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# Urinary MicroRNAs as Non-Invasive Biomarkers for Nephrotoxin-Induced Acute Kidney Injury

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**BACKGROUND**: MicroRNAs are potential diagnostic biomarkers of several diseases. This study aimed to establish whether urinary miRNAs can be used as early renal biomarkers following poison-induced acute kidney injury (AKI) and microRNA signature identify different mechanism of nephrotoxicity (toxic-AKI).

**METHODS**: Urine samples from age and gender-matched patients with acute self-poisoning following Paraquat, Glyphosate, Oxalic acid, and Russell's viper bites were used. Patient groups include those who did not develop AKI (NOAKI) and developed AKI stage 1, 2 &3 (AKIN1/2/3). Three patients from each group from each toxin and healthy controls were profiled through TaqMan discovery microRNAs OpenArray RT-qPCR platform. A panel of 56 microRNAs was selected and validated in a larger cohort of patients (Paraquat=55, Glyphosate=51, Oxalic acid=41, and Russell's viper bite=53) and 27 healthy controls.

**RESULTS**: The expression of microRNAs was significantly upregulated in urine samples of patients poisoned by all nephrotoxic agents in both the discovery and validation cohorts. Variable numbers of microRNAs were altered in AKI depending on the agent (Oxalic acid=14, glyphosate=7, paraquat=38 & Russell's viper=30). Four microRNAs (miR-30a-3p, miR-30a-5p, miR-92a, and miR-204) discriminated AKIN3 patients from NOAKI for all 4 nephrotoxins. No microRNAs distinguished AKI stage 1 & 2 from NOAKI in glyphosate and Russell's viper. Pathway analysis demonstrated these differentially expressed miRNAs were targeted to many genes associated with the regulation of different nephrotoxic signaling pathways. In Russell's viper envenomation, 12 microRNAs were significantly ($p<0.01$, rrCt >3.5) expressed in NOAKI compared with healthy controls.

**CONCLUSION**: Urinary microRNA profiling showed promise in identifying nephrotoxicity after severe AKI in humans. Some (but not all) of these urinary miRNAs (miR-10a, miR-30d, miR-16, miR-192, miR-21, miR-221, miR-320, miR-29c) are also observed in ischemia-reperfusion injury and focal segmental glomerulosclerosis patients. Urinary microRNAs have potential clinical application to use as early non-invasive biomarkers for AKI, toxic-AKI, and also envenomation.