NEW HYPOTHESIS FOR POSSIBILITIES OF PREVENTION AND TREATMENT OF ORGANOPHOSPHATES (TABUN, SARIN, SOMAN) INTOXICATION

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ABSTRACT

Organophosphate compounds are some of the most toxic compounds known at present. Some organophosphate compounds have been used in chemical weapons (for example tabun, sarin, soman) and pesticides (for example malathion, chlorpyriphos). There are some antidotes but the problem of prevention and treatment of such chemical compounds intoxication is yet to be solved. The aim of this article is to justify some new hypothesis for prevention and treatment of intoxication caused by those compounds.

Key words: *organophosphates, pesticides, chemical warfare agent, terrorism, acetylcholine esterase, resveratrol, silybin, vitamin E*

INTRODUCTION

Organophosphate compounds are characterized by their strong toxicity, much stronger than most other chemical compounds known to present (2). Some of these compounds have been used as chemical warfare nerve agents during wars and acts of terrorism (1). For example such compounds are tabun, sarin, soman. The usage of weapons of mass destruction has become a real imminence after the war between Iran and Iraq in the 1980s and the acts of terrorism against civil persons in Tokio subway in 1994 and 1995. They are not only easy to produce but cheap as well. They can cause many deaths and injuries. Nobody can guarantee that they will not be used in the future. Some of these compounds have been used like pesticides, for example malathion, chlorpyriphos, methylcholrpirofos. They cause millions of casualties per year (6) - they are responsible for around 200 000 human deaths per year (5). Organophosphate compounds are the most commonly used suicide poisons in the developing countries. Therefore the World Health Organization emphasizes the need for introducing new methods of improving the results of the classic detoxification therapy. For these reasons, the problems of poisoning organofosfatni compounds are discussed in the course of medical training in many disciplines.

Hypothesis

The acetyl group of acetylcholine connects with the hydroxyl group of amino acid serine in the active side of the enzyme acetylcholine esterase. It releases free choline. In the second step of the reaction the acetyl remainder of the hydroxyl group of serine is also released and the enzyme can attack new molecule acetylcholine (fig. 1) (8).

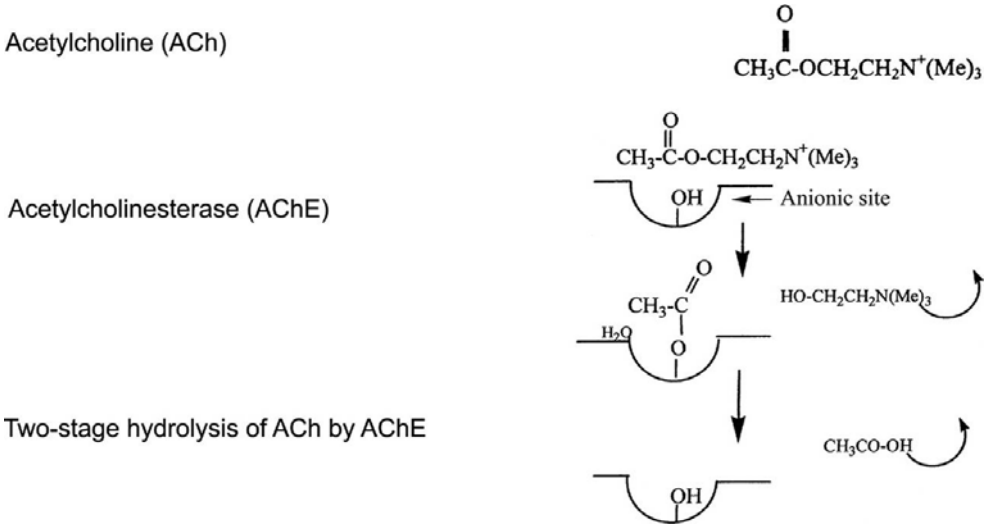

Fig 1 Mechanism of action of acetylcholine esterase

The enzyme is unusually effective. Organophosphate compounds connect with the hydroxyl group of serine in the active side of the enzyme and thus blocks it. As a result the victims are intoxicated because the mediator acetylcholine accumulats in the neuromuscular synapse, which causes continuous stimulation of acetylcholine receptors. Therefore, they are also called anticholinesterase agents. So medical professionals should be aware and learn more about the toxicology and proper management of organophosphorus poisoning.

Organophosphates can form adducts with this or other enzymes like human and animal (for example horse) serum butyrylcholinesterase or albumin. According to some data butyrylcholinesterase (4, 7), which contains amino acid serine and albumin (3), which contains amino acid tyrosine can play a role in the prevention and treatment of organophosphates intoxication. They form adducts with organophosphates and in this way they decrease the rate of inhibited acetylcholine esterase. These compounds are called scavengers. For example an injection of purified horse butyrylcholinesterase decreases the toxicity of organophosphate compounds. What these cases have in common is the presence of amino acids like serine, and tyrosine. These amino acids contain a hydroxyl group which can react with organophosphates. The scavengers connect organophosphates in ratio 1:1. But one disadvantage of butyrylcholinesterase and albumin is the fact that they are high molecular compounds but bound only one molecule of poison which is a low molecular compound.

The author supposes that peptides with lower molecular mass which contain amino acids with hydroxyl group- serine, tyrosine or threonine or even amino acids with hydroxyl group and another compounds with hydroxyl groups (for example resveratrol, silybin, vitamin E, mannitol) can be used for prevention and treatment of organophosphates intoxication.

Conclusion:

This method of prevention and treatment of organophosphate compounds poisoning can be very useful and can save many human lives.

REFERENCE

1. Balali-Mood M, Balali-Mood K. Neurotoxic disorders of organophosphorus compounds and their management. Arch Iran Med. 2008 Jan;11(1):65-89. Review

2. Carpentier P, Foquin A, Lallement G, Dorandeu F. Flunarizine: a possible adjuvant medication against soman poisoning? Drug Chem Toxicol. 2004 Aug;27(3):213-31

3. Li B, Nachon F, Froment MT, Verdier L, Debouzy JC, Brasme B, Gillon E, Schopfer LM, Lockridge O, Masson P. Binding and hydrolysis of soman by human serum albumin. Chem Res Toxicol. 2008 Feb;21(2):421-31. Epub 2007 Dec 29

4. Saxena A, Sun W, Dabisch PA, Hulet SW, Hastings NB, Jakubowski EM, Mioduszewski RJ, Doctor BP. Efficacy of human serum butyrylcholinesterase ageinst serin vapor. Chem Biol Interact. 2008 Sep 25;175(1-3):267-72. Epub 2008 May 23

5. Sogorb MA, Vilanova E, Carrera V. Future applications of phosphotriesterases in the prophylaxis and treatment of organophosporus insecticide and nerve agent poisonings. Toxicol Lett. 2004 Jun 15;151(1):219-33

6. Sogorb-Sánchez MA, Vilanova-Gisbert E, Carrera-González V. Perspectives in the treatments of poisonings by organophosphorus insecticides and warfare nerve agents. Rev Neurol. 2004 Oct 16-31;39(8):739-47

7. Sun W, Doctor BP, Lenz DE, Saxena A. Long-term effects of human butyrylcholinesterase pretreatment followed by acute soman challenge in cynomolgus monkeys. Chem Biol Interact. 2008 Sep 25;175(1-3):428-30. Epub 2008 May 3

8. Weinbroum A. Pathophysiological and clinical aspects of combat anticholinesterase poisoning. British Medical Bulletin 2004; **72**: 119–133