Journal of Positive Psychology & Wellbeing
2022, Vol. 6, No. 3, 688-694

http://journalppw.com
ISSN 2587-0130

An Overview Organophosphate Poisoning, Role Of Anesthesia, Pharmacist, Clinical Laboratory And Paramedics In The Management Approach

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Abstract

Organophosphates are compounds that are frequently employed as pesticides. They function to block acetylcholinesterase, which results in an accumulation of acetylcholine at muscarinic and nicotinic receptors located all throughout the body. Although poisonings are typically thought of as low-volume, chronic cases that are caused by agricultural exposures, they can also manifest as attempts at suicide that are caused by the consumption of organophosphates. When organophosphate poisoning occurs, especially when substantial quantities are consumed, it is imperative that treatment be initiated as quickly and effectively as possible. Literature review give an example that demonstrates how to effectively manage severe organophosphate toxicity symptoms. In the management approach, the roles of anesthesia, chemist, clinical laboratory, and paramedics are extremely important. They work together as a collaborative team beginning with prehospital care and continuing through emergency department admissions and intensive care unit admissions.

Keywords: *Organophosphates, receptors, prehospital care.*

Introduction

OPs, or organophosphates, are a type of chemical that is frequently found in insecticides. They are preferred because of the broad spectrum effect they have against a wide variety of agricultural pests, in addition to the inexpensive cost they have. However, due to the

fact that these chemicals are hazardous to both humans and animals and can cause teratogenic effects, their use has been prohibited and has fallen out of favor over the course of the previous twenty years. Systemic absorption of OPs can take place through inhalation, as well as through absorption through mucous membranes, cutaneous, conjunctival, and gastrointestinal exposure. Due to this particular cause, they have also been utilized as chemical weapons [1]. On the other hand, the majority of exposures that take place in the United States today are related to occupational exposure and take place over an extended period of time among farm workers and their children [2]. There has been some achievement in reducing the use of organophosphates as pesticides all over the world; yet, accidental exposures and ingestions by suicide continue to occur [1].

Acetylcholinesterase inhibitors, often known as OPs, are substances that bind to acetylcholinesterase and help prevent the breakdown of acetylcholine. Synaptic junctions within the autonomic nervous system, the central nervous system, and neuromuscular connections are the locations where they perform their functions. These sites get saturated with acetylcholine as a result of this accumulation, which leads to muscarinic and nicotinic receptors becoming saturated [2]. Due to the fact that the link between the organophosphate chemical and acetylcholinesterase has the potential to become irreversible over time, it is of the utmost importance to administer the antidote, which is 2-pralidoxime (2-PAM) [2]. Activation of the muscarinic receptors leads to cholinergic effects including excessive secretions, diaphoresis, diarrhea, urination, and bronchoconstriction. Activation of the nicotinic receptors can be lethal, particularly stimulation of the nicotinic receptors within the cerebellum which can lead to respiratory depression [1]. It is also possible for acute exposures to result in chronic neuropsychiatric problems, such as motor impairment, psychosis, depression, memory, and cognitive flexibility [1,3].

The treatment that is currently available for organophosphate poisoning is a two-pronged approach that consists of supportive care in addition to atropine and 2-PAM. 2-PAM is necessary for survival because it reactivates the acetylcholinesterase that was previously attached to organophosphate. Additionally, it enables fresh absorption of acetylcholine at the neuromuscular junction, which in turn reverses the effects of the pesticide that were potentially fatal [4]. In addition to boosting the ability to penetrate the blood-brain barrier by increasing lipophilicity and modifying the polarity of N-oxime formulations, efforts are currently being made to determine the most effective formulation of the medicine and the route of administration. In spite of this, it has been demonstrated that 2-PAM is capable of liberating the bulk of the organophosphate-bound acetylcholinesterase and restoring the enzyme's effectiveness [5].

Review:

Organophosphates are a broad collection of chemical compounds that are commonly used in herbicides and pesticides, as well as nerve agents in chemical warfare. Organophosphates are also used in the production of nerve agents. As a consequence of the introduction of organophosphates into the body, the enzyme acetylcholinesterase is inhibited, which leads to an excessive amount of the neurotransmitter acetylcholine. The presence of an excessive amount of acetylcholine in the body is characterized by the presence of cholinergic toxidrome, which includes effects on nicotinic and muscarinic receptors, in addition to the central nervous system. In situations of organophosphate toxicity, the most common cause of death is respiratory failure, which can be caused by bronchospasm and bronchorrhea. In addition, there is a substantial body of evidence demonstrating chronic toxicity and neurological consequences, such as the intermediate syndrome. Despite the fact that wealthy countries have seen a decrease in the number of poisoning cases as a result of more stringent controls on the use of these chemicals, poor countries continue to face a clinical problem, particularly when these compounds are used for the purpose of self-harm. In order to effectively treat organophosphate toxicity and

reduce the risk of morbidity and mortality, it is vital to provide patients with antidotal therapy and complete supportive care from medical specialists [6].

The start, intensity, and duration of toxicity are all determined by the amount of the pesticide that is consumed, the route of absorption, and the toxicokinetics of the particular pesticide. In accordance with the classification system established by the World Health Organization (WHO), these compounds are divided into five distinct classes, ranging from "Extremely dangerous" to "Active components unlikely to create acute hazard in regular usage." This categorization is determined from the data that is based on the median lethal dosage (LD50), which represents the oral fatal dose that the rat receives for fifty percent of the individuals that are exposed to the active ingredient. On the other hand, the LD50 classification has some limitations when it comes to distinguishing more dangerous substances that belong to the same class [7].

The annual reports of the Toxic Exposure Surveillance System (TESS), which is maintained by the American Association of Poison Control Centers, revealed that the number of incidents involving organophosphate exposure reached its peak in 1997 with 20,135 cases, and then declined in the years that followed. This was revealed by a study that was carried out between the years 1995 and 2004. 2079 incidents of organophosphate exposure were registered in the annual report of the National Poison Data System for the year 2020. However, there were no fatalities reported in any of these cases. The decision made by the United States Environmental Protection Agency to eliminate the use of organophosphate pesticides in residential settings is principally responsible for the significant drop in organophosphate exposure that has been seen. This endeavor started in the year 2000 and continued until the year 2005. On the other hand, it is important to point out that the data collected from the surveillance conducted by poison control centers could not be an accurate representation of the entire number of exposures that have occurred in the United States. The reason for this is that these data are either self-reported or derived from reports provided by medical providers, both of which have the potential to underestimate the specific substance involved and lack proof of its presence [8].

It is difficult to correctly determine the entire worldwide exposure rate of organophosphate and the toxicity that is associated with it anywhere in the world. It was estimated that 371,594 people around the world committed suicide by poisoning themselves with pesticides in the year 2007, which accounted for approximately one-third of all suicides that took place in the world. Approximately 20,000 people lost their lives as a result of unintended poisonings caused by pesticides in 1990, according to estimates provided by the World Health Organization (WHO). A study conducted in 2020 estimated that there were 740,000 unintended poisonings caused by pesticides, which led to 7446 deaths across 141 nations. It is highly probable that the true extent of exposure and toxicity is more than what has been reported due to insufficient reporting and a lack of statistical data [9].

When dealing with cases of possible toxicity, it is essential to take into consideration the particular component that is involved as well as the period of exposure. This is especially critical in situations when the patient intentionally ingested the substance. If it is at all possible, an effort should be made to secure the pesticide bottle in order to submit this information to the Poison Control Center or a medical toxicologist. This is something that should be done because the level of toxicity that can be caused by different chemicals can vary significantly. Depending on the method of exposure, the degree or dosage of exposure, and the particular organophosphate substance that is involved, the timing of the start of symptoms and the severity of the toxicity are all determined. Additionally, the toxicokinetics of the compound, which includes its lipophilicity, have a role in determining the duration of the component's hazardous effects. As the molecule is released from its storage in fat, it is possible that cholinergic effects will occur repeatedly in certain instances [10].

In order to properly diagnose organophosphate poisoning, it is necessary to begin therapy prior to test confirmation. This is because the diagnosis is dependent on clinical examination. The presence of a high clinical suspicion for organophosphate poisoning is extremely important, particularly in situations when there is no known history of exposure or ingestion. The most common manifestation of toxicity is a patient who exhibits symptoms such as diaphoresis, miotic pupils, and respiratory distress. The unique odor of garlic or petroleum that is emitted by certain organophosphates can be helpful in the diagnostic process [11]. The administration of atropine may be attempted in the event that organophosphate poisoning is on the differential diagnosis list but has not been established. In the event that symptoms improve after the injection of 0.6 to 1 mg of atropine, this raises the possibility of AChE inhibitor toxicity and should be considered significant. The absence of research, on the other hand, makes it difficult to assess the sensitivity and specificity of this trial, which is especially difficult to do in cases of severe poisoning. Consequently, additional research is required in order to address this phenomenon. When patients have had considerable poisoning, it is possible that they will not show any response to a little dosage of atropine, which can lead to a false-negative test [11].

Although there are certain laboratories that are able to directly detect cholinesterase activity, these tests are frequently contracted out to other facilities that might not give you with results in a timely manner to guide your treatment. The two cholinesterase enzymes that are most frequently measured are called red blood cell AChE (RBC AChE) and buChE. RBC AChE activity is more particular than BuChE activity, which is less specific. In addition, persons who suffer from congenital enzyme failure, hepatic disease, chronic sickness, malnutrition, and iron deficiency anemia may also exhibit low levels of BuChE activity. The level of enzyme inhibition varies depending on the particular organophosphate that is implicated in the poisoning. Furthermore, there are insufficient data available for many chemicals, which further complicates the interpretation of this test. Among the clinical manifestations of organophosphate toxicity, it is hypothesized that RBC AChE activity has a better association with the clinical picture. When more than fifty percent of this enzyme is blocked, symptoms often manifest themselves in clinical settings; however, the threshold for this inhibition can change depending on the molecule in question [12]. There are a variety of crucial laboratory tests that medical professionals may order for their patients. These tests may include particular diagnostic testing for organophosphate poisoning, in addition to other tests that are used to evaluate the patient's overall health. An example of one of these would include a complete blood cell count (CBC), a basic metabolic panel test, tests to evaluate the health of the liver and kidneys, tests to measure glucose levels, an arterial blood gas study, and pregnancy testing. The electrocardiogram (ECG) will often show sinus bradycardia because of the activation of the parasympathetic nervous system. Each and every healthcare professional is required to put on personal protective equipment before evaluating and treating a patient who has organophosphate poisoning. This is done to reduce the likelihood of the provider becoming self-contaminated. The maintenance of a low contamination rate among healthcare personnel is facilitated by the observance of universal precautionary procedures. After the personnel in the healthcare industry have been given the assurance that they are safe through the implementation of suitable protective measures, the first step is to decontaminate the patients. Once this step is complete, the next step is to thoroughly cleanse the patient's skin with soap and water three times. It is the primary objective of this method to clean in a short amount of time without the requirement of certain decontamination fluids. This is because organophosphates can be present in bodily secretions such as vomit and diarrhea, thus it is important to exercise caution while dealing with these fluids. Each and every article of clothes that the patients are wearing ought to be removed and discarded. If washing is unsuccessful, long hair should be trimmed since it has the potential to trap highly lipophilic chemicals. It is imperative that the patient be decontaminated; however, this should not be

done at the expense of delaying timely medical attention for a patient who is experiencing acute distress [13].

The management of the airway is of the utmost significance for treating patients who have been exposed to organophosphate poisoning. Intubation may be necessary for certain patients where bronchospasm, seizures, or bronchorrhea are the underlying conditions. Succinylcholine, on the other hand, should be avoided during intubation since it cannot be digested and causes chronic paralysis. This is an important point to keep in mind. Patients should also be provided with access to intravenous fluids, monitoring of their heart rates, and pulse measurement. Atropine, which competes with acetylcholine at the muscarinic receptors, is the primary treatment, and it is used to treat organophosphate poisoning. When administering atropine intravenously (IV), the initial dose is typically between 2 and 5 milligrams for adults and 0.05 milligrams per kilogram for children. The goal is to obtain the adult dose first. The healthcare team should double the dose every three to five minutes until the respiratory secretions have cleared and there is no bronchoconstriction. This should be done in the event that the patient does not respond to the treatment. At this time, the patient has reached the condition of "atropinization," which is defined by the presence of anticholinergic signs and symptoms in the patient. These signs and symptoms include dry skin and mucosa, decreased bowel noises, tachycardia, the absence of bronchospasm, reduced secretions, and mydriasis [14].

The primary purpose of administering atropine to individuals who are experiencing organophosphate poisoning is to enhance the cardiorespiratory parameters during the course of treatment. Assessing the patient's heart rate, blood pressure, and respiratory condition is more important than determining the size of the pupil or the moisture level of the skin. It may be necessary to administer hundreds of milligrams of atropine to patients who have suffered severe poisoning. This can be done in the form of bolus doses or continuous infusions, and it may take anywhere from a few days to several weeks before the patient indicates signs of improvement. Patients need to be continuously watched for the potential development of neuromuscular junction dysfunction and respiratory failure because atropine does not attenuate the effects of nicotinic acid. The monitoring of parameters such as tidal volume and negative inspiratory force can be of assistance in determining whether or not ventilatory support is required [15].

Through its interaction with the organophosphate, the antidote pralidoxime (2-PAM) is able to reactivate the phosphorylated alternative cholinesterase (AChE). On the other hand, in order for the antidote to be effective, it must be delivered prior to the beginning of the aging process, and the time frame that is required for this is unique to each individual molecule. In addition to being able to be utilized in conjunction with atropine, this drug does not have the ability to depress the respiratory center. On the other hand, the evidence concerning the utilization of oximes as a course of treatment for organophosphate poisoning is inconclusive and open to debate. A number of studies have demonstrated that the incorporation of 2-PAM into atropine did not result in an increase in mortality and might even pose some dangers. When it comes to treating individuals who have been poisoned by organophosphorus compounds, it is recommended that an oxime be administered to each and every one of them until a more comprehensive understanding is achieved and other treatments are developed [16].

Atropine must be given to patients prior to the administration of 2-PAM in order to prevent the symptoms of muscarinic-mediated conditions from becoming more severe. Adults should take a bolus of at least 30 mg/kg, while children should take between 20 and 50 mg/kg. This should be administered over a period of thirty minutes. Due to the fact that the quick delivery of 2-PAM can result in cardiac arrest, it is critically important to exercise caution when delivering the medication to patients. Immediately following the administration of the bolus, it is recommended to commence a continuous infusion of the medicine at a rate of at least 8 mg/kg/h for adults and 10 to 20

mg/kg/h for children. This infusion may be necessary for a number of days [17].

The administration of benzodiazepines is recommended for patients who are suffering seizures. The use of benzodiazepines is not generally recommended until seizures are taking place, despite the fact that there is a single study that suggests the possible benefits of diazepam in avoiding neuropathy. It is possible that extracorporeal elimination is advantageous in the case of particular organophosphate chemicals that have a restricted volume of distribution. Examples of such compounds include dimethoate and dichlorvos. On the other hand, there is a lack of information concerning the efficacy of hemodialysis and hemoperfusion in treating all instances of poisoning from this perspective. Patients should be admitted to the hospital and intensively monitored for a minimum of forty-eight hours inside an intensive care unit (ICU) environment. This is because there is a possibility that the symptoms will return and that they will experience respiratory distress. Patients may be eligible for discharge if they have not experienced any symptoms for a period of twelve hours [18].

Conclusion:

Organophosphorus (OP) chemicals are utilized extensively in a variety of fields, including agriculture, the control of domestic pests, and chemical warfare. Self-inflicted poisoning by pesticides is responsible for one-sixth to one-eighth of all suicides that occur around the world and one-third of all suicide fatalities that occur in rural Asia each year. Cholinesterase enzymes are inhibited by OP pesticides, which increases the amount of cholinergic receptors that are stimulated. Clinical characteristics are determined by the sorts of receptors that are triggered at different locations throughout the body. The history of poisoning, the smell of pesticides, the distinctive clinical indications, and decreased cholinesterase activity are all factors that are considered when making a diagnosis of OP poisoning. The measurement of plasma cholinesterase is helpful for the diagnosis of OP poisoning; nevertheless, it is possible that the measurement does not directly correlate with the severity of the poisoning. In the treatment of opiate poisoning, atropine continues to be the primarystay, and there is convincing evidence that it is beneficial provided it is delivered correctly. When taking atropine, it is important to keep a systolic blood pressure that is greater than 80 mmHg, a pulse that is greater than 80 beats per minute, and a chest that is clear when auscultated. Oximes have the ability to restart cholinesterase enzymes, which enables them to prevent even the nicotinic effects that are caused by OP poisoning. Nevertheless, there is poor evidence to support its efficacy following self-inflicted poisoning. Even though a number of more recent adjuvant medicines are being tested in an effort to produce a better outcome, the prospective benefits of these therapies have not yet been evaluated. Organophosphates have the potential to create severe disorders that pose a significant risk to individual life, including a first acute cholinergic crisis and intermediate syndrome. Each of these disorders carries with it the possibility of respiratory failure, which necessitates the use of ventilatory assistance. It is for this reason that it is of the utmost importance to recognize them at an early stage, particularly in order to implement suitable management. To a large extent, the diagnosis of organophosphate poisoning is determined by a clinical evaluation, which is then followed by laboratory testing. On the other hand, if the neurological disorders that are associated with organophosphate poisoning are well understood, it is simple to differentiate them from other illnesses that are similar to them. It is also extremely important to note that the function that anesthesia, chemists, clinical laboratories, and paramedics play in the management approach is very vital when it comes to the management of patients who have had OP poisoning.

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