Biomarkers of Acute Kidney Injury

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There is an urgent need to identify diagnostic and predictive biomarkers of acute kidney injury (AKI). A change in serum creatinine is the standard metric used to define AKI and monitor its progression. This functional marker is inadequate for a number of reasons including the fact that it only indirectly reflects injury that is not specific to the tubule. Changes in serum creatinine are delayed in time after kidney injury and hence are not good indicators to use in order to target therapy in a timely fashion. Biomarkers can be used to guide and monitor therapy. There are a limited number of biomarkers that are being validated by a number of groups and from this list is likely to derived clinically useful reagents over the next few years.

The overall goal of our ongoing studies has been to identify and qualify biomarkers that are sensitive, specific, and predictive of outcome in acute kidney injury (AKI). We have compared the performance characteristics of kidney injury molecule-1 (KIM-1) with eight promising urinary biomarkers in a cross sectional study involving adult patients with clinically established AKI compared to patients without clinically identified AKI: healthy controls, ICU patients, patients with a UTI and pre-cardiac catheterization patients. Biomarkers tested included neutrophil gelatinase associated lipocalin (NGAL), interleukin-18 (IL-18), hepatocyte growth factor (HGF), cystatin C (Cys), N-acetyl-β-D-glucosaminidase (NAG), vascular endothelial growth factor (VEGF), chemokine interferon-inducible protein 10 (IP-10; CXCL10) and total protein. In another study urinary KIM-1 and NAG levels were found to increase prior to changes in serum creatinine in patients administered cisplatin. Urine was also collected before and 4h, 24h and 48h after cardiac catheterization in 64 patients receiving radiocontrast agents. In renal transplant and native kidney biopsies from patients with various primary renal diseases tissue KIM-1 staining of proximal tubules correlated very well with histological injury and functional significance of the injury.

In summary considerable progress has been made toward the goal of qualifying biomarkers for routine clinical use. Armed with these new tools the future will look much brighter for the patient with AKI as it is likely that early diagnosis and better predictors of outcome will lead to new therapies which can be introduced earlier in the course of disease.