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New Insights into Neurotoxicity and Respiratory Failure in Organophosphorus Insecticide Poisoning

Tharaka Dassanayake

Department of Physiology, Faculty of Medicine, University of Peradeniya
South Asian Clinical Toxicology Research Collaboration

The research that we have been doing over last 6 years at the Toxicology Department of the Teaching Hospital Peradeniya in Sri Lanka is focused on OP-induced intermediate syndrome (IMS), respiratory failure (RF) and neurocognitive deficits.

Classically IMS is characterised by muscular paralysis (neck, limb girdle, proximal limb and respiratory muscles etc.) that sets in 24-96 hours following acute poisoning. Clinical and biochemical parameters recorded in the acute stage of poisoning are only modestly successful in predicting IMS and delayed RF. Given the hypothesis that IMS is a manifestation of deficient neuromuscular transmission, we investigated whether 1) neuromuscular junction (NMJ) dysfunction within the first 24 hours following exposure—quantified by jitter in single fibre electromyography (SfEMG)—can predict IMS, and 2) whether the SfEMG jitter over the course of the illness is different among patients who developed IMS (IMS+) and those who did not (IMS-). Prolonged SfEMG jitter within the first 24 hours following exposure was associated with 9-fold increase in risk of IMS (odds ratio=8.9; 95%CI=2.4, 29.6; $p=0.0003$). The technique showed a high sensitivity (86%), but poor specificity (58%) in predicting IMS. The jitter remained prolonged and the NMJ blocking was more prevalent among IMS+ for 72 hours post-exposure, with some patients having deficits for up to 216 hours post-exposure. For intubated patients, the median time for jitter to normalize and median time to extubate were similar, and the two variables had a moderate positive correlation ($r=0.49$, $p=0.001$); signifying that the time course of electrophysiological recovery of the NMJ mirrors the time course of respiratory recovery in those patients.

RF causes a significant proportion of mortalities in OPI-poisoning. Over last 6 years, we prospectively observed 366 patients poisoned with different OPI formulations, during their hospital stay. Contrary to what we and the pesticide regulatory authorities expected, chlorpyrifos—the most commonly OPI used in self-harm before it was banned in Sri Lanka in 2014—was associated with lower risk of RF (odds ratio=0.35; 95%CI=0.21, 0.61; $p<0.0001$) and mortality (OR=0.29, 96%CI=0.01, 0.85, $p=0.015$), whereas profenofos—an S-alkyl OPI that mainly replaced chlorpyrifos in Sri Lanka—was associated with a higher risk of RF (odds ratio=2.27, 95%CI=1.43, 3.59; $p=0.0006$) and mortality (odds ratio=2.68; 95%CI=1.27, 5.64; $p=0.01$), compared to other OPI formulations.

Our regression models based on preliminary cognitive event-related potential (ERP) data indicate that hypoxia in the acute OPI poisoning is more likely to be associated with delayed neurocognitive deficits.