ACUTE ORGANOPHOSPHORATE POISONING: CLINICAL, DIAGNOSTIC AND THERAPEUTIC APPROACH

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Abstract. Organophosphate poisoning is considered pesticides that have the ability to inhibit the enzyme Acetylcholinesterase to produce an overstimulation of muscarinic and nicotinic receptors present in the CNS, exocrine glands, hollow organs, among others. A narrative review was carried out based on keywords of poisoning, organophosphate, poison and acetylcholine in between 2015 and 2020. Organophosphate poisoning mainly presents in cholinergic syndrome product of overstimulation of the muscarinic receptors. Subacutely, it can present as intermediate syndrome and subsequent consists polyneuropathy induced by organophosphates. The clinical findings pesticide exposure will provide the diagnosis. In the driving initial symptomatic should use atropine, which will act in a competitive with ACh for muscarinic and nicotinic receptors, but the reversal of the action of the organophosphate on AChE is only carried out with the oximes, pradiloxime is the first choice. The reviewed provides updated information about key aspects in organophosphate poisoning as well as a approach in the clinical presentation.
Keywords: *Organophosphates, poisoning, therapeutic, diagnostic*

Short Communication

Organophosphates are pesticides that have represented a weapon of great value in the agricultural industry throughout history, helping to combat pests and weeds that are harmful to crops, however, these compounds have chemical characteristics that can cause great harm to the exposed population. either voluntarily or accidentally. It is known that chronic exposure to these pesticides can considerably increase the risk of suffering from cancer, in addition to negative effects on the human immune system, reproductive system and nervous system, thus being an important cause of morbidity and mortality worldwide (Pérez et al., 2021; Saborío Cervantes et al., 2019).

It is estimated that around 3 million people are poisoned by these pesticides each year in the world, of which 2 million cases are accidental and 1 million with suicidal objectives, reaching this end in around 300 thousand of the cases[2]. In Colombia for the year 2020, the total number of poisonings by chemical substances was 17,270 of which 3,297 were specifically due to this type of pesticide, the most frequent origin of the poisoning being the accidental form presented at the time when farmers irrigated the

compound on their clothes, skin, mucous membranes or they even inhale it, followed by intentional use where consumption is almost always generated orally and other forms such as criminal (Anchatipán-Escobar et al., 2020).

The way in which the organophosphates generate their affection on the body is based on a powerful and irreversible inhibition of the enzyme acetylcholinesterase (AChE) this is achieved by carrying out the phosphorylation of a hydroxyl group present in the active site of the enzyme, achieving that it is kept in a non-functional state. Normally, the function of the AChE enzyme is to separate acetylcholine into two products as they are; the choline that will be reused by the neuron to again synthesize acetylcholine[4] and acetic acid which will be used in the Krebs cycle. This enzyme acts specifically on cholinergic receptors such as nicotinic receptors found in the CNS, exocrine glands and hollow organs, other receptors such as muscarinic receptors, which are present in both the postgannglionic junctions of the sympathetic and parasympathetic nervous systems and the neuromuscular junction. In addition, they are also found in the membrane of red blood cells (Alahakoon et al., 2020; Alozi and Rawas-Qalaji, 2020; Gutiérrez-Jara et al., 2020).

Upon obtaining an inhibition of said enzyme, a consequent accumulation of acetylcholine is generated in the synaptic space, leading to an over stimulation of the previously described receptors, which generates all clinical picture called cholinergic síndrome (Gutiérrez-Jara et al., 2020). Well said, the manifestations of this intoxication will vary in severity and time of appearance depending on the way in which contact with the toxic agent was had, it is also important to take into account the amount of the harmful agent, the age of the patient, if presents or does not present comorbidities since this can further exacerbate the clinical presentation. However, 3 main routes by which exposure can be generated are described;

Airway; which is almost always generated accidentally, in farmers and whose symptoms can present a rapid appearance that varies only from seconds to minutes;

Oral route; represented in most cases in people with suicidal purposes, although also accidentally in the pediatric population, the clinical appearance usually occurs between 30 to 90 min after ingestion, although the clinical appearance can also take up to 3 hours;

Cutaneous route; The form of exposure is accidental, the clinical appearance can take from 12 to 18 hours. However, given that there are some of these agents with lipophilic characteristics, the incubation period can be increased, taking symptoms from 5 to 30 days to appear, aided by the distribution in the adipose tissue of the individual (Alozi and Rawas-Qalaji, 2020; Gutiérrez-Jara et al., 2020; Manohar and Kannawar, 2020).

Clinically, the cholinergic syndrome product of an acute organophosphate poisoning will present itself through a sequence of signs and symptoms starting with the so-called cholinergic crisis, whose appearance lasts from minutes to hours where the patient will manifest the consequences of hyperstimulation of cholinergic receptors, initially muscarinics presenting symptoms such as defecation, urination, miosis, bronchorrhea, bronchospasm, bradycardia, lacrimation, hypersalivation. The presence of symptoms resulting from nicotinic stimulation can manifest itself when there is severe intoxication, presenting symptoms such as tachycardia, hypertension, paleness, myalgia, cramps, twitching at the level of the eyelid and facial muscles, and even hyperglycemia.

Since these receptors are also found in the CNS, symptoms such as drowsiness, confusion, headache, anxiety, depression of the respiratory system and seizures can occur (Gutiérrez-Jara et al., 2020; Manohar and Kannawar, 2020).

In a later period, around 24 to 96 hours of evolution, the intermediate syndrome may appear in up to 20% of cases, which is characterized by presenting a neurological deficit, decreased tendon reflexes, fatigue of the intercostal muscles and of the diaphragm, making this stage the one that represents the highest degree of mortality and that a percentage of patients require ventilatory support for several days, however, the appropriate treatment and support manages to end the condition in around 2 to 3 weeks (Gutiérrez-Jara et al., 2020; Manohar and Kannawar, 2020; Mbah Ntepe et al., 2020). In addition to these presentations, there is organophosphate-induced polyneuropathy, which usually occurs on average from the first to third week after exposure to the poison and is characterized by manifesting very painful paresthesias in a glove and sock pattern, followed by symmetrical weakness. in the lower limbs that can ascend to the upper limbs, where the distal muscles are the most affected by neurotoxicity (Manohar and Kannawar, 2020; Mbah Ntepe et al., 2020).

A prospective observational study conducted at the Acharya Vinoba Bhave Rural Hospital Department of Medicine, India. Between the years of 2014 and 2015 I conclude based on their results that the leukocyte count had a sensitivity of 60%, a specificity of 76% and a negative predictive value of 85% if the counts were more than 12,000 and a sensitivity of 30%, a specificity of 95% and a negative predictive value of 80% if the counts were more than 15,000 in predicting mortality in patients with organophosphate poisoning (Nizami et al., 2020).

The management of organophosphate poisoning must be viewed from several points and carried out in a hasty but effective way to achieve greater expectations of improvement in the patient, initially the approach must be carried out with the ABC protocol, first evaluating the state of the airway since in many cases an early intubation is necessary given the patient's ventilatory compromise, in these cases it is advisable to use a non-depolarizing muscle relaxant during the rapid intubation sequence since succinylcholine is metabolized through AChE and these due to its state non-functional can prolong a muscle block in the patient. During initial handling, it is also vitally important to strip the patient of their clothing in case the exposure has been due to contamination in clothing and to wash the exposed skin with plenty of wáter (Leonel Javeres et al., 2021; Omar et al., 2021; Amir et al., 2020).

Once the patient is stabilized, the application of specific pharmacological management is necessary. In this case, two antidotes are known, which are oximes and atropine, the effectiveness and use of which has been evidenced since 1950. In the initial management, the use of activated charcoal is also possible. at a dose of 1 gr/kg as long as the picture appears maximum one hour after oral exposure, after this time it has been shown that there are no benefits.

Atropine shows great effectiveness against the symptoms produced by muscarinic stimulation since its mechanism is given by a competitive inhibition of these receptors both in the CNS and in the SNP. An initial dose of 2 to 5 mg iv is recommended in adults and 0.05 mg/Kg iv in children, these doses can be repeated every 3-5 min until the symptoms subside (Leonel Javeres et al., 2021; Mbah Ntepe et al., 2020). On the other hand, oximes such as palidoxine have the ability to disinhibit AChE affected by organophosphates. The recommended dose in these patients is 30 mg/kg in adults as an initial dose which should be administered slowly over 30 min and then an infusion of 8

mg/kg/h for 24 hours. In children, the initial dose is 25-50 mg/kg iv with a subsequent infusion of 10 mg/kg/h for 24 hours (Gutiérrez-Jara et al., 2020; Manohar and Kannawar, 2020).

There is another therapeutic arsenal that we can use in the management of this intoxication, such as benzodiazepines, for example diazepam, which has been shown to be beneficial for the management of seizures, fasciculations and agitation during episodes, with a dose of 10mg in adults. which can be repeated every 10 to 15 min maximum 3 times, in children it is recommended to administer 0.3mg/kg in 3 min with a maximum dose of 5 mg in children <5 years and 10mg in children> 5 years (Gutiérrez-Jara et al., 2020; Manohar and Kannawar, 2020; Mbah Ntepeet al., 2020).

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Conflict of interest

The author confirm there are no conflict of interest with any parties involved in this research.

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