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Alzheimer's medication shows promise in treating nerve agent and pesticide poisoning

Drug could be used by soldiers, emergency medical personnel, farm workers and others

A medication used to treat mild to moderate Alzheimer's disease can be used to protect people against the toxic effects of nerve agents and certain insecticides, according to a study led by researchers from the University of Maryland School of Medicine. The findings, published this week in the online edition of the Proceedings of the National Academy of Sciences, provide the basis for further development of a safe and effective treatment to protect people exposed to organophosphorus compounds, including nerve agents that have been used in chemical warfare and terrorist attacks, as well as pesticides used in households and on farms worldwide.

"Nerve agents, such as soman and sarin, are among the most lethal chemical weapons ever developed. They have been used with catastrophic results in wars and terrorist attacks, such as the subway attacks with sarin in Japan in the late 1990s," says Edson X. Albuquerque, M.D., Ph.D., professor and chair of the Department of

Pharmacology & Experimental Therapeutics at the University of Maryland School of Medicine and principal investigator on the study. "The possibility of further terrorist attacks with nerve agents and the escalating use of organophosphorus insecticides underscore the urgent need to develop effective and safe antidotes against poisoning with these compounds."

The study found that galantamine, a drug originally extracted from snowdrop flowers currently approved to treat Alzheimer's disease, could be used as an antidotal therapy to counteract the lethal effects of even the most deadly organophosphorus compounds.

"The only medication currently approved by the Food and Drug Administration to prevent the catastrophic effects of nerve agent poisoning does not protect the brain," says Dr. Albuquerque. "This medication, pyridostigmine, doesn't effectively cross the blood-brain barrier."

Most animals treated with pyridostigmine and exposed to toxic doses of nerve agents survive when they receive a combination of other medications, including atropine, oximes and benzodiazepines. However, even with this drug cocktail, animals surviving the initial nerve agent exposure can develop neurological effects.

Dr. Albuquerque and his colleagues studied the effects of galantamine in an animal model to counteract the neurological devastation caused by nerve agents and organophosphorus pesticides. "We wanted to test a drug with neuroprotective properties that is widely available and safe and could be as effective taken before as it would be taken after an exposure," says Dr. Albuquerque. "Galantamine fit that description."

In the study, those animals treated with galantamine and later exposed to lethal doses of soman or sarin survived and showed no signs of the most common symptoms of exposure to nerve agents, such as convulsions, respiratory distress and loss of coordinated movement. Comparatively, those animals treated with the standard therapy of atropine and benzodiazepines died after exposure. "To our amazement, the animals treated with galantamine behaved as if they had not been exposed to these lethal agents," says Dr. Albuquerque. The researchers repeated the experiments with paraoxon, the active metabolite of the insecticide parathion, and again, all of the animals survived with no signs of toxicity.

Because it is difficult to predict when a person might be exposed to toxic levels of nerve agents on the battlefield or in a terrorist attack, or to toxic levels of insecticides during farm and garden work, the researchers also studied whether treatment with galantamine following exposure could counteract their toxicity effectively.

"All the animals treated with the antidotal therapy consisting of galantamine and atropine within five minutes after an exposure to lethal doses of soman and paraoxon survived with no side effects," says Dr. Albuquerque.

He says these findings have a clear relevance for military personnel under the threat of exposure to the deadly nerve agents and, as importantly, for the general population. "The basic finding of our study is that galantamine effectively penetrates the blood-brain barrier and protects the brain from the toxic effects of organophosphorus compounds, as long as it is administered before or soon after an exposure," says Dr. Albuquerque. "This simple and safe antidotal therapy could be added to the arsenal of

medications carried by all military members and first responders, who could easily administer it to themselves should they suspect that they've been exposed to a nerve agent. Likewise, this therapy could be used worldwide to save the lives of people who come in contact with toxic levels of organophosphorus insecticides."

"These important findings of Dr. Albuquerque and his colleagues will pave the way for further improvements in the current medical countermeasures against intoxication by organophosphorus nerve agents and insecticides," says David H. Moore, D.V.M., Ph.D., Director of Strategic Research Program Development at the U.S. Army Medical Research Institute of Chemical Defense. "By supporting this effort, it is clear that the Department of Defense is committed to quality biomedical research that seeks to improve the health and welfare of U.S. military personnel."

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