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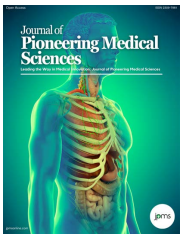

Organophosphate and Carbamate Toxicity: Understanding, Diagnosing and Treating Poisoning

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Abstract Organophosphate (OP) and carbamate pesticides are widely used to control pests in agriculture and households, but they come with serious health risks. These chemicals interfere with an enzyme called acetylcholinesterase, leading to a dangerous buildup of acetylcholine-a neurotransmitter that overstimulates the body's nerves. This overstimulation causes symptoms ranging from excessive saliva, difficulty breathing and muscle weakness to confusion and even paralysis. OP poisoning tends to be more severe because it creates lasting enzyme disruptions, while carbamates have shorter, reversible effects. Recognizing the signs of poisoning quickly is critical for saving lives. Doctors often rely on clinical symptoms to start treatment immediately, administering atropine to control excessive secretions and pralidoxime to help restore normal enzyme function. Laboratory tests can confirm exposure but should not delay treatment. Managing OP and carbamate poisoning involves stabilizing the patient's breathing and heart function, thoroughly cleaning any exposed skin and closely monitoring their progress. This review highlights the importance of safer pest control practices, such as integrated pest management, to reduce dependence on toxic chemicals. Public education about the dangers of improper pesticide use is essential, especially in communities where these chemicals are widely available. Continued research into better antidotes and diagnostic tools offers hope for improving outcomes and reducing the devastating impact of these poisonings on human health and the environment

Key Words Organophosphate, carbamate, acetylcholinesterase, pesticide poisoning, acute poisoning management, diagnosis, treatment

INTRODUCTION

Organophosphates (OPs) and carbamates are commonly used insecticides, both indoors and outdoors. For instance, OPs are often used as bait for houseflies, to treat lice infestations by dipping or spraying and to manage pests like cattle grubs and screwworms. They are also combined with other organic compounds to combat external parasites in livestock such as cattle, sheep and pigs. Similarly, carbamates are used in products like fly and louse baits and are applied directly to livestock in concentrated forms. While these chemicals are effective, their misuse can pose significant risks. Problems arise from improper handling, advances in application techniques that increase exposure to people and animals, the development of more potent formulations and a tendency to prioritize quick fixes over comprehensive pest management strategies. This highlights the importance of safe practices and integrated approaches to pest control [1].

These insecticides are well-known for their severe toxicity to the nervous system, which has resulted in numerous poisoning incidents in humans and animals. OP and carbamate compounds inhibit acetylcholinesterase (AChE) activity, causing an excessive buildup of acetylcholine (ACh) at synaptic junctions [2]. This causes cholinergic receptors (both nicotinic and muscarinic) to be overstimulated, resulting in symptoms of cholinergic toxicity such as excessive salivation, tearing, urination, defecation and vomiting [3].

The overstimulation of these receptors can result in a variety of symptoms, such as bronchoconstriction, bradycardia and miosis, as well as muscle weakness, confusion and respiratory distress. Given their widespread use, particularly in agriculture, pesticides can pose a significant health risk if not effectively managed. This emphasizes the importance of caution and awareness when managing these chemicals to avoid acute poisoning [4].

Proper management and handling practices are critical for reducing the severe health risks associated with OP and carbamate insecticides. The widespread use of these insecticides in agriculture and domestic settings emphasizes the importance of integrated pest management (IPM) strategies. IPM emphasizes the use of multiple methods to control pests, reducing reliance on chemical insecticides and thus lowering the risk of poisoning [5].

Organophosphate (OP) and carbamate poisoning represents a significant global health challenge, with a large proportion of cases arising from occupational exposure and intentional ingestion. Developing countries, where regulatory controls on pesticide usage are often inadequate, bear the heaviest burden of this issue [6]. OP poisoning is one of the leading causes of self-poisoning and suicide worldwide, with mortality rates varying from 10% to 50%, largely dependent on the availability of healthcare resources and specific antidotes [6]. In rural Asia, these pesticides are directly implicated in thousands of suicides annually, highlighting their deadly impact [7].

The regional distribution of the burden shows marked disparities. Sri Lanka and India, for example, report significantly high mortality rates due to pesticide poisoning, surpassing global averages. This is largely attributable to the widespread availability and inherent toxicity of these substances [8]. African nations are also increasingly witnessing rising cases, particularly in regions experiencing rapid agricultural expansion, where the use of these chemicals is growing [9].

Improper handling, unsafe application methods and the development of more potent formulations of OPs and carbamates have heightened risks to human and animal health while compromising environmental safety [10]. Although these chemicals are well-documented toxins, there is a significant research gap regarding the long-term environmental consequences and societal burden associated with their exposure. This is particularly concerning in low-resource settings where safety regulations are inadequate or poorly enforced.

While acute poisoning incidents are widely recognized, there is limited data on sub-lethal, chronic exposures and their impacts on neurological, developmental and ecological systems. This knowledge gap is alarming given the profound societal implications of OP and carbamate misuse. High-risk groups, such as farmers, pesticide applicators and vulnerable populations-including children and pregnant women-face heightened exposure, raising serious public health concerns. Environmentally, these chemicals contaminate soil and water, harm non-target organisms and disrupt ecosystems and biodiversity, contributing to ecological imbalance.

The societal and environmental impact of OP and carbamate misuse underscores the urgent need for safer pest control alternatives, enhanced educational initiatives and integrated pest management (IPM) strategies. These approaches must balance pest control demands with the imperative of protecting human health and preserving ecosystems. This review highlights the critical importance of addressing these gaps through the development of sustainable solutions, improved treatment protocols and increased public awareness to mitigate the long-term consequences of OP and carbamate exposure.

METHODS

Relevant studies were identified through a thorough search of electronic databases, such as ScienceDirect, Scopus, PubMed and Google Scholar. The relevant articles published were studied in detail and a manuscript was prepared and written. The databases were searched using the keywords "Organophosphates" or "Carbamates" or "Carbamate poisoning" or "Carbamate poisoning," and "Management" or "Treatment" were the main keywords used to search for articles.

Inclusion criteria comprised peer-reviewed articles published in English, focusing on organophosphate and carbamate poisoning, their management, treatment protocols and relevant case studies. Studies discussing acute, chronic poisoning or emerging management approaches were prioritized. Exclusion criteria included duplicate publications, conference abstracts, non-English papers, or studies lacking detailed methodologies and outcomes.

To minimize potential selection bias, multiple independent reviewers screened articles based on relevance, method, quality and inclusion criteria.

Findings from selected studies were synthesized through narrative analysis, summarizing key themes, including clinical features, treatment protocols and preventive measures. Where applicable, data from quantitative studies were compared to highlight trends and discrepancies across regions. Systematic comparison ensured that conclusions reflected robust evidence drawn from diverse sources.

The management of regional or language-specific data prioritized studies published in English to maintain consistency and accessibility throughout the review process. Regional data sources were considered; however, non-English studies were excluded unless significant findings were available through translations.

The potential limitations of the selected studies in representing global trends stem from several factors: First, reliance on studies primarily published in English may exclude valuable research from non-English-speaking regions, leading to an underrepresentation of findings from countries where local languages dominate academic publication. This exclusion can create gaps in understanding trends specific to certain regions, particularly in low- and middle-income countries where pesticide use and its associated health impacts may differ significantly from those in higher-income nations. Second, the databases used, such as ScienceDirect, PubMed and Google Scholar, may favor

research from regions with better access to publishing resources and established academic infrastructure, while studies from underrepresented regions, particularly in Africa, South Asia and Latin America, may be overlooked. This imbalance could skew the interpretation of global trends, making the findings less applicable to regions where organophosphate and carbamate poisoning is most prevalent. Third, variations in study design, sample size and quality across different regions can contribute to inconsistencies in findings. Many studies from high-burden areas might lack rigorous methodologies or detailed reporting, which can limit their comparability with higher-quality studies from well-resourced settings. Lastly, socioeconomic and environmental factors influencing pesticide exposure-such as regulatory enforcement, agricultural practices and healthcare access-differ globally. Studies focused predominantly on specific regions may fail to capture these broader determinants, reducing the generalizability of findings to other settings.

OPs and Carbamate Proprieties

OPs are chemical compounds that can exist as esters, amides, or thiol derivatives of phosphoric, phosphonic, or phosphinic acids. Their general structure includes two side chains, R1 and R2, which can be made up of alkyl, alkoxy, alkylthio, or amido groups and a third component, X, which is an acyl residue. This residue can be a labile group like fluorine, cyano, or a substituted or branched aliphatic, aromatic, or heterocyclic group. The structural variations of these compounds significantly influence their properties and reactivity [11] (Figure 1).

Initially developed in the early 19th century, the insecticidal properties of OPs, which resemble their toxic effects in humans, were only discovered in 1932. Some of these compounds, due to their high toxicity, were used as nerve agents during World War II. Today, several OPs pesticides, such as parathion, malathion, methyl parathion, chlorpyrifos, diazinon, dichlorvos, phosmet, fenitrothion, tetrachlorvinphos and azinphos methyl, are in use [12]. Additionally, the carbamate group of insecticides, containing a carbamate ester group derived from carbamic acid, includes compounds like aldicarb, carbofuran, carbaryl, ethienocarb, fenobucarb, oxamyl and methomyl [13] (Figure 2).

Both OPs and carbamates inhibit the enzyme AChE, which is crucial for the proper functioning of the central nervous system in humans and insects. Inhibiting AChE leads to an accumulation of ACh, disrupting muscle responses and potentially causing severe respiratory and heart problems, which can be fatal [14]. Given the varied toxicity of these compounds, accurate detection in environmental samples is essential for health and safety. Modern electrochemical biosensors for detecting these chemicals leverage cholinesterase inhibition to deliver highly sensitive and rapid monitoring, offering precise and timely detection capabilities [15].

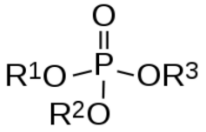

Figure 1: Chemical structure of OPs

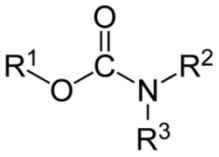

Figure 2: Chemical structure of Carbamates

Toxicokinetics and Metabolism

OPs and carbamates inhibit AChE by binding to the enzyme's active site, preventing ACh from being broken down into choline and acetate [16]. This causes an accumulation of ACh in the synaptic cleft. While OPs are considered irreversible inhibitors, some, such as echothiophate, exhibit slightly reversible interactions. OPs and carbamates have similar binding mechanisms to AChE, implying that their toxicokinetic properties are likely comparable. These compounds inhibit AChE, which disrupts standard synaptic transmission and leads to overstimulation of cholinergic receptors (Figure 3) [17].

The toxicokinetic parameters of OPs and carbamates include several critical factors: the fraction absorbed into the body, the fraction unbound in the bloodstream, the blood-to-air partition coefficient, the duration of the AChE reaction and the extent of irreversible inhibition [18]. Additional factors include the fraction of the compound that ionizes at physiological pH, the proportion of the reaction with AChE that is rapidly reversible, the dose fraction absorbed into peripheral blood and the fraction available to inhibit plasma cholinesterase. Together, these parameters determine how much of the parent compound is bioavailable and capable of inhibiting cholinesterase, thereby influencing the severity and duration of toxicity [19].

Clinical Features of OPs and Carbamates Poisoning

The clinical symptoms of OP poisoning can be grouped into three categories based on their onset, progression and mechanism of action: acute systemic effects, cholinergic syndrome and intermediate syndrome. The acute systemic effects are mainly caused by excessive acetylcholine accumulation due to inhibition of AChE. These effects are mediated through muscarinic receptors (bronchospasm, bradycardia, miosis), nicotinic receptors (tachycardia, muscle weakness) and central nervous system involvement (anxiety,

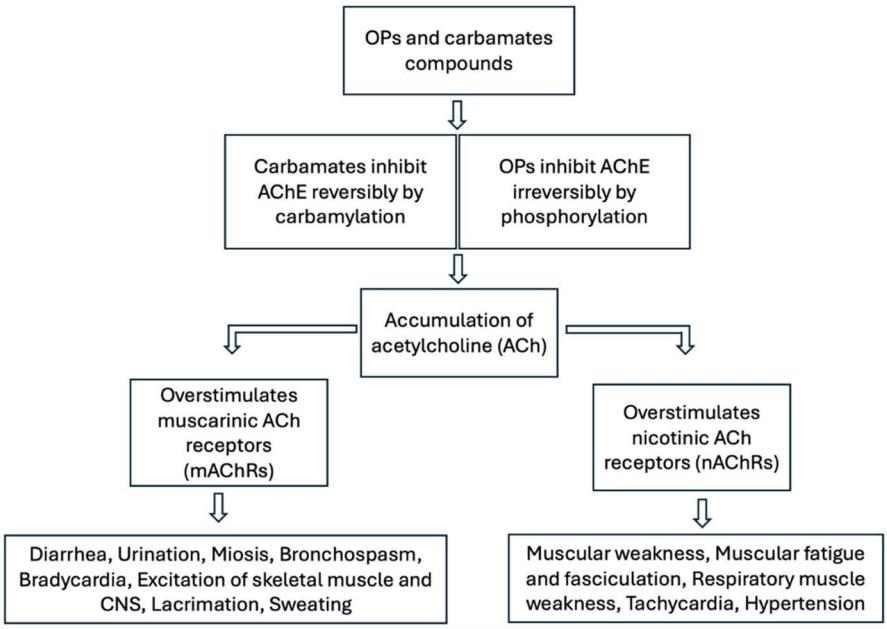

Figure 3: Schematic diagram showing the mechanism of action and sequence of events involved in the toxicity of OPs and Carbamates

respiratory depression). The cholinergic syndrome is the combination of all acute systemic effects and is referred to as cholinergic crisis [20]. The intermediate syndrome develops one day or more after OP or carbamate exposure. The symptoms are characterized by weaknesses in respiratory and proximal muscles and cranial nerve palsies [21]. While systemic effects are fundamental to OP poisoning, treatment primarily targets the cholinergic crisis. Cholinergic toxidromes can be categorized into central and peripheral manifestations, with central ones including mental status changes and muscle twitching and peripheral ones involving various muscarinic and post-ganglionic effects. The activation of central and peripheral cholinergic receptors results in typical cholinergic symptoms. Clinical signs of OP poisoning are generally easy to identify when there is a known history of chemical exposure. Common symptoms include nausea, vomiting, diarrhea, excessive salivation, bronchorrhea, respiratory distress, fever, rapid heartbeat, low blood pressure, dilated pupils and decreased bowel sounds. However, vague descriptions during initial medical assessments can lead to misdiagnosis or missed cases [20, 22].

For oral exposure, gastric decontamination with activated charcoal is recommended. Treatment should include administering atropine or other anticholinergic medications. Monitoring cholinesterase levels and closely tracking patients' progress are also critical. In cases of carbamate poisoning, supportive care combined with anticholinergic therapy is vital for symptom management [23, 24].

Mild carbamate poisoning typically results in less severe symptoms than OP poisoning. Individuals exposed to low doses of carbamate insecticides may experience mild cholinergic syndrome symptoms like chest tightness, palpitations, dry mouth and nonspecific abdominal cramps [25]. They may also have difficulty concentrating, along with minor headaches or dizziness. In suspected cases of carbamate poisoning, oral atropine is often administered before laboratory tests confirm cholinesterase inhibition, as waiting for laboratory results can delay symptomatic relief [26].

Diagnosis and Differential Diagnosis

Clinical evaluation is the primary method for identifying OP or carbamate poisoning. In cases of suspected acute poisoning, healthcare providers should look for cholinergic symptoms that indicate muscarinic, nicotinic, or central nervous system receptor activation [27]. A typical response to therapeutic doses of atropine or standard muscarinic agonists indicates acute cholinergic poisoning. It is critical to monitor both peripheral and central effects, as threshold between cardiovascular and pulmonary effects can lead to significant management mistakes. Although atropine can be useful and may help confirm a diagnosis, its overuse as a diagnostic tool is dangerous and should be avoided [28].

There are several methods for diagnosing acute OP and carbamate poisoning. Basal blood cholinesterase (ChE) levels can indicate early effects, but they are not associated with morbidity or mortality and are frequently unavailable in emergencies [29]. A reduction in erythrocyte ChE levels by more than 20% from average on two occasions, combined with clinical symptoms and relevant history, suggests a presumptive diagnosis. However, demonstrating decreased in

vitro red cell ChE activity is not required for the diagnosis. If normal RBC ChE levels are detected, OP intoxication is highly unlikely [30].

Laboratory Investigations

Laboratory tests play a minor role in early treatment of acute OPs and carbamate poisoning. In critically ill patients who require intubation, symptoms such as hypothermia and elevated lactate levels may necessitate the use of more advanced life support measures [31]. Delaying certain lab tests can help to speed up decisions about additional supportive and surgical care. Clinical chemistry tests are used in laboratories to detect abnormalities such as elevated serum creatinine phosphokinase or alanine aminotransferase, which can indicate multi-system organ failure, liver damage, or rhabdomyolysis. AChE and butyrylcholinesterase levels can also be measured, both specifically and non-specifically. Low-cost methods for measuring AChE have been validated for use in rural developing countries to indicate high levels of exposure [32].

Despite their low cost, the required reagents and equipment are frequently unavailable. Rapid identification of cholinesterase inhibitors is critical for initiating antidote treatment. Ellman's reagent can be used to assess the activity of AChE [33,34]. Ongoing research is aimed at determining the most effective measure for low-dose exposure, with studies showing that serial measurements of cholinesterase activity are more predictive of exposure risks than single tests [35]. High-dose exposure is usually diagnosed based on clinical symptoms. Data show that 98% of symptomatic individuals, including those who were asymptomatic but were exposed to sulprofos, had a cholinesterase activity decrease of more than 20% from baseline. Future research should focus on determining the best type of cholinesterase and antibodies for detecting low-dose exposure [36].

Management Principles

The primary strategy for treating poisoned patients is to rapidly stabilize them and then use both general and specific methods to eliminate the poison. Initially, stabilization should focus on securing and maintaining the airway, ensuring adequate oxygenation and ventilation, maintaining stable hemodynamic parameters and managing seizures or other critical emergencies [37]. Once these broad safeguards are in place, specific interventions tailored to the type of poisoning can be implemented. These interventions may include decontamination, improved elimination techniques and the administration of antidotes [21].

Decontamination

The primary goal of decontamination is to prevent further toxin absorption while also removing any residual toxins that have already been absorbed. In an emergency, securing the patient's airway and ensuring adequate oxygenation and ventilation is critical. Decontamination should begin immediately [38]. Depending on the type of poisoning, irrigation and bathing may be necessary to thoroughly cleanse the skin and hair. Contaminated clothing must be handled with caution to avoid exposing the medical team, who should also be wearing appropriate protective gear during treatment [39]. If the poisoning involves eye contact, the eyes should be rinsed with normal saline or a 0.9% salt solution before beginning skin decontamination. In cases where a small amount of liquid OP has been consumed, the mouth should be rinsed with water; however, vomiting should be avoided due to the risk of rapid absorption and respiratory complications [40].

For oral poisonings involving OPs or carbamates, stomach emptying is not recommended. Absorbent materials, such as activated charcoal, can help prevent further toxin absorption and are helpful in cases of overdose where the poison is consumed orally or has an effective antidote. However, these adsorbents can occasionally produce unstable gases or interact with other treatments, so they must be used cautiously [41]. Consulting a poison control center can provide guidance, especially since elderly patients may require lower charcoal doses due to aspiration risk. Alternatives to inhaled syrup include sodium hexamine salts and charcoal, as they do not require additional saline or sorbitol. Also, emergency personnel frequently carry various antidotes, including thiamine and N-acetyl cysteine. Animal poison response centers can also provide assistance and professional advice for treating poisoned animals [42].

Decontamination Techniques

Decontamination is the first step in treating people who have been exposed to OPs or carbamate poisoning. It should be done at the scene or while being transported to a medical facility. Those exposed through skin contact should remove all clothing and wash their skin with water and nonabrasive soap. Substances such as activated charcoal Fuller's earth can be applied to the skin and then removed at the medical facility, but using a barrier film is not recommended. Massaging the affected muscles is recommended for dealing with prolonged paralysis. Furthermore, maintaining the airway, breathing and circulation is critical. Once at the medical facility, supportive care should focus on managing respiratory failure caused by the extended inhibitory effects of ACh on muscles, with particular emphasis on providing oxygen and ventilation support [43, 44].

Decontamination should occur immediately following pesticide exposure, but transportation to a medical facility for further observation and assessment should not be delayed. Decontamination is critical for reducing the effects of exposure. First responders must take precautions to keep themselves safe during this process. Patients frequently seek medical attention for symptoms of pesticide exposure, which can occur when personal protective equipment is improperly removed, a large amount of pesticide is inhaled, or there is extensive skin contact. While not everyone may require

Table 1: Antidotes for organophosphates (OPs) poisoning

Antidote	Mechanism of Action	Dosage and Administration	Key Notes	References
Atropine	Competitive antagonist of muscarinic acetylcholine receptors Reverses the effects of excessive acetylcholine at muscarinic sites (e.g., secretions, bradycardia) Signs of adequate atropinization: dry mucous membranes, tachycardia, clear lungs	**Initial dose:** 1-2 mg IV every 5-15 minutes until secretions are controlled and heart rate normalizes	Maintain infusion if required Does not reverse nicotinic effects	[48-50]
Pralidoxime (2-PAM)	Reactivates acetylcholinesterase inhibited by organophosphates Restores standard neuromuscular transmission by cleaving OP-enzyme complex	Loading dose: 30 mg/kg IV over 15-30 minutes Maintenance dose: 8-10 mg/kg/hr as continuous infusion for 24-48 hours	Most effective if given within 24 hours Ineffective against carbamate poisoning	
Diazepam	Enhances GABAergic activity in the central nervous system to control seizures	Seizure control: 5-10 mg IV, repeat as needed	Used to treat OP-induced seizures Adjunct therapy alongside atropine and pralidoxime	
Obidoxime	Similar to pralidoxime but with a broader spectrum of reactivation	Dose: 250 mg IV or IM every 6-12 hours	Limited availability compared to pralidoxime	
Glycopyrrolate	Anticholinergic agent that reduces secretions without crossing the blood-brain barrier	Dose: 0.2-0.4 mg IV every 4-6 hours	Alternative to atropine for controlling peripheral symptoms	

emergency intervention, everyone who is aware of their exposure should have their symptoms thoroughly evaluated and addressed to reduce anxiety [45].

Antidotes for OPs Poisoning

Atropine is the most effective antidote for OP poisoning because it reduces the muscarinic effects of excessive ACh. It is primarily used to treat muscarinic toxidrome, a condition characterized by pinpoint pupils, blurred vision, slow heart rate, respiratory depression, excessive bronchial secretions and increased gastrointestinal activity [46]. Clinical end-organ toxicity is the most reliable indicator for administering atropine. Atropinization is attained when the patient's heart rate normalizes and lung sounds return to normal. The recommended initial dose of atropine is 2 to 4 mg slowly administered intravenously in adults, 0.02 mg/kg in children and 0.05 mg/kg in infants. Dosage and frequency are determined by the severity of the symptoms and the patient's response, to reduce clinical symptoms while avoiding atropine toxicity [47,48] (Table 1).

Intravenous atropine is preferred for treating OP-induced bronchorrhea and bronchoconstriction because intramuscular atropine is less effective. In severe cases, medications such as pentobarbital or phenobarbital may be used to treat bradycardia and excess airway secretions following atropinization. In North America, transvenous cardiac pacing is recommended for OP-induced bradycardia. Intravenous magnesium sulfate can help treat bronchoconstriction and hyperkalemia caused by OP poisoning. Pralidoxime is the only available agent capable of counteracting the neuromuscular toxicity caused by OP poisoning [49].

Antidotes for Carbamate Poisoning

There are two main antidotes for carbamate poisoning. Pyridine-2-aldoxime methiodide (2PAM) is generally preferred due to its longer duration of action compared to the much shorter effect of edrophonium-choline. If edrophonium-choline must be used, it is best to supplement it with neuromuscular blocking agents after an initial trial of 2PAM. In anesthetized animals, 2PAM improves depolarizing neuromuscular blockades more than edrophonium-choline. However, either antidote can be given before starting treatment at 2PAM [50,51].

Edrophonium undergoes hydrolysis in the liver, resulting in the production of pyridine-2-aldoxime. When Edrophonium is administered, the pyridine acts as a cholinesterase reactivator, inhibiting the breakdown of endogenous ACh. In addition to its antimuscarinic effects, edrophonium is more effective in this role than pyridine and 2PAM combined and slightly better than pyridine alone. However, its effects usually last no more than 15 minutes and may even be shorter in some animals [10].

Supportive Care and Monitoring

Providing extensive and specialized supportive care is critical for successfully treating patients with severe poisoning because it addresses both the indirect effects of low oxygen levels and blood pressure, as well as the direct toxic damage to organs [6]. The type of supportive care required depends on the state of the vital organ systems. Vital signs, blood oxygen (PO2) and carbon dioxide (PCO2) levels, ECG, pulse oximetry, and, possibly, arterial pH and serum electrolyte levels should all be monitored. Additional laboratory tests and diagnostic procedures should be tailored to the clinical findings, cholinergic symptoms and the extent of the poisoning [52,53] (Table 2).

The first step in treating poisoned patients, regardless of the route of exposure, is advanced cardiac life support, which includes airway management, ventilatory support and hemodynamic stabilization. Establishing an emergency

Table 2: Supportive care and monitoring measures for organophosphates (OPs) and carbamates poisoning

Category	Supportive Care Measures	Monitoring Parameters	References
Airway and Breathing	Secure airway to prevent aspiration Provide oxygen supplementation as needed Consider mechanical ventilation for severe respiratory distress	Monitor oxygen saturation (SpO2) Arterial blood gas (ABG) analysis for acidosis or hypoxemia	[56]
Cardiovascular Support	Treat hypotension with fluids and vasopressors (if needed) Avoid atropine overdose during treatment of bradycardia or hypotension	Regular blood pressure (BP) and heart rate (HR) monitoring ECG for arrhythmias	[59]
Neurological Support	Administer antidotes: atropine (to reverse muscarinic effects) and pralidoxime (to reactivate acetylcholinesterase) Manage seizures with benzodiazepines if necessary	Regular Glasgow Coma Scale (GCS) assessment Monitor for signs of atropinization (e.g., dry mouth, tachycardia)	[60]
Decontamination	Remove contaminated clothing Wash skin thoroughly with soap and water Gastric lavage or activated charcoal (if ingested within 1 hour)	Skin and ocular examination for chemical burns Stomach content monitoring for signs of ingestion	[61]
Fluid and Electrolyte Balance	Correct dehydration with intravenous fluids Monitor for electrolyte imbalances (e.g., hypokalemia or acidosis)	Serum electrolyte levels (Na+, K+, Cl-, bicarbonate) Urine output monitoring	
Renal Support	Ensure adequate hydration to prevent acute kidney injury Dialysis may be considered in severe poisoning cases	Monitor renal function (serum creatinine and BUN) Urine output and signs of oliguria or anuria	[62]
Long-term Monitoring	Provide psychological support for anxiety or post-exposure stress Monitor for long-term neurological sequelae (e.g., intermediate syndrome)	Periodic neurological examination Quality of life assessments post-recovery	[63]

airway, supporting ventilation, fluid resuscitation and administering inotropic agents may all be necessary for initial stabilization. Emergency airway management should be done with caution to avoid exposing healthcare professionals to toxic substances, which includes limiting contact with hazardous chemicals and controlling the release of harmful vapors. To prevent the release of toxins from the stomach during endotracheal intubation, it is critical to secure the airway, ensure proper ventilation and use an orogastric tube [54,55].

The comparative analysis of intervention outcomes between the two tables (Table 1 and 2) highlights the complementary roles of pharmacological antidotes and supportive care measures in managing OP and carbamate poisoning. The pharmacological antidotes table focuses on agents like Atropine, Pralidoxime (2-PAM), Diazepam, Obidoxime and Glycopyrrolate, which target specific physiological mechanisms affected by poisoning. Atropine, for instance, effectively addresses muscarinic symptoms by blocking acetylcholine receptors, while Pralidoxime and Obidoxime work to reactivate acetylcholinesterase, countering the fundamental toxic effect. Diazepam is essential for managing seizures and Glycopyrrolate serves as an alternative to Atropine by reducing muscarinic symptoms without crossing the blood-brain barrier, limiting its central nervous system effects. The efficacy of these pharmacological interventions depends heavily on the timing of administration, with early treatment offering the best outcomes in reducing toxicity and preventing complications.

In contrast, the supportive care measures table emphasizes the critical role of airway and breathing management, which is foundational for stabilizing patients in severe poisoning cases. Interventions such as ensuring adequate oxygenation, ventilatory support and continuous monitoring of vital signs address respiratory compromise, a major cause of mortality in OP and carbamate poisoning. While pharmacological antidotes directly target the toxin's physiological effects, supportive care provides essential stabilization, ensuring survival in cases where antidotes alone may not suffice, particularly in prolonged or severe poisoning.

In terms of outcomes, pharmacological antidotes like Atropine and Pralidoxime are most effective when administered promptly, as they mitigate the direct toxic effects of OP and carbamates. However, supportive care measures play a critical role in managing life-threatening complications such as respiratory failure, which cannot be addressed by antidotes alone. Together, a combination of pharmacological interventions and supportive care ensures the best clinical outcomes, as antidotes work to counteract the poisoning's cause while supportive care stabilizes vital functions and prevents secondary complications.

If peripheral nerve stimulation responds to anticholinesterase therapy, it is best to avoid neuromuscular junction blockade for assisted ventilation in cases of ventilatory failure, particularly when it occurs late in the poisoning process. Patients may require prolonged or intermittent positive-pressure ventilation, with the option of using high ventilator settings for brief periods during nerve stimulator train-of-four assessments [56]. Although normal end-tidal CO2 levels are frequently maintained until late in the course, rapid improvement is usually observed after atropine and oxime treatment. However, it is critical to monitor for signs of increased intracranial pressure and, if necessary, use controlled hyperventilation [57].

Most patients with severe poisoning should receive intensive care first, which often necessitates the assistance of a critical supportive care specialist. This includes rapidly replacing fluids and electrolytes, administering atropine with caution based on muscarinic symptoms and heart rate and treating sympathomimetic and cholinergic symptoms with

short-acting sedatives rather than anticholinergic agents [56,58]. High doses of atropine, given repeatedly ("atropine lo "ding"), may be required for cardiorespiratory stabilization. Patients should be admitted to hospital units with rapid access to advanced airway management and comprehensive monitoring, such as oximetry, electrocardiography and pulse oximetry [59].

Efficacy of Diagnostic Tools in Resource-Limited Settings

In resource-limited settings, diagnosing OP and carbamate poisoning presents significant challenges due to limited access to sophisticated equipment, trained personnel and financial constraints. Clinical diagnosis often remains the primary tool, relying on patient history, symptoms and physical examinations. While effective, this approach may lack precision, especially when patients present with atypical symptoms.

Point-of-care diagnostic tools such as acetylcholinesterase (AChE) testing offer significant promise. A study in Sri Lanka demonstrated that rapid AChE testing improved clinicians' knowledge and facilitated early intervention for OP poisoning, thereby improving patient outcomes [60]. However, the widespread availability of these tools is constrained by cost and resource limitations, which hinders their use in rural healthcare settings.

In addition, mobile health (mHealth) applications have emerged as low-cost diagnostic aids. A study in South Africa explored a mobile application designed to assist healthcare professionals in diagnosing pesticide poisoning and streamlining reporting. The app significantly improved the identification of OP poisoning cases and enhanced data collection, which is crucial in rural areas with limited medical infrastructure [61]. Such tools can be highly beneficial in resource-poor settings where traditional laboratory diagnostics are unavailable.

The reliance on clinical scoring systems as a substitute for laboratory confirmation has also been explored. For example, tools like the Poison Severity Score (PSS) and simplified prognostic systems based on vital parameters have shown utility in emergency departments with constrained resources [62]. These systems provide rapid assessments to guide treatment decisions and predict outcomes but are less accurate compared to laboratory-based biomarkers.

Despite their utility, these diagnostic methods face challenges such as inadequate funding, poor availability of reagents and a lack of trained personnel. Additionally, the absence of centralized reporting systems in many low-income regions complicates surveillance and effective diagnosis.

While point-of-care diagnostics, mobile technologies and clinical scoring systems offer viable alternatives for OP poisoning diagnosis in resource-limited settings, their efficacy depends on accessibility, cost-effectiveness and proper implementation. Addressing these challenges through innovative, low-cost tools and better healthcare training is crucial for improving diagnostic capacity in underserved regions.

Less toxic alternatives - Biological Control Methods

Biological control involves using natural predators, parasites, or microbial agents to manage pest populations, offering an environmentally sustainable alternative to chemical pesticides. Natural enemies such as parasitoid wasps, predatory beetles and microbial pesticides like *Bacillus thuringiensis* (Bt) are essential tools in reducing chemical dependency [63]. These biological agents can effectively regulate pest populations while preserving biodiversity and minimizing environmental contamination. For instance, microbial pesticides derived from fungi and bacteria have been increasingly adopted as safer pest control solutions in organic farming systems [64].

Botanical Pesticides

Botanical pesticides are plant-based alternatives that are eco-friendly and pose lower toxicity risks to humans and animals. Products such as neem oil (Azadirachta indica) are widely recognized for their insecticidal properties, effectively disrupting insect feeding and reproduction while being biodegradable [65]. Essential oils from plants like garlic and peppermint are also explored for their pesticidal activity against various crop pests. These plant-based solutions have shown minimal effects on non-target organisms and provide a viable alternative for sustainable agriculture, particularly in regions reliant on chemical pesticides [66].

Nanotechnology in Pesticide Development

Advances in nanotechnology have revolutionized pesticide formulations, leading to the development of nanopesticides that offer targeted pest control with reduced environmental contamination. Nanocarriers enhance the delivery of active ingredients, allowing lower dosages while improving effectiveness against pests [67]. Encapsulated pesticides also exhibit slower release rates, minimizing off-target impacts and increasing stability under environmental conditions. Such innovations significantly reduce human exposure and ecological toxicity, presenting a promising direction for sustainable agriculture.

Integrated Pest Management (IPM)

Integrated Pest Management (IPM) combines multiple pest control strategies to reduce reliance on chemical pesticides while maintaining effective pest suppression. IPM incorporates biological control, crop rotation, habitat manipulation and selective pesticide use to achieve long-term pest management goals [68]. For example, introducing natural predators alongside cultural practices has proven successful in reducing pesticide applications by up to 70% in certain

cropping systems. Case studies highlight how IPM enhances agricultural productivity while safeguarding human and environmental health [69].

Regional Variations in Pesticide Use, Regulatory Enforcement and Access to Healthcare Influence Poisoning Prevalence and Outcomes

Pesticide Use in Developing Regions: In many low- and middle-income countries (LMICs), such as in South Asia and Sub-Saharan Africa, pesticides are widely used due to their affordability and effectiveness. However, misuse is common because of inadequate education, lack of safety training and absence of protective gear. For example, studies in Sri Lanka revealed that unrestricted access to highly hazardous pesticides significantly contributed to acute poisoning deaths [70]. Additionally, poor awareness regarding safe pesticide handling increases both occupational and accidental poisoning risks.

Regulatory Enforcement

Variations in regulatory frameworks significantly influence pesticide poisoning outcomes. Countries with weak pesticide regulations or limited enforcement mechanisms struggle to restrict access to highly toxic substances. In contrast, countries with robust policies, such as bans on highly hazardous pesticides, have observed notable declines in poisoning cases. For instance, the phased ban on specific pesticides in Sri Lanka resulted in a significant reduction in mortality rates [71]. On the other hand, regulatory lapses in parts of Latin America and Africa have allowed continued use of banned substances, exacerbating the poisoning burden [72].

Healthcare Disparities and Outcomes

Access to healthcare profoundly affects the outcomes of pesticide poisoning. In many rural regions of Africa and South Asia, healthcare facilities lack essential resources, including ventilators, antidotes (e.g., atropine and pralidoxime) and trained personnel to manage poisoning cases effectively [73]. As a result, the case-fatality rates remain disproportionately high in these regions. In contrast, high-income countries benefit from prompt access to advanced medical interventions, leading to better survival outcomes [74].

Socioeconomic Inequalities

Pesticide poisoning disproportionately impacts marginalized populations, including smallholder farmers and agricultural workers in developing regions. Economic pressures often force these groups to rely on cheaper, more hazardous pesticides while ignoring safety precautions. Additionally, healthcare costs can be prohibitive, leading to delayed treatment and increased mortality [72].

Regional Patterns in Suicide Trends

Pesticides are often used as a means of suicide in rural regions, where their availability is high and healthcare access is limited. In India and China, self-poisoning with organophosphates and carbamates accounts for a significant proportion of suicides, particularly in agricultural communities. Effective pesticide regulation, such as restricting access to highly toxic chemicals, has been shown to reduce suicide rates in these settings [75].

Regional variations in pesticide use, regulatory enforcement and access to healthcare play critical roles in shaping the prevalence and outcomes of pesticide poisoning. Countries with weak regulations, inadequate healthcare systems and high socioeconomic disparities face a disproportionate burden. Addressing these disparities through policy interventions, improved healthcare infrastructure and education on pesticide safety is essential to reducing global poisoning rates.

Critical Evaluation of Study Limitations and Potential Biases

Sample Size and Study Design Bias: Many studies on organophosphate poisoning suffer from small sample sizes and non-randomized designs, which may limit their generalizability and statistical power. For instance, Eddleston *et al.* [8], noted that smaller sample sizes reduce the robustness of conclusions, particularly in cohort studies that analyze the efficacy of oximes like pralidoxime in OP poisoning management [6]. Additionally, heterogeneity in study design, such as variations in data collection methods, can introduce inconsistencies in findings.

Selection and Publication Bias

A common limitation is selection bias, where studies focus on patients with severe poisoning admitted to tertiary care centers, neglecting mild or unreported cases in rural areas. As noted in Kharel *et al.* [76] publication bias further skews findings since studies with significant results are more likely to be published, leading to an overestimation of treatment efficacy and underreporting of adverse outcomes [76].

Regional and Language Bias

Studies often rely on research published in English, which excludes findings from non-English-speaking regions where pesticide misuse may be more prevalent. This bias reduces the representation of data from high-burden areas like South Asia and Latin America, as highlighted by London *et al.* [77]. Regional disparities in healthcare access further exacerbate inconsistencies, making it challenging to generalize findings globally.

Lack of Longitudinal Data

Most studies focus on acute poisoning outcomes, neglecting the long-term effects of chronic exposure to

organophosphates. Neurobehavioral deficits and developmental issues caused by low-dose, prolonged exposure remain underexplored. Ross *et al.* [78] emphasize that systematic reviews often lack longitudinal data, limiting insights into the chronic health burden.

Methodological Weaknesses

Inadequate reporting of inclusion/exclusion criteria and lack of blinding in clinical trials are significant methodological concerns. For example, meta-analyses of oxime therapy by Peter *et al.* [79] highlight that concealment methods and trial randomization were poorly described, raising concerns about internal validity and bias in treatment outcomes.

Confounding Variables

Studies rarely account for confounding factors such as co-exposure to other pesticides, pre-existing health conditions and environmental influences. Munoz-Quezada *et al.* [80] argue that failing to adjust for these variables can misattribute outcomes to OP poisoning alone, leading to flawed conclusions.

Recommendations for Improving Pesticide Safety and Reducing Misuse

To improve pesticide safety and reduce misuse, several strategies can be implemented across regulatory, educational and technological domains:

Strengthening Regulatory Frameworks: Governments should enforce strict regulations on the sale, distribution and use of highly hazardous pesticides (HHPs). Phasing out the most toxic pesticides, as successfully done in countries like Sri Lanka, can significantly reduce poisoning incidents and suicides [70]. Policies must mandate safer alternatives and ensure regular monitoring of pesticide markets to prevent illegal sales.

Promoting Integrated Pest Management (IPM): Encouraging farmers to adopt IPM practices can minimize reliance on chemical pesticides. IPM integrates biological control methods, crop rotation and the use of less toxic botanical pesticides, ensuring sustainable pest management while reducing health risks [81].

Improving Farmer Education and Awareness: Training programs must educate farmers on proper pesticide handling, storage and disposal practices. Farmers should be taught to use personal protective equipment (PPE), follow label instructions and understand the dangers of improper usage [82]. Educational campaigns in rural communities can further raise awareness.

Ensuring Access to Safer Alternatives: Governments and agricultural agencies should promote the use of safer, eco-friendly alternatives such as biopesticides, microbial agents and nano-formulated pesticides. Subsidies and incentives can facilitate their adoption among farmers, particularly in low-resource settings [83].

Enhancing Healthcare Infrastructure: Strengthening rural healthcare systems to improve the management of pesticide poisoning is crucial. Healthcare facilities should be equipped with antidotes like atropine and pralidoxime, along with training programs for medical personnel to diagnose and treat poisoning cases effectively [6].

Implementing Pesticide Stewardship Programs: Establishing community-based stewardship initiatives can improve the lifecycle management of pesticides, including safe storage, responsible use and disposal [84]. These programs involve multi-stakeholder participation, including farmers, regulators and industry.

Increasing Research and Surveillance: Enhanced research on pesticide toxicity, exposure risks and safer alternatives is needed. Developing robust surveillance systems for pesticide poisoning cases can help identify trends, inform policies and target interventions in high-risk regions [85].

Improving Labeling and Packaging Standards: Pesticide products must include clear, multilingual labeling with instructions for safe use, hazard symbols and emergency response guidelines. Packaging improvements, such as childproof containers, can prevent accidental poisoning [86].

By implementing these recommendations, pesticide safety can be significantly improved, reducing misuse and minimizing the adverse health and environmental impacts of pesticide exposure.

Specific Recommendations for Policymakers and Healthcare Providers

For Policymakers: Policymakers must strengthen regulatory frameworks to phase out highly hazardous pesticides (HHPs) and promote safer alternatives. Evidence shows that restricting access to highly toxic pesticides reduces poisoning rates, as demonstrated in Sri Lanka where bans led to significant declines in pesticide-related suicides [87]. Policies should mandate regular monitoring of pesticide markets and enforce stricter guidelines for pesticide registration and labeling. Furthermore, multi-stakeholder initiatives involving industry, governments and farmers are necessary to reduce pesticide risks and encourage sustainable agricultural practices [88].

For Healthcare Providers

Healthcare providers play a vital role in managing pesticide poisoning and preventing adverse outcomes. Providers should receive regular training on the diagnosis and management of organophosphate and carbamate poisoning, ensuring proper use of antidotes like atropine and pralidoxime. Establishing

clinical protocols for early intervention and improving access to essential antidotes in rural healthcare settings are critical steps [89]. Additionally, healthcare systems must integrate public education programs on pesticide safety, targeting agricultural communities to raise awareness about proper handling, storage and disposal of pesticides.

For Joint Implementation

Both policymakers and healthcare providers must collaborate on surveillance systems to monitor pesticide poisoning trends and outcomes, which would inform evidence-based policies and resource allocation. Integrating technology, such as mobile applications for poisoning detection and reporting, can improve case identification and treatment in resource-limited settings [90].

By addressing these recommendations, policymakers and healthcare providers can reduce pesticide misuse, improve safety and enhance clinical outcomes in affected populations.

Ethical Implications of Publishing Findings That May Affect Public Perceptions of Pesticide Use

Publishing findings on pesticide use that may influence public perceptions raises significant ethical considerations. Researchers and publishers must balance transparency, public safety and the potential socioeconomic consequences of their work.

Public Right to Information: It is ethically imperative to share findings that reveal risks associated with pesticide use, such as health hazards and environmental damage. Failing to disclose such information compromises public trust and prevents communities, policymakers and farmers from making informed decisions [89].

Avoiding Misinformation or Panic: While transparency is crucial, presenting findings without context or clear explanations may create public fear, misinformation, or panic. Researchers should communicate findings responsibly, ensuring that risks and benefits are clearly articulated to avoid overgeneralization or misinterpretation [91].

Impact on Agricultural Communities: Publishing data highlighting the adverse effects of pesticides may affect farmers' livelihoods, particularly in developing regions where alternatives are unavailable or unaffordable. Ethical research dissemination should include practical solutions, such as safer alternatives (IPM or biopesticides), to minimize economic impacts while advocating for change.

Regulatory and Policy Implications: Findings that expose regulatory gaps or inadequate safety enforcement may pressure governments to improve pesticide regulations. This can be ethically positive but may create resistance from stakeholders, including industries and policymakers. Researchers must navigate these complexities, emphasizing evidence-based recommendations that prioritize public health and sustainability.

Conflicts of Interest: Ensuring neutrality and transparency in pesticide research is essential to avoid conflicts of interest. Findings influenced by corporate or political agendas can erode public trust and hinder ethical decision-making regarding pesticide use [92].

Balancing Health and Food Security: Findings on pesticide risks must acknowledge the importance of pest control for global food security. Ethical communication should highlight solutions that protect human health and the environment without compromising agricultural productivity.

By considering these ethical implications, researchers can ensure their work contributes to public health, environmental sustainability and informed policymaking while mitigating unintended consequences.

CONCLUSION

This review emphasizes the continued importance of OP and carbamate pesticides, which are still widely used in developing countries and are occasionally misused in developed countries. The high mortality rates and numerous cases highlight the toxic effects on humans and animals. Although clinical presentations vary, the presence of nicotinic signs without muscarinic signs is a strong indicator of severe poisoning. Patients, particularly children, with large amounts of powdery substances on their hair, face, or clothing should be treated with caution because this could indicate phosphoric acid ester or carbamate pesticide poisoning. Thyroid storm, myasthenia gravis and botulism can cause similar symptoms but are less common. The simple McMaster Protocol can help diagnose and monitor the severity of these conditions. Clinical diagnosis of OP/carbamate poisoning is based on exposure history, sudden onset of cholinergic symptoms and respiratory failure following atropine and/or oxime administration. Important laboratory tests include blood pressure, pulse, oximetry, cholinesterase activity and a metabolic panel. Respiratory function must be monitored in all moderate to severe cases, with both non-invasive and invasive monitoring used to determine the need for intubation and mechanical ventilation.

Immediate decontamination therapy, followed by multiple doses of atropine and oxime, is critical for saving lives. The burden on healthcare systems is expected to remain significant, necessitating public health campaigns to educate communities and families about pesticide use properly and safely. Products containing boric acid or white phosphorus can result in significant morbidity and mortality in large groups, such as families or factory workers. To summarize, OP and carbamate poisoning are medical emergencies that are expected to continue in the foreseeable future. Recognizing

the theft and misuse of these hazardous substances is critical. Public health education remains a critical component of efforts to combat OP pesticide poisoning.

Actionable Steps for Implementing Safer Pest Control Alternatives

Promote Integrated Pest Management (IPM): Implement farmer education programs that focus on Integrated Pest Management (IPM) strategies. IPM combines biological control methods, crop rotation and habitat manipulation to reduce pest populations naturally. Case studies in countries like India and China demonstrate that IPM can reduce chemical pesticide use by up to 70% while maintaining crop yields.

Adopt and Subsidize Safer Alternatives: Governments should incentivize the adoption of botanical pesticides, such as neem oil and biopesticides, including microbial agents like *Bacillus thuringiensis* (Bt). Subsidies, technical support and pilot projects will encourage farmers to transition to these eco-friendly alternatives.

Invest in Research and Development: Increase funding for the development and testing of nanotechnology-based pesticides and other advanced formulations that reduce toxicity and improve target specificity. Collaboration between governments, research institutes and agricultural stakeholders can accelerate innovation in safer pest control options.

Regulate and Phase Out Highly Hazardous Pesticides (HHPs): Policymakers must enforce the gradual phase-out of highly hazardous pesticides and restrict their availability in agricultural markets. Establishing pesticide registries and monitoring systems can ensure compliance with safety regulations.

Educate Farmers and Communities: Conduct regular awareness campaigns to educate farmers on the benefits and usage of safer alternatives. Programs should include training on proper pesticide application techniques, protective measures and the economic advantages of IPM and biopesticides.

Enhance Supply Chains for Safer Products: Strengthen agricultural supply chains to ensure that safer alternatives are affordable, accessible and available in rural markets. Partnerships with agricultural cooperatives and local distributors can facilitate distribution.

Monitor Environmental Impact: Implement surveillance programs to monitor the environmental and health outcomes of pest control practices. Real-time feedback will help assess the efficacy of safer alternatives and inform necessary adjustments.

Support Certification Programs: Promote certification for organic farming and sustainable agriculture practices that prioritize safer pest control methods. Certified farmers can gain access to premium markets, creating economic incentives for adoption.

By systematically implementing these actionable steps, the transition to safer, sustainable pest control alternatives can be accelerated, reducing health risks and environmental contamination while supporting global food security.

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