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ORGANOPHOSPHATE POISONING: A NARRATIVE REVIEW

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ABSTRACT Organophosphates (OP) and carbamates, despite structural differences, share potent cholinesterase inhibition, posing risks of severe cholinergic toxicity through various exposures. Global estimates indicate over 3 million annual exposures, causing up to 300,000 fatalities. This review explores their poisoning, emphasizing recent events like the Tokyo sarin attack and Novichok incidents. Organophosphorus compounds initiate toxic effects by inhibiting acetylcholinesterase (AChE), leading to cholinergic excess. Carbamates act as transient inhibitors, hydrolyzing within 48 hours. Clinical manifestations involve cholinergic excess, nicotinic effects, cardiac complications, respiratory failure, and delayed neuropathy. Management includes resuscitation, atropine, pralidoxime, seizure control, decontamination, and individualized approaches. Prognostication involves considering factors like the Glasgow Coma Score and specific OP agents. Ongoing research is crucial for refining diagnostic and therapeutic strategies, considering the diverse clinical responses and individualized care required for organophosphate poisoning.

KEYWORDS : Organophosphates, Cholinergic toxicity, Poisoning management, Prognostic factors, Neurological effects.

INTRODUCTION

Organophosphates and carbamates, distinct in structure but sharing potent cholinesterase inhibition, pose risks of severe cholinergic toxicity via cutaneous exposure, inhalation, or ingestion. This overview focuses on their poisoning, with a concise emergent management table. Global exposure estimates exceed 3 million people annually, causing up to 300,000 fatalities. In the U.S., over 8000 exposures were reported in 2008, resulting in fewer than 15 deaths. Sources include agricultural pesticides and contaminated food or clothing. Notable agents include carbamates (methomyl, aldicarb) and organophosphates (parathion, malathion). Recent events, like the 1995 Tokyo sarin attack and Novichok incidents, emphasize the importance of recognition and treatment (1,2).

METHODS

The methodology of the narrative review on "Organophosphate Poisoning" involved a meticulous exploration across three comprehensive databases: PubMed, Scopus, and Embase. A systematic search strategy was implemented, employing a nuanced combination of keywords such as "organophosphate toxicity," "chemical pesticide exposure," and "neurological effects." The inclusion criteria encompassed studies published within the last decade, focusing on human subjects. Following the exhaustive search, a refined selection process identified 15 seminal references. The synthesis of this narrative review involved a rigorous scrutiny of each source, emphasizing the contextual interplay of findings. This methodological framework ensured a nuanced and thorough exploration of the multifaceted landscape surrounding organophosphate poisoning.

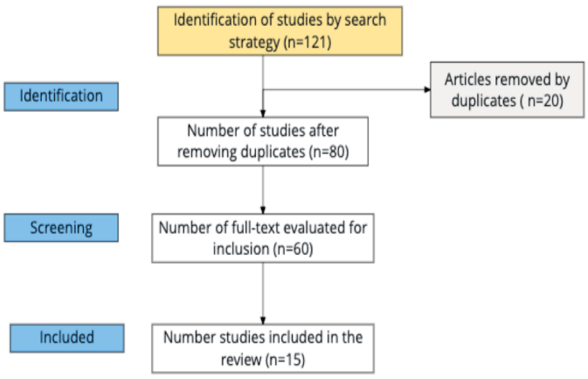

Figure 1. PRISMA.

Mechanism of Action

Organophosphorus compounds, composed of carbon and phosphorous acid derivatives, initiate their toxic effects through intricate processes. These substances swiftly penetrate the skin, lungs, and gastrointestinal tract upon exposure, binding to acetylcholinesterase (AChE), including red blood cell (RBC) acetylcholinesterase. This renders the enzyme non-functional, disrupting the breakdown of acetylcholine into choline and acetic acid. The inhibition leads to an accumulation of acetylcholine at neuronal synapses and the neuromuscular junction, heightening cholinergic activity (3).

Over time, depending on the organophosphorus agent's chemical structure, the AChE-organophosphorus compound undergoes an irreversible conformational change known as "aging," resisting reactivation by antidotal oximes. Organophosphorus agents also inhibit plasma cholinesterase (or butylcholinesterase [BuChE]) and neuropathy target esterase (NTE), with uncertain clinical implications (4).

In contrast, carbamate compounds, derived from carbamic acid, rapidly absorb through various exposure routes. Unlike organophosphates, carbamates act as transient cholinesterase inhibitors, spontaneously hydrolyzing from the enzymatic site within 48 hours. This results in a shorter duration of carbamate toxicity compared to equivalent doses of organophosphates, while mortality rates associated with exposure to both chemical classes remain comparable (5).

Clinical manifestations

Organophosphate poisoning manifests through a myriad of clinical features, with onset and duration varying based on factors such as the specific agent, route of exposure, and lipophilicity. The toxic effects are predominantly cholinergic, affecting the autonomic nervous system, neuromuscular junction, and the central nervous system (CNS). In acute toxicity, cholinergic excess dominates, presenting as bradycardia, miosis, lacrimation, salivation, bronchorrhea, bronchospasm, urination, emesis, and diarrhea. Noteworthy are muscarinic signs encapsulated by the mnemonics SLUDGE/BBB and DUMBELS, illustrating a range of symptoms affecting multiple systems. Concurrently, nicotinic effects involve fasciculations, muscle weakness, and paralysis, akin to succinylcholine's neuromuscular blockade. (6).

Cardiac manifestations, including arrhythmias and

myocardial ischemia, underscore the systemic impact of organophosphates. Respiratory failure, a critical outcome, results from CNS depression, neuromuscular weakness, excessive secretions, and bronchoconstriction. The intermediate syndrome, occurring post-cholinergic excess resolution, presents distinctive neurologic findings, emphasizing the complex nature of organophosphate toxicity (6).

Delving further, delayed neuropathology, exemplified by organophosphate-induced delayed neuropathy (OPIDN), unfolds one to three weeks after exposure. This syndrome, associated with specific agents, showcases symptoms such as "stocking-glove" paresthesias and a motor polyneuropathy. Distinct nerve conduction abnormalities and histopathologic evidence highlight the multifaceted nature of organo phosphate-induced neurotoxicity. Long-term consequences are evident, with survivors facing neurobehavioral deficits, including decreased memory and attention, along with potential permanent Parkinsonism. Additional complications encompass acute kidney injury and acute pancreatitis, further underscoring the diverse systemic impact of organo phosphate poisoning (7).

Recognizing the variability in toxicity among organo phosphorus agents, the complex interplay of cholinergic and nicotinic effects, and the potential for delayed and long-term neuropathological consequences, underscores the importance of tailored medical interventions. Future studies must consider each agent independently to deepen our understanding of the intricate mechanisms driving organophosphate toxicity (7,8).

Management

The comprehensive management of organophosphate poisoning integrates emergent measures, specific antidotes, and ongoing supportive care. The complexity of this toxicological challenge requires a systematic approach, encompassing a range of interventions tailored to the severity of the poisoning (8).

Initial Resuscitation and Airway Management

In cases of markedly depressed mental status, immediate endotracheal intubation and 100 percent oxygen administration are imperative. Respiratory failure can ensue rapidly due to various mechanisms, including CNS depression and excessive secretions. Notably, succinylcholine is avoided during rapid sequence intubation (RSI) due to its interaction with acetylcholinesterase, which is inhibited by organophosphates, leading to prolonged neuromuscular blockade. Nondepolarizing agents like rocuronium are preferred, with awareness of potential increased dosage requirements (8,9).

Cardiovascular Support

Bradycardia and hypotension are common in moderate to severe poisonings, necessitating adequate volume resuscitation with isotonic crystalloid. Tachycardia or hypertension may transiently occur due to direct sympathetic stimulation. Continuous monitoring of vital signs and electrocardiograms is essential, with aspirin considered for non-occlusive myocardial ischemia (9).

Atropine Administration

Atropine, a key component in managing cholinergic toxicity, competes with acetylcholine at muscarinic receptors. Dosages are titrated based on the therapeutic endpoint of alleviating respiratory symptoms. Tachycardia and mydriasis are not reliable markers; therefore, atropine dosing should focus on clinical response, adjusting the infusion to avoid toxicity. In certain cases, high doses may be required, and the addition of epinephrine is an option for non-responsive patients (9,10).

Pralidoxime (2-PAM) Therapy

Administered in conjunction with atropine, pralidoxime addresses both muscarinic and nicotinic symptoms. Its slow infusion prevents transient acetylcholinesterase inhibition and associated muscle weakness. Evidence on the efficacy of oximes is variable, with a need for individualized approaches based on clinical response (10).

Seizure Management

Organophosphate-induced seizures warrant benzodiazepine treatment, with prophylactic diazepam considered to mitigate neurocognitive dysfunction. Phenytion is not recommended, and diazepam autoinjectors may be employed for rapid chemical attack response (10,11).

Decontamination and Gastric Lavage

Aggressive decontamination involves removing contaminated clothing, thorough skin washing, and discarding belongings due to potential reexposure. While gastric lavage is generally avoided, activated charcoal is administered within one hour of ingestion. Forced emesis is contraindicated. Monitoring for myocardial ischemia may include serial electrocardiograms and serum troponin concentrations (12).

Additional Considerations

Patients exhibiting signs of intermediate syndrome require meticulous neurologic monitoring and respiratory support. Oxime therapy is beneficial in cases of neuromuscular dysfunction. Long-term follow-up is essential for survivors facing potential neurocognitive deficits and permanent sequelae (12,13).

Research and Evolving Strategies

The multifaceted nature of organophosphate toxicity underscores the need for ongoing research to refine diagnostic and therapeutic approaches. As the clinical response to treatments varies among patients and organophosphorus agents, individualized strategies should guide future studies. Continuous updates and advancements in management protocols will contribute to more effective and personalized care for individuals affected by organo phosphate poisoning (13).

Prognostic

Understanding the prognosis of organophosphate (OP) poisoning involves a multifaceted consideration of various factors, with recent studies shedding light on key prognostic indicators. The Glasgow Coma Score (GCS) emerges as a valuable tool, especially when evaluating patients acutely poisoned with OP or carbamate. A GCS of less than 13 is identified as a predictor of poor outcomes, offering a practical and reliable assessment comparable to the International Program on Chemical Safety Poison Severity Score (IPCS PSS).However, the nuances of OP agents cannot be overlooked. In instances where the specific agent is a lipophilic OP, such as fenthion or parathion, the prognosis may deviate from general trends. Remarkably, a retrospective study emphasized the importance of considering the OP agent involved, revealing that fenthion-poisoned patients who succumbed to the poisoning had initially presented with only mild symptoms (14).

The complexity of prognostication further unfolds when examining the performance of standard clinical scoring systems in OP poisoning. While the Acute Physiology and Chronic Health Evaluation II (APACHE-II), Simplified Acute Physiology Score II (SAPS-II), and Mortality Prediction Model II (MPM-II) demonstrated efficacy in predicting death in nearly 400 OP-poisoned patients, their performance was contingent upon the specific OP agent. Lipophilic OPs, once again, presented a unique challenge, emphasizing the need for tailored approaches (15).

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