THE EFFECT OF RACE AND GENETIC VARIANTS ON DIURETIC REQUIREMENTS IN PATIENTS WITH SYSTOLIC HEART FAILURE

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1. Abstract:

Rational/Significance: Heart Failure (HF) accounts for over 55,000 deaths annually in the United States and nearly 20% of hospital admissions for persons over age 65 years.[1] Along with disease modifying agents, loop diuretics are the mainstay treatment for managing fluid and congestive symptoms in patients with HF. Optimal loop diuretic dosage is critical in heart failure patients as under-dosing results in worsening functional status, HF symptoms, and an increased risk for hospitalization, while overdosing increases the risk for loop diuretic adverse effects, volume depletion, and acute renal injury. There are several factors that pre-dispose HF patients to higher diuretic requirements including increased sodium intake, concomitant NSAID therapy, renal insufficiency, nephrotic syndrome, and hepatic cirrhosis.[4] However, these factors alone do not completely explain the variable diuretic response seen in patients with systolic HF. Preliminary data (unpublished) from our group suggest that race may contribute to loop diuretic dose requirements. Genotype for the renal sodium transporters has also been identified as a determinant of loop diuretic response in healthy volunteers.[5] However, the effect of genotype on diuretic response in HF patients has not been examined. We hypothesize that both race and genotype for renal sodium transporters influences response to loop diuretics in HF.

Objectives: The primary objective of this study is to investigate the association between race and genotype and chronic oral loop diuretic dose requirements in patients with systolic HF. Our secondary objective is to examine whether race or genotype influences response to IV loop diuretic therapy in a subset of patients recruited for this study who are hospitalized for decompensated HF. Our study objectives are consistent with the specific grant focus and strategic priorities of the ASHP Research and Education Foundation. Specifically, positive associations between race and/or genetics and diuretic requirements in HF could eventually lead to individualized diuretic therapy. This in turn, would advance the safety and efficacy of medication-use systems and patient medication outcomes in the HF patient population.

Study Design and Methods: This will be a prospective observational cohort study evaluating the association between race and genotype and chronic loop diuretic dose requirements in patients with systolic HF. After obtaining written informed consent, baseline data, including diuretic dose and a buccal cell sample for genetic analysis will be collected. The contribution of race and presence of a genetic variant to loop diuretic dose requirement will be examined.