

Advances in toxicology and medical treatment of chemical warfare nerve agents

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Organophosphorous (OP) Nerve agents (NAs) are known as the deadliest chemical warfare agents. They are divided into two classes of G and V agents. Most of them are liquid at room temperature. NAs chemical structures and mechanisms of actions are similar to OP pesticides, but their toxicities are higher than these compounds. The main mechanism of action is irreversible inhibition of Acetyl Choline Esterase (AChE) resulting in accumulation of toxic levels of acetylcholine (ACh) at the synaptic junctions and thus induces muscarinic and nicotinic receptors stimulation. However, other mechanisms have recently been described. Central nervous system (CNS) depression particularly on respiratory and vasomotor centers may induce respiratory failure and cardiac arrest. Intermediate syndrome after NAs exposure is less common than OP pesticides poisoning. There are four approaches to detect exposure to NAs in biological samples: (I) AChE activity measurement, (II) Determination of hydrolysis products in plasma and urine, (III) Fluoride reactivation of phosphorylated binding sites and (IV) Mass spectrometric determination of cholinesterase adducts. The clinical manifestations are similar to OP pesticides poisoning, but with more severity and fatalities. The management should be started as soon as possible. The victims should immediately be removed from the field and treatment is commenced with auto-injector antidotes (atropine and oximes) such as MARK I kit. A 0.5% hypochlorite solution as well as novel products like M291 Resin kit, G117H and Phosphotriesterase isolated from soil bacteria, are now available for decontamination of NAs. Atropine and oximes are the well-known antidotes that should be infused as clinically indicated. However, some new adjuvant and additional treatment such as magnesium sulfate, sodium bicarbonate, gacyclidine, benactyzine, tezampanel, hemoperfusion, antioxidants and bioscavengers have recently been used for OP NAs poisoning.

Keywords

Nerve agents, Chemical warfare agent, Organophosphorous compounds, Pesticides, Sodium bicarbonate, Magnesium sulfate, Iran