IS02

Oximes to treat organophosphate nerve agent victims

Dr Bruno Mégarbane
Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris Cité Université

Aim and objectives: Organophosphorus (OP) nerve agent exposure may result from multiple scenarios as illustrated by the Sarin attack in Tokyo's metro in 20/03/1985, the civil war in Syria, and the successful (such as Kim Jong-nam in 13/02/2017 using VX) or attempted murder of individuals (Sergueï Skripal and his daughter in 04/03/2018). We aim to describe the exact place of oximes in the management of OP nerve agent poisoning.

Methodology: Narrative review of the literature.

Results: Oximes are acetylcholinesterase (AchE) enzyme reactivators effective to accelerate the removal of the phosphoryl group from the inhibited AChE enzyme, before ageing onset (covalent link with the OP compound). Although their exact contribution to improve organophosphate pesticide poisonings is still questioned, their immediate use in chemical warfare exposure is highly recommended before the onset of AChE enzyme ageing, which onset is relatively rapid after exposure with the majority of the OP compounds. Several oximes have been produced since the fifties including pralidoxime, obidoxime, and HI-6. Several in vitro and in vivo experimental works, mainly conducted by the German Army Institute of Pharmacology and Toxicology in Munich, have shown the effectiveness of all oximes to reactivate AchE enzymes and limit toxicity of nerve agents. However, published findings suggest that oximes are afflicted with numerous disadvantages (variable reactivating potency, limited agent spectrum, poor blood-brain barrier penetration, and reduced stability). When considering the theoretical conditions of oxime usefulness defined as follows (half-life of AchE enzyme reactivation of 5 min and blood concentration below the maximal tolerance of 50-100 µM), obidoxime appears to be the most effective oxime with the broadest spectrum available at present. Pralidoxime usefulness at the current recommended dosages seems questionable in most nerve agent compound except with sarin. HI-6 use might be suggested to close some persistent therapeutic gaps.

Conclusions: Oxime administration is recommended in the management of OP nerve agent poisoning, including in case of mass attack. However, additional data are still requested to improve recommendations.