Management of insecticide poisoning

Hyung-Keun ROH
Division of Clinical Pharmacology, Department of Internal Medicine, Gachon University Hospital, Korea

Organophosphate poisoning is the most frequent among acute poisoning with insecticides and can be managed by anti-muscarinic agents and acetylcholinesterase reactivators. A number of researches on organophosphate poisoning have suggested some treatment guidelines through animal studies and acute human poisoning cases. These guidelines generally have rational to treat the acute organophosphate poisoning properly, but we often encounter perplexing and difficult cases to treat in clinical situation, especially when patients ingested very large amount of organophosphate insecticide in suicide attempts. Many study recommendations show considerable variations in atropine doses and are still confounding how much and how long the pralidoxime dose should be given in severe cases. There have been some randomized controlled studies suggesting proper use of pralidoxime, but these results are often inappropriate to decide the dose and duration of treatment. Lipid solubility of organophosphate is one of the important factors influencing rapid distribution and redistribution in the body after ingestion. Furthermore, clinical evaluation of the severe organophosphate poisoning with large amount is not easy and often misleading in the course of treatment. Studies in clinical toxicology have limitation and are different from the clinical trials for new drug development. Even though randomized controlled trials may be better than observational studies, those are not well-controlled studies. Therefore, the treatment course should be guided by frequent acetylcholinesterase monitoring especially in severe acute organophosphate poisoning with large amount.

How should we evaluate causality for adverse reactions during clinical trials?

Stewart GEARY
Eisai Co., Ltd., Japan

Information on the safety profiles of medications that is critical for making decisions in clinical toxicology initially relies on the profile of adverse reactions determined during clinical development. Adverse reactions can be heuristically classified into types A (Augmented pharmacologic effect), B (bizarre or idiosyncratic effects), C (Chronic effects), D (Delayed effects), E (End-of-treatment effects), F (Failure of therapy) or G (Genetic reactions) and of these categories type A reactions can be expected to be of greatest interest during acute overdose. Causality assessments of individual adverse events during clinical trials are often unreliable, as evidenced by cases where an adverse reaction is assessed as being "related" to study drug but on unblinding the subject is found to have been on placebo. The determination of what adverse reactions can be expected depends on careful review of aggregate clinical trial data comparing the adverse events and clinical testing abnormalities for the investigational compound to placebo and active comparators. The Bradford-Hill criteria, the recommendations of CIOMS VI on evaluating clinical safety data and the FDA's internal guidance for its reviewers on performing Clinical Safety Reviews are useful guides when evaluating clinical trial safety data. The interpretation of clinical trial safety data, selection of safety issues for future monitoring in Risk Management Plans and considerations for selecting information for the Warnings & Precautions and other Adverse Reactions sections of Package Inserts will be presented and discussed.