"Catch-up" therapy: Combining antidotal treatment with dermal application of AHA following percutaneous VX poisoning in the domestic swine

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Abstract

Low volatility organophosphorus chemical warfare agents are cholinesterase inhibitors which rapidly absorb into the skin, leading to the formation of a dermal depot from which they slowly enter the bloodstream. This leads to sustained cholinergic hyperstimulation, which if untreated may lead to death. Current available countermeasures are not adequate to neutralize the agent residing in the dermal depot. Herein, we evaluated the efficacy of the potassium salt of acetohydroxamic acid (AHAK), as a potential "catch-up" therapy lotion intended to neutralize the dermal depot by penetrating the skin and decomposing it before it reaches the bloodstream. We compared the clinical outcome following skin surface decontamination combined with antidotal treatment, to that following the same antidotal treatment combined with dermal application of AHAK at the site of VX exposure, against percutaneous poisoning by a lethal neat dose of the low volatility nerve agent VX, in an unanesthetized swine model. Following skin surface decontamination and antidotal treatment, recurrence of intoxication signs and a prolonged recovery time was observed. In contrast, similar antidotal treatment combined with dermal application of AHAK significantly reduced intoxication signs recurrence and accordingly medical supervision duration needed, paralleled by a significantly faster recovery of whole blood ChE activity. An initial evaluation demonstrated the safety of prolonged whole-body AHAK application. By quickly penetrating the skin at the site of exposure and degrading the depot within it, the AHAK lotion may act as an efficient "catch-up" therapy against percutaneous poisoning by low volatility OP CWAs, thus improving the clinical outcome and reducing the burden on medical staff.

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