Numerical and Computational Analysis of a Pharmacokinetic Model of Organophosphorus Compound Poisoning

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Abstract:

Chemical warfare nerve agents include highly toxic organophosphorus compounds (OPs) that inhibit acetylcholinesterase (AChE). This inhibition induces central respiratory depression and may lead to respiratory failure and death. To better understand the toxicokinetics of poisoning and to determine the efficacy of drugs to either prevent or treat OP attack, several mathematical models have been created. In particular, Green's 1958 paper assumes that the body acts as one homogeneous, well-mixed compartment. His model accounts for the interaction of OPs with both AChE and a therapeutic agent,and also shows what happens when an organism is treated with a substance that mediates toxicity by reactivating inhibited AChE. We re-examine Green's model using numerical and computational methods unavailable at the time to find solutions to the equations that enable us to determine the protection level of different or combination treatments. Given a particular dose of OP, we show the duration of time it takes to reach a critical level of AChE in a subject, thereby determining how quickly treatment must take place.

KEY WORDS: toxicokinetics, organophosphates, scavengers, differential equations, multi-compartment modeling

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