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Serum microRNA as biomarkers for acute kidney injury following poisoning with potassium permanganate and oxalic acid

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Objectives: Early detection of acute kidney injury (AKI) is difficult due to the lack of sensitive and specific biomarkers. MicroRNAs are stable biomarkers, which are released following cellular injury. Local and systemic effects of tissue injury can be captured via efficient detection of microRNAs in bio-fluids. This study aims to identify a signature of serum microRNAs as early biomarkers of AKI in patients following poisoning with oxalic acid and/or potassium permanganate.

Methods: Serum samples from age and gender-matched patients with acute self-poisoning following oxalic acid/potassium permanganate (Patients who did not develop AKI - NOAKI=6, AKI stage 2 &3 -AKIN2/3=13) and healthy controls (n=4) were profiled through a TaqMan discovery microRNAs OpenArray quantitative real-time PCR (qPCR) platform. A panel of 56 microRNAs was selected (42 from discovery, 11 from other publications & 3 spike control microRNAs) for validation in a larger cohort of patients (NOAKI=15, AKIN2/3=36) and 23 healthy individuals.

Results: The expression of 44 microRNAs was significantly downregulated in serum samples of AKIN2/3 patients compared to healthy control and NOAKI in the smaller discovery cohort. Validation study confirmed that 32 microRNAs were significantly downregulated ($p<0.05$, DDCt >1.5) in AKIN2/3 compared with healthy control. A set of six microRNAs (miR-21, miR-92a, miR-20a, miR-191, miR-574-3P, and miR-122), distinguished AKIN2/3 patients from NOAKI. miR-451, miR-25, miR-19b, miR-16 and miR-92a discriminated AKIN2/3 patients with an area under the curve greater than 0.88. Significant ($P<0.05$) correlations were observed between traditional biomarkers of AKI, such as peak serum creatinine with miR-25 (r=0.54), miR-451 (r=0.75); estimated glomerular filtration rate with miR-20a, miR-93, miR-451 and miR-16 with; and normalized urinary albumin with miR -16, miR-451, miR-21 miR-30a-5p, miR-20a, miR-19b. Several microRNAs (miR-15 miR-16, miR-21, miR-24, miR-26b, 29a-3p, miR-93, 146a) that we identified have also been reported in other types of AKI (Intensive care unit AKI and post-cardiac surgery AKI) in humans.

Conclusion: A microRNA signature indicative of AKI was identified in human serum samples. Differences in relative abundance of dysregulated microRNAs in serum may provide insights into understanding their potential as early biomarkers of AKI. Our study identified that miR-451 could be a novel biomarker for oxalic acid and potassium induced AKI.