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CASE REPORT

Case Report of Acute Kidney Injury in Organophosphorus Poisoning and Potential Association with Oxime Use

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Abstract

Introduction: Organophosphorus poisoning (OP) represents a significant public health issue, particularly in developing countries, due to its extensive availability and high toxicity. Standard management includes atropine and oximes such as Toxogonin; however, emerging evidence suggests potential adverse effects associated with oximes.
Case presentation: This case report examines the uncommon occurrence of acute kidney injury (AKI) in a 64-year-old Egyptian farmer following accidental dermal and inhalational exposure to OP pesticides. The patient presented with symptoms of OP poisoning, including dizziness, sweating, and fasciculations. Initial treatment with atropine and Toxogonin (obidoxime) resulted in temporary symptomatic improvement. Nevertheless, renal function progressively deteriorated after initiating Toxogonin therapy, evidenced by elevated urea and creatinine levels. Renal impairment coincided temporally with Toxogonin administration and improved following its cessation.
Discussion: Potential mechanisms of Toxogonin-induced AKI include direct nephrotoxicity, altered renal perfusion, or immune-mediated injury. Other causes, such as rhabdomyolysis, systemic hypotension, or intrinsic OP nephrotoxicity, were ruled out to reinforce the likelihood of oxime-related renal impairment. While oximes are essential in OP poisoning management, this case emphasizes the necessity for clinical vigilance concerning their potential nephrotoxic effects.
Conclusion: The findings highlight the need to reassess the use of oximes, especially in patients with pre-existing renal conditions. Furthermore, additional research is required to elucidate the mechanisms and determine risk factors associated with oxime-induced nephrotoxicity.

Keywords: Organophosphorus Poisoning, Acute kidney injury, Toxogonin nephrotoxicity

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INTRODUCTION

Organophosphorus poisoning (OP) and its associated lethal outcomes remain a significant public health issue worldwide, especially in developing countries. This issue stems from the widespread use of OP compounds, inadequate awareness and education regarding the risks of pesticide contamination, absence of protective measures, and insufficient governmental regulation of their production [1,2].

Organophosphorus chemicals are the most commonly used pesticides in Egypt. They were identified as the most frequently involved toxic substances, accounting for 6,920 cases among all admissions to the Alexandria Poison Control Center over five years [3]. Approximately 40 different types have been identified and utilized, either individually or in combination [4].

These chemicals infiltrate the human body via ingestion, inhalation, or skin absorption. Their primary pharmacological action is the irreversible inhibition of the enzyme acetylcholinesterase (AChE), which degrades acetylcholine (ACh). Subsequent ACh accumulation overstimulates muscarinic and nicotinic receptors at peripheral and central nervous system synapses, precipitating neurotoxic effects with high mortality rates. Consequently, the standard treatment involves the use of atropine to counteract cholinergic effects, along with oxime-based enzyme reactivators, such as pralidoxime and obidoxime, to address nicotinic effects [5,6].

Nevertheless, emerging evidence contests the assumption that cholinesterase inhibition solely accounts for the wide range of morbidity associated with OP poisoning [7]. Recent findings indicate that OP compounds can induce multisystem toxicity, which, while less common, may exacerbate clinical presentation and prognosis. The kidneys are among the organs impacted. Several hypotheses have been proposed to explain the mechanism underlying AKI; however, the exact process of OP-induced renal toxicity remains unclear [8].

The present study investigates a rare case of acute kidney injury (AKI) in a patient accidentally exposed to OP compounds. The renal function deteriorated following oxime

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(Toxogonin) administration but improved upon discontinuation, as evidenced by clinical and laboratory evaluations. This study aims to determine the potential correlation between oxime administration and the development of AKI regarding OP toxicity.

CASE PRESENTATION

History

A 64-year-old Egyptian male farmer presented to the Alexandria Poison Control Center six hours after suspected exposure to a pesticide mixture containing lannate (methomyl) and lambda-cyhalothrin. The patient exhibited symptoms of dizziness, sweating, recurrent vomiting, and diarrhea, which manifested after inhalation, ocular exposure, and dermal contamination during a one-hour pesticide spraying session conducted without personal protective equipment. No history of seizures, loss of consciousness, or drug overdose was noted. The patient's medical history includes treatment of hepatitis C and a left renal stone managed via left open pyelolithotomy.

Clinical Examination:

The patient was alert with bilaterally constricted, sluggishly reactive pupils. The cardiovascular assessment indicated a blood pressure of 100/70 mmHg, and the ECG demonstrated sinus bradycardia (50 bpm on electrocardiogram). Auscultation of the chest revealed clear but bilaterally reduced breath sounds. The abdomen was soft, non-tender, and lax. Bilateral spontaneous fasciculations were observed in the neck, upper, and lower limbs.

Arterial blood gas analysis showed normal results (pH: 7.39, $PaCO_2$: 40 mmHg, PaO_2: 123 mmHg, HCO_3: 24 mEq/L and SO_2: 96%). The patient's body temperature was 37°C, and random blood sugar was 162 mg/dL.

The laboratory investigations were performed during hospitalization, including a variety of biochemical and hematological parameters:

- **Alanine Aminotransferase (ALT)**: Remained within the normal range (20-40 U/L) throughout the observation period, with minor fluctuations.
- **Aspartate Aminotransferase (AST)**: Initially within the normal range (15-40 U/L), followed by a mild increase (40-60 U/L), and returned to near baseline levels (20-40 U/L) by the end of the observation period.
- **Sodium (Na)**: Fluctuated within the normal range (135-145 mmol/L) during the observation period.
- **Potassium (K)**: Initially within the normal range (3.5-5.0 mmol/L), with a slight increase (4.0-4.5 mmol/L) on Day 5, followed by a decrease (3.0-3.5 mmol/L) on Day 6.
- **Creatine Kinase (CK)**: Initially elevated (160-180 U/L), followed by a gradual decline (80-100 U/L) to near normal levels (30-50 U/L) by the end of the observation period.
- **Troponin**: Consistently undetectable (<0.01 ng/mL) throughout the observation period.
- **Prothrombin Time (PT)**: Remained stable within the normal range (11-13 seconds) throughout the testing period.
- **Prothrombin Activity (%)**: Remained stable within the normal range (70-110%) throughout the observation period.
- **International Normalized Ratio (INR)**: remained stable within normal ranges (0.9-1.1) throughout the testing period.

Management and Outcome:

The patient managed with immediate decontamination of the skin and eyes, supplemented by intravenous fluid resuscitation, supplemental oxygen therapy, and incremental intravenous and nebulized atropine dosing until full atropinization was achieved, requiring a total dose of 7 mg.

He was administered a loading dose of Toxogonin (250 mg), followed by a maintenance dose of 750 mg according to approved guidelines. Despite marked initial improvement, persistent lower limb fasciculations necessitated five additional maintenance doses of Toxogonin over the subsequent five days.

Laboratory investigations for renal functions were conducted upon admission and continued at 24-hour intervals until discharge on Day 9, as shown in Table 1. The patient maintained a daily urine output of 2.5–3 L/day. However, following the initiation of Toxogonin infusion, there was a gradual increase in renal function markers. On the second day of Toxogonin treatment, the patient developed perioral numbness, headache, generalized fatigue, and constipation, which persisted until Toxogonin was discontinued on Day 6. Renal function showed improvement the day following the final Toxogonin dose (Day 8), though the patient declined further follow-up.

Abdominopelvic ultrasonography on Day 5 revealed normal-sized kidneys without calculi, cystic lesions, or hypertensive nephropathy. The chest X-ray was also normal. The patient's condition stabilized, culminating in discharge on Day 9.

Ethical Considerations

Informed consent was obtained from the patient. All patient information was managed with strict confidentiality. Additionally, ethical approval for this case report was granted by the Ethical Committee of the Faculty of Medicine, Alexandria University.

DISCUSSION

AKI has been observed in cases of OP poisoning, though it is an uncommon occurrence with only a limited number of cases documented in the medical literature. The precise pathophysiological mechanisms underlying OP compound-

Table 1. Laboratory investigations conducted over consecutive days of admission.

Day	Urea (mg/dL)	Creatinine (mg/dL)	BUN (mg/dL)
1st day	-	0.7	19
2nd day	38.52	1.1	18
3rd day	49	2.1	23
4th day	70.62	2.6	33
5th day	71	2.6	33
6th day	73	2.9	34
7th day	96	2.9	45
8th day	75	2.5	40
9th day	68	2.2	31

induced AKI remain controversial. Various pathways have been proposed, including hemodynamic instability, oxidative stress, rhabdomyolysis, and direct cytotoxic effects mediated by the parent compound or its metabolites [9].

Experimental studies have demonstrated that AKI may arise after OP poisoning, underscoring the nephrotoxic properties of these compounds. Animal models of OP exposure demonstrated dose-dependent renal dysfunction, characterized by elevated serum creatinine levels and reduced glomerular filtration rate. In addition, there was increased urinary flow with low osmolarity, indicating a direct effect on tubular function and histopathological damage to renal tubules [10,11].

Oximes are crucial in managing OP pesticide poisoning, functioning as enzyme reactivators that directly address the core mechanism of acetylcholinesterase (AChE) inhibition. OP compounds irreversibly bind to AChE, accumulating acetylcholine and a subsequent cholinergic crisis. Oximes, such as pralidoxime and obidoxime (Toxogonin), work by reactivating AChE by cleaving the bond between the enzyme and the OP compound, thereby mitigating both nicotinic and muscarinic effects. Consequently, oximes are essential in the treatment protocol, serving as a complement to atropine, which primarily addresses muscarinic symptoms. Toxogonin, an oxime used as an antidote for organophosphate poisoning, is poorly absorbed after oral administration in humans, is less than 1 % bound to human serum albumin, and is mainly renally excreted. [12-14].

Toxogonin is linked to various adverse effects. Cardiovascular effects such as tachycardia and hypertension are frequently observed, likely due to cholinergic activity or sympathetic nervous system stimulation. Additionally, a dose-independent symptom complex has been reported, which includes sensations of peroral warmth, paresthesia, hypalgesia, and a distinctive menthol taste [15].

This case report investigates the rare association between AKI and OP poisoning, focusing on the potential link between the use of oxime reactivators, such as Toxogonin, and renal impairment.

The observed AKI may be due to direct OP nephrotoxicity, rhabdomyolysis secondary to persistent fasciculations, a pre-existing history of renal disease, or the administration of oximes as a therapeutic intervention.

OP poisoning is unlikely to be the primary cause of renal impairment, as OP compounds are generally not linked to direct nephrotoxicity. Renal dysfunction associated with organophosphate poisoning generally arises from major systemic complications such as hypovolemia, hypotension, or rhabdomyolysis [9]. However, the clinical data in this case do not support these mechanisms. The patient presented with normotension (100/70 mmHg) and maintained hemodynamic stability throughout admission. Serum electrolytes remained within normal ranges, and arterial blood gas analysis showed no significant metabolic acidosis or other derangements.

Rhabdomyolysis due to persistent fasciculations was considered a potential cause of renal impairment; however, this can be excluded in this case. Creatine kinase (CK), a key marker of rhabdomyolysis, was only mildly elevated on Day 1 (169 U/L) and progressively decreased to 68 U/L by Day 7, suggesting that the severity of rhabdomyolysis was inadequate to cause renal dysfunction. Furthermore, the patient maintained normal urine output (2.5–3 L/day) throughout the hospitalization, effectively ruling out myoglobin-induced acute tubular necrosis. Additionally, no dark-colored urine or myoglobinuria was observed during the hospital stay [16].

The patient received five repeated doses of Toxogonin over five days, potentially exceeding cumulative exposure. The temporal association between the onset of symptoms, including perioral numbness, headache, and generalized fatigue, and the elevation of renal function markers strongly indicates Toxogonin-related toxicity. Notably, the clinical symptoms and renal function markers immediately improved within 24 hours of discontinuing oxime therapy, further supporting a causal relationship.

The proposed mechanisms of Toxogonin-induced renal dysfunction include direct nephrotoxicity, characterized by the accumulation of Toxogonin or its metabolites that impair renal tubular function, and immune-mediated mechanisms, which may involve rare hypersensitivity reactions leading to interstitial nephritis.

The renal impairment observed in this case is more likely attributable to Toxogonin treatment rather than to OP poisoning or rhabdomyolysis resulting from fasciculations. Renal function deterioration commenced following the initiation of Toxogonin treatment on Day 1 and progressively worsened throughout its administration. Improvement in renal function was observed immediately after the discontinuation of Toxogonin on Day 6.

The findings indicate that oxime therapy, particularly Toxogonin, may lead to renal impairment via mechanisms including altered renal perfusion, direct tubular toxicity, or immune-mediated reactions. While the precise mechanism remains undetermined, the resolution of AKI following the discontinuation of Toxogonin further implicates it as a potential causative factor.

LIMITATIONS

This report is limited by the absence of advanced diagnostic tools, such as renal biopsies or tubular injury markers, to elucidate the precise mechanism of AKI. Furthermore, the brief follow-up period limits the evaluation of long-term renal outcomes.

CONCLUSION

Oximes play a critical role in the treatment of OP poisoning. However, this case underscores the previously underrecognized nephrotoxic risks linked to Toxogonin despite the essential role of oximes in reversing acetylcholinesterase inhibition during OP poisoning. These findings highlight the necessity for ongoing research to more clearly delineate their therapeutic role and improve outcomes for patients affected by OP poisoning.

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