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Animal models to measure kidney injury post-poisoning

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Objective: Glyphosate-surfactant herbicides (GPSHs), paraquat (PQ), *4-chloro-2-methylphenoxyacetic acid* (MCPA) are used in South East Asia due to its low cost and its effectiveness in wide-range weed control. Renal failure is a very common toxic effect due to the role of the kidney in actively excreting these herbicides. This study aimed to demonstrate the potential utility of acute kidney injury (AKI) biomarkers in herbicide-induced nephrotoxicity animal models.

Methods: Male Wistar rats were dosed orally with 4 different doses of PQ or Roundup® or Ospray® MCPA 500 and the biomarker patterns in urine and plasma were investigated at 8, 24 and 48 hours after exposure. Biomarkers were quantified by absolute concentration; by normalising to urine creatinine; and by calculating the excretion rate. The ROC diagnostic performances of each method in predicting of acute kidney injury were compared.

Results: Urinary kidney injury molecule-1 outperformed other biomarkers in predicting histological changes in the PQ and Roundup® nephrotoxic models. Plasma creatinine was still the best marker for early detection of acute kidney injury after MCPA dosing. The performance of plasma cystatin C in mirroring renal function was similar to that of plasma creatinine and creatinine clearance.

Conclusion: This translational research contributes significantly to the identification of more sensitive and specific markers for pre-clinical identifying of markers for predicting outcome after exposure to nephrotoxic agents and in assessing the extent to which animal acute kidney injury biomarker data can inform risk assessment in humans.