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Recent developments in toxicity and treatment of organophosphates and carbamates

Currently, there are more than 250 synthetic organophosphate (OP) and two dozen carbamate (CM) compounds that are commonly used in agriculture and human and animal health protection; in addition, those compounds are also involved in malicious and suicidal intents. As a result of their extreme toxicity, lack of species selectivity and worldwide use, OPs and CMs continue to pose serious threats to animal and human health. In the current world situation, the biggest threat is from the use of OP nerve agents. Depending upon the dose and duration of exposure, OPs can cause acute or chronic toxicity. More than a dozen OP pesticides also produce an intermediate syndrome, which is a separate clinical entity from acute and chronic toxicity. OPs primarily affect the nervous system and skeletal muscles and cause hypercholinergic preponderance due to acetylcholinesterase (AChE) inactivation at the synapses and neuromuscular junction. Some OPs and CMs directly interact with cholinergic receptors. In addition to cholinergic elements, they interact with many other critical molecules, including receptors (NMDA, cannabinoids and others) and enzymatic and non-enzymatic proteins. OPs have complex chemical structures (>13 types) and with varying affinities, they interact with the above molecules and each OP produces a different toxicological profile. OPs and CMs exert oxidative/nitrosative stress, which is involved in neurotoxicity, neuroinflammation, dendritic damage and other toxic effects. Biomarkers of exposure (OPs, CMs and/or their metabolites), effects (at molecular, cellular, morphological, inflammation and behavioral levels), and susceptibility (cytochrome P-450, PON-1) to OPs have been proposed but many of them have yet to be validated. Because of the complex mechanisms involved in the toxicity of OPs, treatment with atropine sulfate and 2-PAM is not always successful. Therefore, in recent years, novel oximes have been developed that seem to be quite effective against certain types of OPs, such as nerve agents. To date, treatment of CM poisoning rests with atropine sulfate. Current efforts in the area of OP/CM research are to explore the novel toxicological mechanisms, identify the most sensitive and quantifiable biomarkers and develop a universal antidote.

Biography

Ramesh C Gupta has obtained his DVM, MVSc and PhD from India and currently serves as Professor and Head of Toxicology Department. For decades, he has conducted experimental brain research in relation to pesticide toxicity. He has made presentations in Australia, Italy, Japan, Germany, France, Switzerland, Spain, Czech Republic, Sweden, South Korea and China. He has served the panels of NIH, CDC, NIOSH and NAS and has published >350 publications, including 7 books: *Toxicology of Organophosphate & Carbamate Compounds*, *Veterinary Toxicology*, *Handbook of Toxicology of Chemical Warfare Agents*, *Anticholinesterase Pesticides*, *Reproductive & Developmental Toxicology*, *Biomarkers in Toxicology and Nutraceuticals*. In 2006, he has received the Murray State University's Distinguished Researcher Award. He is a Diplomate of American Board of Toxicology and Fellow of American College of Toxicology, American College of Nutrition and Academy of Toxicological Sciences.

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