ABSTRACT:

Tabun belongs to the group of highly toxic organophosphorus compounds, which may be used as chemical warfare agents for military as well as terrorists purposes. Tabun differs from other highly toxic organophosphates by the fact that commonly used antidotes are not able adequately to prevent tabun-induced acute toxic effect.

At first, we studied neuroprotective effects of newly developed oximes (K074, K075) and currently available oximes (obidoxime, HI-6) in combination with atropine in rats poisoned with tabun at a subletal dose (80 % LD_{50}). Neurotoxicity was monitored using a functional observational battery and automatic measurement for motor activity at 24 hours and 7 days following organophosphorus challenge. The neuroprotective efficacy of obidoxime in combination with atropine is similar to the potency of newly developed oxime K075, however, the ability of the oxime HI-6 to counteract tabun-induced acute neurotoxicity si significantly lower.

In the second test, we compared neuroprotective effects of four bispyridinium oximes - the newly developed oximes K075 (the best according to the previous test), and commonly used oximes (trimedoxime, HI-6, obidoxime) in combination with atropine. The animals were poisoned with tabun at subletal dose (80 % LD_{50}) too. We used the same methodology - the functional observational battery which consists of 47 measurements of sensory, motor and autonomic nervous functions. Trimedoxime combined with atropine was the most effective antidote in tabun-induced neurotoxicity in the case of sublethal poisoning. Due to its neuroprotective effects, trimedoxime may be considered to be more suitable oxime for the antidotal treatment of acute tabun exposure if compared with currently used oximes (obidoxime, HI-6) and the newly synthesized oxime, K075.

In the latest test, we studied soman which is one of the most resistant organophosphorus compound, because of the rapid aging of soman-inhibited acetylcholinesterase (creation of non-reactivable enzyme). We compared the neuroprotective effects of new oximes (K074, K075) and currently available oximes (obidoxime, HI-6) in combination with atropine. The soman-induced neurotoxicity was monitored using the functional observational battery, too. The results indicate that the oxime HI-6 is still the best acetylcholinesterase reactivator for the antidotal treatment of acute poisoning with soman. Both newly developed oximes (K074, K075) are not suitable oximes for the antidotal treatment of soman intoxications.