OP13

The relationships of plasma profenofos and ethanol to clinical outcome in acute profenofos self- poisoning

Dr Jeevan Dhanarisi[1], Michael Eddleston[1,2], Klintean Wunnapuk[3], Indika Gawarammana[1,4], Fahim Mohamed[1,5,6]

[1]South Asian Clinical Toxicology Research Collaboration, Faculty of Medicine, University of Peradeniya,
[2]Pharmacology, Toxicology, & Therapeutics, University/BHF Centre for Cardiovascular Science, and Centre for Pesticide Suicide Prevention, University of Edinburgh, Edinburgh, UK
[3]Department of Forensic Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand
[4]Department of Medicine, Faculty of Medicine, University of Peradeniya, Peradeniya, Sri Lanka
[5]Department of Pharmacology, Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia
[6]Edith Collins Centre for Translational Research, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia.

Aim and objectives: Currently the S-alkyl OP, profenofos EC50, is commonly ingested for self-harm in Sri Lanka. Although clinical experience suggests that ethanol co-ingestion makes management more difficult, the relationship between plasma concentrations of ethanol and of profenofos to clinical outcome is unknown. Therefore, we aimed to determine the relationships between plasma ethanol concentration and plasma profenofos toxicokinetics with clinical outcome in acute profenofos poisoning.

Methodology: Demographic and clinical data, including an ethanol history and blood samples were prospectively collected from all cases of acute poisoning with profenofos EC50 presenting to Teaching Hospital Peradeniya, Sri Lanka over four years from 2017 to 2021. Plasma samples were analysed by Gas Chromatography- Mass Spectrometry to quantify the ethanol (n=99) and profenofos (n=30 [15 no ethanol, 15 with ethanol]) concentrations. The PKSolver program was used to calculate the toxicokinetic parameters such as, plasma absorption (pt1/2a), elimination (pt1/2e) half- lives, etc.
Results: Of 99 patients (male 78/99, 78.8%) with acute profenofos self-poisoning, 50 (50.5%) reported history of alcohol co-ingestion. Plasma from 44 of 99 (44.4%) profenofos-poisoned patients had detectable alcohol

(median 88.8, interquartile range [IQR] 26.6–122.2) $mgdL^{-1}$. Alcohol co-ingestion (ALC+) group had a non-significant higher risk of death than those who had not co-ingested alcohol (ALC-
) group (5/44 [11.4%] vs 3/55 [5.5%]; p = 0.461). The median pt1/2a for the ALC+ group and the ALC- group (0.1 h and 0.1 h respectively, time 0–24 h) were not statistically different (p= 0.6594), however median pt1/2e value was significantly higher in the ALC+ group than ALC- group (23.1 h and 9.9 h, time 0–24 h, p=0.0002) suggesting that patients in ALC+ group had a longer elimination half-life. The extent of profenofos absorption (area under the curve [AUC]) was significantly higher in ALC+ compared to AlC- (62644 [IQR 18928 to 107880] vs. 14946 [IQR 8201 to 18707] $ngmL^{-1}*h$; p = 0.0002).

Conclusions: Ethanol co-ingestion leads to alter the toxicokinetic of profenofos insecticide by slowing elimination rate, and possibly increasing risk of death and worsening the hospital outcome.