Urine NGAL May Reveal Kidney Failure Etiology

BY DIANA MAHONEY

BOSTON — Measuring urine neutrophil gelatinase–associated lipocalin upon hospital admission in patients with cirrhosis and renal failure can distinguish hepatorenal syndrome and acute kidney injury from other forms of kidney dysfunction and might help predict inpatient mortality, a study has shown.

If the findings are confirmed, a single measurement of neutrophil gelatinase–associated lipocalin (NGAL), an acute-phase protein, may help guide early, disease-specific therapy for patients with cirrhosis and renal failure, Dr. Elizabeth C. Verna said at the annual meeting of the American Association for the Study of Liver Diseases.

"Determining the etiology of acute renal failure in patients with cirrhosis, ascites, and edema remains an important clinical challenge, and it is particularly important in patients awaiting liver transplantation," said Dr. Verna of Columbia University in New York.

Although urine NGAL has been shown to predict the onset or severity of acute kidney injury, and to predict clinical outcomes, "it has not been tested in the setting of cirrhosis or hepatorenal syndrome," she noted.

Dr. Verna and her colleagues conducted a prospective cohort study of 115 adults admitted to the general medical service or ICU with either biopsy-proven cirrhosis or a combination of imaging, laboratory, and clinical data with documentation of cirrhosis. The study excluded patients with chronic end-stage renal disease on dialysis as well as those who were anuric on presentation with significant proteinuria, active urinary tract infection, HIV infection, or a previous solid organ transplant.

A single measurement of NGAL, an acute-phase protein, may be instrumental in directing early, disease-specific therapy for patients with cirrhosis and renal failure.

The primary outcomes included inpatient mortality and category of renal failure—normal renal function, stable chronic kidney disease, prerenal azotemia (PRA), hepatorenal syndrome (HRS), or acute kidney injury (AKI). Urine was collected from all patients within 24 hours of admission, and NGAL measurement was determined with Western blot and confirmed using ELISA, then corrected for urine creatinine for each case. The final adjudication of renal function was determined by an attending nephrologist who was blinded to both urine NGAL measures and clinical outcomes.

The mean age of the patients was 56 years, and 70% were men. Most had hepatitis C, alcohol dependence, or a combination of both. "Many of the patients had suffered previous consequences of cirrhosis, including ascites, variceal bleeding, and hepatocellular carcinoma," she said. About 14% of the patients had previous transjugular intrahepatic portosystemic shunt, and 18% had a history of at least stage 2 chronic kidney disease. The median model for end-stage liver disease (MELD) score on admission was 17, and median hospital stay was 6 days.

With respect to renal function category, 43% had normal kidney function, 11% had stable chronic kidney disease, 25% had PRA, 11% had HRS, and 9% had AKI. Urine NGAL was elevated in both AKI (1,000 mcg/g) and HRS patients (318 mcg/g), compared with PRA (111 mcg/g), while the admission values of creatinine were elevated only in AKI.

About 12% of the patients died while in the hospital, 22% required ICU admission, 17% had a nephrology consultation, and 10% underwent inpatient dialysis. "The majority of patients who died during admission were in the HRS or AKI groups," Dr. Verna said. "The log transformation of urine NGAL was predictive of all of our other binary outcomes including inpatient mortality, dialysis, combination of dialysis and mortality, ICU admission, and renal consultation. This finding was strongest for inpatient mortality, where for every log increase in urine NGAL, the odds ratio for mortality was 1.9."

In multiple logistic regression models, "a urine NGAL cutoff of 165 was significantly predictive of mortality and when controlling for creatinine at a cut point of 1.2, age, and [HRS]," she said. The strongest predictor of inpatient mortality was HRS as a diagnosis of acute renal failure; adding the MELD score did not significantly change these relationships.

The study findings suggest that, in patients with cirrhosis, "a single urine NGAL measurement may distinguish HRS and AKI from PRA, and that HRS is a strong predictor of mortality in this setting," Dr. Verna said. "Additional studies are required to understand why urine NGAL may be elevated in HRS. We think it perhaps is due to subtle and reversible tubular damage in these patients."

If these findings are confirmed, Dr. Verna noted, "urine NGAL could be used clinically to discriminate HRS from PRA, which is usually a very difficult decision to make, and to direct early therapy." ■

Disclosures: *Dr. Verna reported having no relevant financial disclosures.*