Journal of Cardiac Failure Vol. ■■ No. ■■ 2018

Clinical Investigation

Spot Urine Sodium as Triage for Effective Diuretic Infusion in an Ambulatory Heart Failure Unit

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ABSTRACT

Background: Admission for diuresis remains a common and costly event in patients with advanced heart failure (HF). We tested whether spot urine sodium could identify patients likely to respond to ambulatory diuretic infusion without hospitalization.

Methods and Results: We prospectively followed 176 consecutive patients with advanced heart failure receiving intravenous furosemide for congestion in an ambulatory clinic. Spot urine sodium was measured in 1st voided urine after diuretic infusion and compared with 3-hour urine output and subsequent risk of 30-day hospitalization or emergency department (ED) visit.Spot urine sodium was significantly associated with urine output in a model adjusted for age, renal function, and blood urea nitrogen ($P = .02$). Higher urine sodium was associated with lower risk of hospitalization or ED visit within 30 days (odds ratio [OR] 0.82 [95% confidence interval 0.72–0.94] per 10 mmol/L increase; $P < .001$), in a model adjusted for hemoglobin (OR 0.80 [0.66–0.97]; $P = .02$) and systolic blood pressure (OR 0.82 [0.67–1.0]; $P = .05$). Spot urine sodium ≥65 mmol/L and urine output ≥1200 mL identified a lower-risk group for outpatient management.

Conclusion: High spot urine sodium after diuretic administration identifies HF patients likely to respond to an ambulatory diuretic infusion with lower rates of hospitalization or ED visits at 30 days. (*J Cardiac Fail 2018;*■■:■■–■■)

Key Words: Heart failure, hospitalization, urine sodium, outcomes.

There are more than 1 million hospitalizations and ~550,000 emergency department visits for heart failure (HF) each year.[1] Hospitalizations account for the majority of costs of treatment for HF patients and affect quality of life.[2] Most HF admissions are attributed to volume overload which is treated with intravenous (IV) loop diuretics. However, 27% of these patients are readmitted within 30 days,[3] and there are few interventions proven to be effective at preventing readmission. Current efforts focus on improving the discharge process, early follow-up, and changing oral diuretics in response to weight gain or signals of increasing pulmonary pressures from hemodynamic monitoring devices. Despite these efforts, some patients develop recurrent symptoms and signs of congestion sufficient to warrant consideration of hospital admission.

Ambulatory IV diuretic infusion has been identified as safe and cost-effective alternative to hospitalization for selected patients with decompensated HF.[4–9] However, the time and resources required for outpatient infusion are not well spent on patients who proceed on to hospitalization. Triage of patients likely to have a durable response to ambulatory intervention has not been established. Because loop diuretics induce natriuresis, urine sodium concentration may serve as a surrogate for diuretic responsiveness. Indeed, a recent study of inpatients found that high urine sodium concentration assessed at steady state during continuous infusion of furosemide was associated not only with volume of urine output but also with fewer adverse events.[10] However, it takes hours to reach a steady-state condition, making this method

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Manuscript received August 21, 2017; revised manuscript received December 26, 2017; revised manuscript accepted January 23, 2018.

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1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2018.01.009

less than ideal to identify responders and nonresponders. A spot urine sodium can be readily measured in the outpatient setting to assess initial response. We hypothesized that higher spot urine sodium following outpatient administration of an IV loop diuretic bolus would predict greater urine output and lower risk of subsequent emergency department (ED) visit or hospitalization.

Methods

Patient Selection

The Ambulatory Cardiac Triage, Intervention, and Education (ACTIVE) unit at Brigham and Women's Hospital is a multidisciplinary ambulatory intervention clinic for HF patients, offering infusions of diuretics, iron, and other replacement therapies in conjunction with pharmacology consultation for reconciliation, revision, and education concerning medication regimens and coordination of urgent consultations such as rhythm device management or palliative care social work, as has been previously described.[4,9] Before IV diuretic infusions, nurse practitioners confirm signs and symptoms of clinical congestion and hemodynamic stability with no evidence of critical hypoperfusion. Patients with severe symptoms sitting at rest, concern for an acute condition precipitating HF, predialysis advanced chronic kidney disease, or other perceived high risk of clinical instability with outpatient treatment are referred to the ED or directly admitted. Diuretic dose is determined with the use of an algorithm designed with the pharmacy team based on home diuretic dose.[4] For the present study we enrolled consecutive patients presenting to the ACTIVE unit from June 2013 to July 2015 and followed them for a median 16 months. Baseline characteristics and laboratory values were recorded on the initial visit. Ischemic etiology was defined as any history of obstructive coronary artery disease (CAD), including previous myocardial infarction, coronary artery bypass, percutaneous coronary intervention, or severe stenosis. Diabetes was defined as use of any oral hypoglycemic therapy or insulin. Diuretic doses were converted to furosemide equivalents, where 40 mg oral furosemide = 20 mg torsemide = 1 mg bumetanide, and 40 mg IV furosemide = 1 mg bumetanide.[11] Glomerular filtration rate (GFR) was estimated with the use of the Modification of Diet in Renal Disease equation.[12] Intravenous loop diuretic bolus and subsequent 3-hour infusion dosing were determined with the use of a standardized algorithm based on home dose, as previously validated.[4] Diuretic efficiency was defined as mL urine per 40 mg furosemide equivalent.[13]

We prospectively collected the 1st voided urine sample after administration of IV diuretic, measured 3-hour urine output, and recorded hospital/ED visits within the following 30 days. All spot urine samples were obtained within 3 hours. Although the protocol called for voiding before initiating diuretic infusion, this was not always followed. Urine sodium was measured using a Roche Cobas C501 chemistry analyzer. All patients received telephone follow-up within 30 days to assess clinical status, including hospitalization at other institutions.

Statistics

Data were analyzed with the use of Stata 14 (Statacorp, College Station, TX). Baseline characteristics across tertiles of urine sodium were compared with the use of the Cuzick trend test, and characteristics by outcome were compared with the use of the Wilcoxon rank sum test or Fisher exact test. The relationship between predictors and continuous urine sodium and urine volume was analyzed by means of multiple linear regression with robust standard error. Variables were transformed with the use of functions minimizing the difference from the normal distribution when necessary. Oral diuretic dose was log transformed, and diuretic efficiency was square-root transformed. The relationship between predictors and events was analyzed by means of logistic regression. Univariate predictors with $P < .10$ were entered with a stepwise forward-selection strategy and retained in the final model if $P \leq .05$. Models were assessed for residual distribution, multicollinearity, Hosmer-Lemeshow goodness of fit, and the effect of outliers. Optimal thresholds were determined with the use of receiver operating characteristic (ROC) curve analysis by means of the Youden method (CUTPT package). Two-sided P values are reported, with $P < .05$ considered to be statistically significant.

Results

Patient Characteristics

Baseline characteristics for the 176 enrolled subjects are listed according to tertile of spot urine sodium in Table 1. The median age of the patients was 70 years (interquartile range [IQR] 58–79). Patients were predominantly male (65%) and white (78%). They typically had HF with reduced ejection fraction (61%), New York Heart Association (NYHA) functional class III–IV symptoms (89%), and frequent diabetes and renal dysfunction. Home oral diuretic medication was furosemide for 44% and torsemide for 53%. In our practice, thiazides are typically prescribed only as needed, and only 8 patients (<5%) had taken a thiazide dose on the day of infusion.

Urine Sodium

As urine sodium tertile increased from low to high across tertiles (Table 1), there were more women ($P = .01$), more nonwhites ($P < .01$), and less advanced disease, as characterized by lower blood urea nitrogen (BUN; $P < .001$), lower home diuretic dose ($P < .001$), less CAD ($P = .04$), higher systolic blood pressure ($P < .001$), higher GFR ($P = .01$), higher hemoglobin ($P = .03$), higher serum sodium ($P < .001$), and higher diuretic efficiency ($P < .001$). Multiple linear regression was performed to determine factors associated with continuous urine sodium concentration (Supplemental Table S1). Total dose of IV furosemide ($\beta = -0.10$; $P < .001$), serum sodium ($\beta = 2.13$; $P < .001$), BUN ($\beta = 0.35$; $P = .001$), and white race ($\beta = -13.53$; $P < .001$) were independently associated with urine sodium (model $r^2 = 0.35$). Lower urine