Oral Presentation - 28

Mechanisms Underlying Early Rapid Increases in Creatinine in Paraquat Poisoning

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Abstract

Objectives: Acute kidney injury (AKI) is common after severe paraquat poisoning and usually heralds a fatal outcome. However, the very rapid rise in serum creatinine exceeds what can be explained by creatinine kinetics based on loss of renal function. This prospective multi-centre study compared the kinetics of two surrogate markers of glomerular filtration rate (GFR), serum creatinine and serum cystatin C following paraquat poisoning.

Methods: This study enrolled 66 patients with paraquat poisoning. Serial blood and urine samples (4, 8, 16 and 24 hours post ingestion and then daily until discharge) were collected to measure different biomarkers and paraquat levels. Relative changes in creatinine and cystatin C, and influence of non-renal factors were studied. AKI was diagnosed using the Acute Kidney Injury Network (AKIN) criteria.

Results: Of 66 patients with paraquat poisoning, 37 rapidly developed severe AKI (AKIN 2 & 3) and 17 died. All 37 patients had a rapid increase in creatinine of >100% within 24 hours, >200% within 48 hours and >300% by 72 hours. In contrast, cystatin C levels increased by 50% at 24 hours and then remained constant for several days. The creatinine to cystatin C ratio increased up to 8 fold by 72 hours. Non-creatinine chromogen contributions were excluded by using an enzymatic creatinine assay. There was only a modest fall in urinary creatinine and plasma/urine creatinine ratios and a moderate increase in urinary paraquat.

Conclusions: While loss of renal function contributes to the large increases in creatinine following severe paraquat poisoning the most plausible explanation of the large increase is increased production of creatine and creatinine to meet the energy demand from severe oxidative stress. Minor contributions include increased cyclisation of creatine to creatinine because of acidosis and competitive or non-competitive inhibition of creatinine secretion. Creatinine is not a good marker of renal functional loss after severe paraquat poisoning and renal injury should be evaluated using more specific biomarkers of renal injury.