EFFECTS OF ATROPINE SULFATE AFTER POISONING WITH ORGANOPHOSPHORUS COMPOUNDS

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Abstract: Organophosphorus compounds are most toxic synthesized substances. This group consists of the substances used in the composition of chemical weapons. Less toxic substances in this group are used as insecticides. These compounds are inhibitors of the enzyme esterase-holing. First aid and treatment of poisoning with these substances is achieved by atropine sulfate.

Keywords: organophosphorus compounds, insecticides, toxic effects, atropine sulfate, first aid

1. Introduction

Development of organophosphorus compounds begins in the nineteenth century. They penetrate organism through the respiratory system, skin and digestive tract. They act directly on the central nervous system, depending on the dose can in a short period of time, lead to death. At higher doses, there is a so-called momentary effect, death occurs immediately. For this substance is also typical to have a cumulative effect.

The organophosphorus compounds are among the most toxic compounds synthesized and their part in chemical weapons and insecticides is significant.

2. Toxic Substances

The most important representatives of the toxic chemicals from the composition of chemical weapons, here in after referred to PCS, as sarin, soman and tabun. The mechanism of action of the substance is the same. Chemically speaking, all PCS paralytic nerve activity are organophosphorus

compounds. There are over a thousand different organophosphorus compounds, in addition to soman, sarin and tabun.

Between themselves PCS this type there is a difference in the level of toxicity that can be manifold.

Tab. (1) Inhalation toxicity of paralytic OHS neural activity in the form of vapor or aerosol to people of average weight

OHS	Lethal contretation LC ₅₀ (mg in min/m ³)	Start of effect (min)
VX- poison	4 – 5	4-10
Soman	45 – 70	1-15
Sarin	70 -100	2-15
Tabun	300 – 400	10-15

PCS nerve paralytic effects are irreversible inhibitors of cholinesterase in the human body. Inhibition of this enzyme leads to the accumulation, endogenous acetylcholine", so that each new quantity of the release of acetylcholine cause a longer and more intense effects on organs. Excess acetylcholine in the body initially stimulates and then paralyzes impulse transmission at all synapses where acetylcholine appears as a mediator, in:

- The central nervous system,
 - Neuromuscular coupling,
 - Sensory nerve endings,
 - Ganglionic synapses
- holinergic and adrenergic (sympathetic and parasympathetic) nerves,
- Post ganglionic drenergic nerve terminals that innervate glands and blood vessels,

- Adrenergic nerve terminals (without ganglionic synapses) in the adrenal gland and

- Post ganglionic cholinergic nerve terminals.

When it comes to toxicodynamics, there are three main activities of the effect of acetylcholine.

- The biochemical structures innervated cholinergic nerves, leading to stimulation of bronchial smooth muscle, organs, abdomen, heart muscle, sweat and mucus glands and others., These effects are also called acetylcholine muscarinic and, due to the analogy with the effect of alkaloid muscarine,

- The biochemical structure of ganglion cells and nerve endings in the cross-striped muscle. This action is called nicotian, because of the similarity with the effects of nicotine,

- The biochemical structure of the central nervous system that has muscarinic and nicotian receptors.

These substances do not cause any inflammatory changes in the points of entrance in the body and they don't cause irritation of nerve endings sensible nerves.

Volatile substances are non polarised, with high liposolubility, which is very well absorbed from the mucous membranes, even through intact skin. At these features is their use as agents. Repeated exposure of the organism to low doses repeatedly in a relatively short period of time can cause poisoning and even death.

Disorders that cause these substances are grouped into the following categories:

- Acetylcholine-cholinesterase system,

- Nervous system,
- Respiratory system,
- Cardiovascular system
- Digestive system and
- Certain organs.

On the nerve endings there are specific microscopic entities on which delivery is made through nervous impulses from one neuron to another or from the nerve to the effector organ. These structures are called synapses. Submissions of impulses in the synapses are made by the mediator. In the peripheral nervous system mediator is acetyl-choline. In the central nervous system, there are multiple mediators, and plays an important role of acetylcholine. That is, the transmission of nerve impulses in a healthy organism is produced by a compound acetylcholine. Created acetyl-choline, influenced enzyme cholinesterase breaks down and it stops the muscle contractions that seemed. PCS paralytic nerve activity is associated with the enzyme cholinesterase, resulting in the accumulation of acetylcholine. The increased amount of acetyl-choline in the body cause disorders that impair the normal functioning of all organs, especially of the respiratory and circulatory system. In normal conditions, the effect of acetylcholine is a millionth of a second, and the active center of cholinesterase in these conditions can be hydrolyzed 300,000 molecules of acetylcholine.

More serious forms of poisoning have the following layout and flow: secretion from the nose, chest tightness, constriction of pupil (miosis) and visual impairment-eclipse, difficulty in breathing, fascial muscle spasms, excessive sweating, nausea, vomiting, uncontrolled release of urine and diarrhea, muscle twitching, staggering, severe headache, confusion, drowsiness, convulsions and death by paralysis. These symptoms develop rapidly and death can occur in about 10 minutes.

Code for mild poisoning or exposure at lower concentrations, show the following symptoms of poisoning:

pupil constriction and impaired vision, chest tightness and shortness of breath, anxiety, eye pain and headaches. In further developing the symptoms of poisoning are severe, but in a milder form. In the use of antidotes atropine sulfate syringe these symptoms are starting to lose after several hours.

When PCS neural effects of paralytic effects on the nervous system it can be concluded that:

- Central nervous system stimulant react at first, and later inhibition,

- In the pathological process all parts of the central nervous system are involved and

- The rate of participation of certain parts of the nervous system in the pathological process of distortion and intensity of its functions is not equal, that is the most sensitive cortex.

PCS paralytic nerve activity and cause of disruption in the work of the organs and glands that have smooth muscle fibers (eye, intestines, bronchi, gland).

It also causes disturbances in motor nerves and muscles, a consequence of convulsive contraction of muscle spasms muscle fibers muscle weakness, etc..

The immediate cause of death in the PCS effects of neural activity is a paralytic disorder breathing function.

Breathing disorder occurs in the early stages of poisoning, and under the influence of small amounts of these substances these disorders arise from effects of action on the central nervous system, the peripheral nervous system and the effector organs.

The disorder breathing function involved several factors:

- Bronchospasm (a consequence of the effects on the structure holino reactive bronchial bronchospasm may be one of the reasons for the occurrence of death, bronchospasm

and is the main reason for the heavy breathing and the occurrence of man feeling of tightness in the chest),

- Respiratory center (changes can be quantitative and qualitative changes in the flow in two phases that in the first short-term toxicity observed irritation of respiratory center, which was later reduced long-term depression, but if you are organized enough to resuscitate a long (2 to 3 hours) may be established functions of breathing),

- Respiratory muscles (poisoning causes characteristic changes in the muscle's breathing muscles as well; appear jerky muscle contractions, tremors muscle fibers, partial or complete muscle weakness).

PCS paralytic nervous activities also act on the cardiovascular system. In this system, there are changes of vascular tone and the functional state of the heart muscle.

These substances slow the heart rate and reduce the force of contraction of the muscle as a result of the action of acetylcholine muscarinic receptors in the heart. With this disorder leads to the disruption in the electrical conductivity of the nervous system of the heart.

PCS nerve paralytic causes heavy salivation, increased secretion of glands and increased contractions of the stomach and intestines, which among other things has resulted in listless bowel movements.

A sign in the action of these substances is miosis (constriction) pupils. It is stable and depending on the concentration of the poison that has acted may last for days.

Toxic chemical type VX for its toxic effects belonging to the group of toxic chemicals neuro-paralytic action, or a group of toxins that irreversibly inhibit cholinesterase. In its chemical structure are organophosphorus esters.

VX most toxic poisons are toxic chemicals. From other listed

toxic nerve agents are up to a hundred times. Work quickly through respiratory, skin and digestive tract.

Act as poisons and neuro-paralytic or block cholinesterase and cause general poisoning organism. Symptoms of poisoning toxic chemicals VX types are: muscle tremors, difficulty breathing, excessive salivation, convulsions, muscle paralysis and death. First aid are used as antidotes for nerve agents such.

3. Organophosphorus insecticides

Insecticidal effects of organophosphorus compounds have been known since 1935. During the synthesis of these insecticides it was found that in addition to insecticidal properties are very toxic to warm-blooded animals, especially humans. After detection of these insecticides, it was found that the basic mechanism of the toxic action of the enzyme acetylcholinesterase inhibition.

All insecticides of this group share a common structure and are considered esters of phosphoric acid or phosphoric. Thus phosphorylated inactivated enzyme is very stable and there is no hydrolysis and recovery of enzyme activity depends on the synthesis of new enzyme compounds. The mechanism of toxic effects are a group of general functional toxin.

Figure 1. Degradation of acetylcholine by ache

After penetration in to the organism into the bloodstream and maturity, uniformly transmitted to all

organs and tissues. The effect of these compounds is based on the irreversible inhibition of the enzyme acetylcholinesterase (AChE).

The clinical picture of poisoning by organophosphorus pesticides is displayed through three effects:

- Muscarinic effect, which is manifested by chest pain, coughing, shortness of breath, pulmonary edema, diarrhea, pupils, narrowed, blurred vision, slow heart operations and a drop in blood pressure,
- The effect of nicotine, which is manifested muscle twitches, fine muscle tremors, muscle weakness, muscle cramps and all
- The effect of the central nervous system that is manifested by dizziness, pressure in the head, restlessness, drowsiness, headache, uncertainty in gait and coma.
- Great importance in the development of organophosphorus insecticides had fluorophosphates ester synthesis (soman and sarin) 1930. Year 1935. showed strong physiological effects of organophosphorus compounds, and originated the rapid development of insecticides.
- A certain number of organophosphorus compounds have systematically insecticide-effect, or when adsorbed by plants, included in the vascular system of the plant and insect remains in the body.
- Organophosphorus insecticides are usually liquid. Have high vapor pressure and act via the respiratory tract. Good to dissolve in fats and penetrate through the skin. Some

organophosphorus insecticides are not toxic, but only after it became transformation in the liver (cholinesterase inhibitor parathion has not been transformed into paraoxon, which is an inhibitor).

The most important types of organophosphorus insecticides are:

- Tionophosphorous acid esters-tionophosphate representatives are parathion, fenthion and others.,
- Esters of phosphoric acid (phosphate), representatives are mevinfos, fosfamidin, monocrotophos and others.,
- Ditiofosforne acid esters (dithiophosphate), representatives are disulfon and tiometon,

- Pirofosforne acid esters (pyrophosphate), Representative: sulfotep,
- Esters of phosphorus acid (phosphonates), Representative trihlorfon.

USE OF atropine sulfate poisoning organophosphorus compounds

Atropine Sulfate is a tool without which it is impossible to imagine a first-aid and treatment of people poisoned by organophosphorus compounds. Clinical experience has shown that the organism is poisoned with organophosphorus compounds, tolerated doses of atropine" enormous, and in the first hour after administration and in the later stages of treatment.

Tab. (2) Average dose of atropine required for effective treatment of different stages of acute poisoning

Stage of poisoning	Oral atropisation in first hour (mg)	Atropisation maintainance In next three days since poisoning (daily dose in mg)
Easy	2-3	4-5
Medium - Heavy	20-25	30-50
Heavy	30-50	100-150

Atropine sulfate in large doses effectively antagonises the muscarine-like manifestations of poisoning in the periphery and partly in the central nervous system. Relatively ineffective against the actions of the mediators in the autonomic ganglia and has no effect on muscle weakness. Pharmacologically speaking, atropine sulfate acts by blocking muscarinic receptors, making them, in effect" insensitive to acetylcholine.

Therapeutic effects of the substance can be explained in two ways:

First Reactivation of inhibited cholinesterase allows the enzyme to exhibit the physiological function of acetylcholine degradation accumulated,

Second Creating complex reactivators-venom in most cases makes the poison harmless and allows the organism to various metabolic processes release toxins.

It is theoretically possible that every person, regardless of clinical form of poisoning be saved by appropriate treatment. However there are the following problems that can occur:

- Presence of the treatments in the immediate vicinity and in sufficient quantity,

- Vocational training to provide therapy

- Evaluation of dose in relation to the image of poisoning and others.

No matter whether you are a first aid or treatment is necessary:

- Break contact between the toxin and the man,

- Immediately inject 2mg atropine sulfate intramuscularly with autoinjectors or Syringe,

- Repeated injection of atropine sulfate every 3 to 10 minutes until the occurrence of signs atropisation,

- If there are conditions, atropine sulfate may be injected and intravenously.

On the first day of treatment, especially in severe poisoning, it is necessary to use up to 50 mg of atropine sulfate. Easy to maintain a degree of atropisation giving oral atropine sulfate (1 to 2 mg) in appropriate intervals, and as long as there is any symptom of poisoning.

When there are signs of marked disturbance of pulmonary ventilation and the patient shows signs of cyanosis, artificial respiration should be given to the disappearance of these symptoms, and then access the injection of atropine sulfate. Injection of atropine sulfate during cyanosis is contraindicated, as administration of atropine sulfate in a state of anoxia can cause fibrillation cardiac chambers.

To remove a local disturbance in the eyes-miosis, it is necessary to instill atropine 1% solution.

Conclusion

Organophosphorus compounds are highly toxic substances and only some natural toxins, such as botulinum toxin, is more toxic of these toxins.

Synthesized over a thousand different organophosphorus compounds, in addition to soman, sarin and tabun, and there are several extremely toxic.

These substances are most toxic substances from the family of synthetic poisons. They act very quickly, and in high concentrations rapidly.

These compounds are inhibitors or blocking or decreasing the activity of cholinesterase in the human body. Except as may be used in the composition of chemical weapons, many of the family of compounds that are less toxic and are used as insecticides. These compounds have a cumulative effect. First aid and medical treatment can be carried through atropine sulfate.

5. References

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