. In patients with underlying renal disease, treatment must be adjusted after renal function of the patient is accurately evaluated.

CONFLICT OF INTERESTS AND FUNDING

None to declare.

REFERENCES


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