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Editorial

Treatment of Organophosphorus Exposure and Precautions in Using Succinylcholine

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Organophosphate is a toxic and lethal chemical compound. Organophosphate toxins are available in the form of repellents for plant pests and chemical warfare gases. Organophosphorus (OP) pesticide poisoning is intoxication due to organophosphates contamination, inhalation or swallow. This is a significant clinical problem in developing countries. Its Medical management is difficult, with more than 15% mortality [1-2].

OP poisoning is due to inhibition of acetylcholinesterase (AchE) at synapses and membranes of red blood cells and butyrylcholinesterase in plasma. OP shows its affection by phosphorylating serine hydroxyl residues on AChE, which inactivates AChE. Although acute inhibition of butyrylcholinesterase does not appear to have significant clinical features, inhibition of AChE leads to acetylcholine (Ach) accumulation and causes major clinical manifestations [2-3].

ACh is an essential neurotransmitter for neuromuscular function, and irreversible inhibition of cholinesterases causes the accumulation of acetylcholine and over-stimulation of nicotine and muscarinic receptors. Excessive stimulation of nicotine receptors in neuromuscular junction causes muscle weakness, muscle cramps, fasciculation, and finally paralysis; In addition, there is accumulation of ACH in the autonomic ganglia which causes overstimulation of nicotinic expression in the sympathetic system [3-4]. Excessive stimulation of nicotinic acetylcholine receptors in the central nervous system leads to shortness of breath, anxiety, tremors, headache and convulsion [2-4].

Accumulation of ACH in muscarinic receptors leads to visual disturbances, wheezing due to bronchoconstriction and bronchial secretions, increased salivation, lacrimation, sweating, peristalsis and urination [2-4].

The core treatments of OP poisoning are atropine, oximes, agitation treatment by benzodiazepines,

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ventilation support and tight monitoring for conditional therapy (hyperthermia and cardiac arrhythmia) [3-4]. Small studies suggest benefit from new treatments such as magnesium sulphate. Use of morphine, theophylline, aminophylline, reserpine, and phenothiazine-type tranquilizers should be avoided in patients with organophosphate poisoning. Consensus believes, early scientific approach is needed to improve outcome of Organophosphorus poisoning [2-4, 6]

Gastric lavage and detoxification are considered if the patient has been exposed to a toxic dose of OP and has been hospitalized in the early hours. For gastric lavage, after aspiration of gastric contents, cold normal saline in amounts of 250-300 ml is given through the nasogastric tube. Larger volumes of fluid may push the toxin into the small intestine. At the end of the lavage, some activated charcoal can be placed in the stomach [2-4].

Atropine competitively blocks the acetylcholine effects on muscarinic cholinergic receptors on smooth muscle and heart, secretory glands and peripheral autonomic ganglia, and central nervous system but, nicotine receptors remain defenseless against excess acetylcholine [3-4,6].

Oxymes (pralidoxime, obidoxime) are wide spectrum with different potencies and are known as phosphorylated AChE reactivator by binding to the OP molecule [5,7]. Abidoxime is stronger than pralidoxime (2-PAM). The potency of oxymes varies with temperature and pH [5-6].

Enzyme reactivation has been shown to be effective when pralidoxime is administered within 1 hour of exposure and continue for 24 hours but, it is effects vary according to the chemical structures of OP [5-7]. The guidelines recommend that the loading dose be 30 mg/kg of pralidoxime for 10 to 20 minutes (no more than 2000 mg), followed by continuous infusion of 8 to 10 mg/kg/h until clinical recovery (12 to 24 hours after atropine is no longer needed or the patient's endotracheal tube is removed) or 7 days, whichever is longer [2, 4-5].

However, treating OP poisoning can be difficult with conventional therapies, especially which could band to AChE and make aging phenomenon. The rate and magnitude of aging of the enzyme is also different with various OP compounds. When aging of the enzyme-OP complex occurs, reactivation of the enzyme is not possible [5-7].

Intermediate syndrome is defined as a state of muscle weakness and paralysis which occurs 1-4 days after cholinergic symptoms of organophosphate poisoning. Ventilator requirement and incidence of prolong intermediate syndrome was seen higher in the patients that treated by Pralidoxime with lag time. There are reports that late and long-term administration of pralidoxime has adverse effects on respiratory force in intubated patients. In high dose poisoning with potent agents, even recommended dose of Pralidoxime may not be effective in reactivating the enzyme [2,6-7].

There is controversy over the administration of pralidoxime in severe poisoning, and some research has questioned the effectiveness of the drug because it did not make any suitable changes on the aging phenomenon and outcomes [5-6, 8]. Some patients will suffer from long term disability no matter how well managed [3,6-9].

OP binding to the AchE is irreversible and recovery will occur when the enzyme is made and replaced. This recovery will be a relative improvement and will occur with increasing enzyme levels. In severe cases, the healing process may take more than 3 weeks, during which time the patient will need respiratory support [2-4].

One of the drugs that are used as a fast-acting muscle relaxant is succinylcholine (Suxamethonium chloride), which is used to facilitate tracheal intubation. Suxamethonium chloride (Sux) is a depolarizing muscle relaxant consisting of two molecules ACh. Similar to ACH, sux binds to cholinergic receptors of the motor endplate of postsynaptic neuromuscular junction to induce membrane depolarization. End plate depolarization initially stimulates muscle contraction; but, sux is not degraded by AchE and remains at the neuromuscular junction to cause continuous end plate depolarization and resulting muscle relaxation. This block is called phase I. Sux has a longer and stronger effect than ACH and in the presence of cholinesterase inhibitors such as OPs, this effect can be exacerbated. This exacerbated effect lead to two collateral consequences, sever hyperkalemia and strange behavior in muscle relaxation (phase II) [7, 9-10].

The muscle relaxant properties of sux will vary at the nerve-muscle junction that has been exposed to higher doses of sux for a long time, and as a result it is possible to enter the phase II of muscle relaxation. Continuous stimulation of the terminal plate of the neuromuscular junction by Sux leads to phase II blocks. Prolonged paralysis has been reported in patients receiving sux who are exposed to toxins with anticholinesterase activity [9-11].

In a normally functioning muscle, acetylcholine receptors (NAChRs) are located only at the junction area. Patients with severe OP poisoning who need respiratory support remain in the intensive care unit (ICU) for a long time, so neuromuscular junctions have changed as AChRs are distributed throughout the muscle membrane, with the additional expression of two new AChR isoforms. The new AChRs do not have normal physiological function. Depolarization of these AChRs, which are distributed throughout the muscle membrane, results in the release of potassium from the muscle. These patients experience longer and stronger stimulation by sux due to AchE inhibition. The combination of these two subjects predisposes patients to severe and fatal hyperkalemia [9-12].

In summary, organophosphorus poisoning causes acetylcholine to accumulate and over-stimulate muscarinic and nicotine receptors. Atropine competitively inhibits the symptoms associated with muscarinic receptors but has no specific antidote to nicotine receptors [2-4]. In these cases, attempts are made to use oxymers (pralidoxime) to reduce the concentration of free organophosphors in the body, help excrete them, and inhibit the strong binding of organophosphate toxins to acetylcholinesterase (AchE). The effects of pralidoxime on organophosphate poisoning are controversial [5-8].

However, people exposed to organophosphate toxins are affected by enzyme inhibition, which can persist for a long time even after the initial symptoms have improved. These patients are at potentially fatal risk if exposed to depolarizing muscle relaxants and should be avoided [9-11].

It makes sense to avoid succinylcholine for at least 4 weeks after discharge from the hospital if mechanical ventilation is not required and; for 3 months if endotracheal intubation is performed besides 3 days or more of artificial ventilation.

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