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Long term effects of acute kidney injury from agrochemicals

Fahim Mohamed
SACTRC, Faculty of Medicine, University of Peradeniya, Sri Lanka
Department of Pharmacy, Faculty of Allied Health Sciences, University of Peradeniya

Deliberate self-poisoning with pesticides is common and occurs in millions of people each year, predominantly affecting healthy young adults. Several common pesticides cause acute kidney injury (AKI) after poisoning, e.g. paraquat, glyphosate, MCPA. Although AKI is generally regarded as reversible, it may increase the risk of a subsequent diagnosis of chronic kidney disease (CKD). AKI may contribute to CKD in at least two possible ways. Firstly, although AKI may apparently resolve, the patient is left with residual damage and reduced capacity to deal with further physiological stresses to the nephron. Secondly, AKI (and sub-clinical CKD) may impair renal elimination of nephrotoxic chemicals which then induce direct injury.

Animal studies demonstrate the 'proof of concept' that AKI can lead to CKD. However, this relationship and how to identify those at risk of subsequent CKD needs to be defined in humans, particularly following pesticide exposure. The rates of CKD in rural communities are often much higher and not explained by the better known risk factors and aetiologies of CKD. CKD of unknown aetiology (CKDu) is a leading cause of death in the North Central province of Sri Lanka. There are epidemiological/ecological associations with a range of toxicological causes including agrochemicals. A few medium-term (<6 month) follow-up clinical studies have demonstrated acute ingestion of toxic pesticides and chemicals may lead to CKD.

The value of long-term functional measures other than those based around GFR is shown from a study of Chinese herbal, cadmium and analgesic nephropathy which indicated that functional deficits in beta-2 microglobulin reabsorption could be detected despite NAG and creatinine were in the normal range. Similarly, following acute poiosning with glyphosate, paraquat and oxalic acid poisoning, renal biomarkers concentrations were elevated at 3 months in a subset of patients, including those who had developed AKI by conventional criteria but also some who did not. Elevated urinary biomarkers at 1-3 month follow-up might indicate on-going nephrotoxicity. Data on long-term effects of pesticide exposure is lacking and further studies are warranted including novel markers and techniques.

Early identification of patients who are likely to develop CKD is important since renal replacement therapy is unaffordable for both patients and the government in the developing world. Novel biomarkers of renal damage may be superior since extensive damage is required to lead to a rise in urea and creatinine and the effect is delayed. Empirically, in animal studies biomarkers other than creatinine are greatly superior in accurately detecting renal damage. For example, progression of CKD has been predicted by elevated serum cystatin C and beta-trace protein over 7 years of follow-up. Increased urinary albumin excretion predicts CKD progression and is used in both clinical practice and research. NGAL, KIM-1 and Liver-type fatty acid-binding protein (L-FABP) predict progression of CKD and have been used to evaluate treatment response. Predictive utility of oxidative markers has also been evaluated.

Apart from renal biomarkers, recent studies suggest a possible role for Doppler ultrasound in diagnosis and prognosis of CKD. Renal resistive index (RRI) and renal functional reserve (RFR) may play an important role predicting the progression of CKD. A reduction in RFR is an indicator of glomerular hyperfiltration, and this has been associated with a range of renal diseases. The mean RFR falls to 6.7% in CKD stage 4 compare to healthy volunteers (23 %). RRI and RFR may provide insights into pathophysiological contributions to the development of CKD, and relationship between RFR/vascular function and biochemical injury/functional biomarkers.

CKD is a major health burden in Sri Lanka and other part of the world. Risks associated with long-term effects in young people may affect their health over a very long time frame. An evidence-base on risk factors for long-term complications has many potential implications for policy and public health interventions.