OP-25

Identification of nephrotoxic mechanisms and early biomarkers of acute kidney injury following intentional self-poisoning with chlorophenoxy herbicide [2-Methyl-4-chlorophenoxyacetic acid (MCPA)]

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Objective: Nephrotoxic acute kidney injury (AKI) is common in less developed countries. Self-poisoning with chlorophenoxy herbicide [2-Methyl-4-chlorophenoxyacetic acid (MCPA)] has been associated with acute kidney injury (AKI) and high case fatality of up to 11% [1]. The current study aims to determine the nephrotoxic mechanisms and early renal biomarkers that could diagnose AKI following MCPA poisoning.

Methods: Clinical and demographic data were collected from 58 patients. Serial blood and urine samples were collected 4 hourly till day 1 and then daily till discharge. Serum biochemical parameters; creatinine (sCr), cystatin C (sCysC), albumin (sAlb) and creatine kinase (CK) were measured. Samples were also analyzed for urinary biomarkers; kidney injury molecule – 1 (KIM – 1), clusterin, albumin, beta-2-microglobulin (β2M), cystatin C, neutrophil gelatinase associated lipocalin (NGAL), osteopontin and trefoil factor 3 (TFF3) using enzyme linked immunosorbent assay (ELISA). Maximum biomarker concentrations observed within 24 hours post-ingestion (Cmax24) were noted. Performance of biomarkers was assessed using spaghetti plots and receiver operating characteristic (ROC) curves. AKI severity was defined by AKI Network (AKIN) criteria.

Results: 28 patients developed AKI (AKIN1 n = 23, AKIN2 n = 4, AKIN3 n = 1). sCysC levels of AKI group (except one patient) remained within the normal range. Several patients with AKI had increased levels of KIM-1 and β2M compared to the normal range. Area under curve (AUC) of ROC for β2M and KIM – 1 at Cmax24 were 0.68 (95% CI: 0.53 – 0.81, p = 0.03) and 0.67 (95% CI: 0.51 – 0.84, p = 0.05) respectively. Median CK level in AKI group was 163 U/L (range: 53 U/L – 3071 U/L). Patients without AKI had median CK level of 149 U/L (range: 22 U/L – 919 U/L). Serum concentrations of sCr Vs CK and sCr Vs sCysC were moderately correlated (r = 0. 442, p < 0.0001 and r = 0.282, p = < 0.0001 respectively).

Conclusion: Ingestion of MCPA caused mild AKI. Structural damage (proximal tubular damage) was more prominent than functional damage. Part of the elevation of sCr may be due to decreased mitochondrial respiration and decreased ATP. Mechanisms of renal effects of MCPA poisoning can be due to rhabdomyolysis, renal tubular injury and cellular damage.

Reference: [1] Mohamed, F., Z.H. Endre, and N.A. Buckley, Role of biomarkers of nephrotoxic acute kidney injury in deliberate poisoning and envenomation in less developed countries. Br J Clin Pharmacol, 2015. 80(1): p. 3-19.