

Toxicokinetics of Propanil Following Acute Self-Poisoning

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Introduction : Propanil self-poisoning is reported in parts of Asia where it is one of the most toxic herbicides available. (1) *In vivo*, propanil is hydrolysed to 3,4-dichloroaniline (DCA) which is subsequently oxidised to 3,4-dichlorophenylhydroxylamine which is a potent inducer of methaemoglobin. However, there is limited information about the toxicokinetics of propanil. Such information may assist in the management of patients with acute poisoning by guiding the administration of antidotes such as methylene blue which has a relatively short half-life of 5 hours. **Methods** : A total of 356 blood samples were available for inclusion in this study, including serial samples in 26 patients from which kinetic analyses could be conducted. The plasma concentration of propanil and DCA were determined by HPLC. On the basis of clinical criteria (1), the dose-response relationship was determined for both propanil and DCA. The best-fit apparent elimination half-life was determined using non-linear regression by global fitting of the rate constant in a monoexponential decay model. **Results** : 451 patients presented to study hospitals over a 5 year period, 10.7% of whom died. The median admission propanil concentration was significantly higher in patients who died compared with those with mild clinical toxicity (72 μ M vs 1.3 μ M; $P < 0.001$). The absorption phase appeared to persist for up to 10 hours. First order elimination for propanil and DCA was noted in some patients while in others it was less predictable. The elimination half-life of propanil was 3.2 hours (95% confidence interval 2.6 to 4.1 hours) while the concentration of DCA was generally higher, more persistent and more variable than propanil. In survivors, by 36 hours post-ingestion the concentration of DCA in survivors was low or negligible, so clinical toxicity is not likely to increase beyond this time. **Conclusions** : Propanil-induced toxicity appears to be dose-dependent. Due to ongoing absorption and prolonged elimination of DCA in a number of patients, continuous infusion of methylene blue may be preferred to intermittent bolus dosing. More research is required into the optimal management of acute propanil poisoning. **Reference** : 1. Roberts DM. Clinical outcomes from acute intentional self-poisoning with the herbicide propanil (3,4-dichloropropoanilide). Proceedings from the Asia Pacific Association of Medical Toxicology 5th International Congress, Sri Lanka, 2008.

Propanil concentration

