No evidence that WHO-recommended treatment for insecticide poisoning improves survival

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A study published this week in the open access journal *PLoS Medicine* finds no evidence to suggest that a controversial antidote recommended by the World Health Organisation (WHO) to treat patients poisoned with highly toxic insecticides improves their chance of survival. The results may even add weight to existing concerns about pralidoxime, the treatment recommended by the WHO, by suggesting that it could be harmful in patients who have deliberately poisoned themselves with insecticides.

Poisoning with organophosphorous pesticides - toxic chemicals commonly used in agriculture in developing countries is a global public health problem causing an estimated 200,000 deaths a year. Deliberate self-poisoning with pesticides is a common method of suicide in some countries- in Sri Lanka, more than 50% of fatal suicide attempts are a result of pesticide poisoning.

Michael Eddleston, from the University of Edinburgh, and colleagues conducted a clinical trial to study the effects of WHO-recommended pralidoxime treatment in patients who had been admitted to two hospitals in Sri Lanka for insecticide self-poisoning. If ingested by humans the pesticides disrupt the communication between the brain and body, inhibiting the activity of a neurotransmitter called acetylcholine, which plays a crucial role in the central nervous system and the control of breathing. To treat organophosphate poisoning, the WHO

recommends that in addition to atropine, an antidote that is known to reverse some but not all of the effects of the poisoning, a regimen of pralidoxime should be used to reactivate acetylcholine activity. As the authors of this study mention, few randomized clinical trials have been conducted into its use, meaning that there is a lack of evidence for its effectiveness, in particular relating to dosage.

The researchers enrolled 235 patients at two Sri Lankan hospitals who had self-poisoned with organophosphate insecticides, determining how much, and which, pesticide each patient had been exposed to, and randomly allocating them to receive either the WHO-recommended regimen of pralidoxime or a salt water placebo. However, the trial was stopped early and did not reach its intended study size owing to discussions surrounding the results of another trial of pralidoxime therapy, carried out in India at the same time which led to a fall-off in recruitment of patients. In the Sri Lankan trial, published in PLoS Medicine, more patients in the pralidoxime arm died than in the placebo arm, despite the fact that pralidoxime was shown to aid acetylcholine activity. Whilst the difference in mortality between arms was not statistically significant, it is suggestive of a higher mortality rate resulting from pralidoxime treatment.

Acknowledging the difficult situation that clinicians now face when deciding whether or not to administer pralidoxime to patients poisoned with organophosphorous pesticides, the authors conclude that there is no consistent clinical evidence for the use of pralidoxime in patients who have self-poisoned with organophosphorous pesticides. They argue that further trials are needed to explore the risks and benefits of oximes and dosing regimens.

More information: Eddleston M, Eyer P, Worek F, Juszczak E, Alder N, et al. (2009) Pralidoxime in Acute Organophosphorus Insecticide Poisoning—A Randomised Controlled Trial. PLoS Med 6(6): e1000104.

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