

COMPARATIVE EFFICACY AND SAFETY OF REFRACTORY DIURETIC REGIMENS IN ACUTE HEART FAILURE.

Patients with heart failure (HF) are frequently hospitalized for acute decompensation secondary to intravascular volume overload and subsequently treated with loop diuretics. Unfortunately, in patients who present with more advanced stages of HF or those who have been on chronic diuretic therapy, loop diuretics alone may fail to garner adequate diuresis despite more aggressive intravenous bolus doses. This phenomenon, known as diuretic resistance or refractory diuresis, contributes to the morbidity and complexity of managing these patients. Various strategies are used to overcome diuretic resistance, however, there continues to be a lack of data on efficacy and potentially more importantly, the safety associated with these refractory diuretic regimens. One major safety issue is the effect of these regimens on renal function. Renal impairment in heart failure has become increasingly recognized as an independent risk factor for morbidity and mortality.

The purpose of this study is to evaluate for potential clinical differences between the common therapeutic regimens used for enhancing diuresis in acute HF, and to determine if we can identify predictors of response which could then be used to potentially guide optimal therapy. Our hypothesis is: the comparison of the efficacy and safety of various diuretic regimens, as assessed by urine output and incidence of renal insufficiency respectively, will differ between refractory diuretic regimens used in acute HF patients. We will test the hypothesis through 3 specific aims: 1) To compare the efficacy of various diuretic regimens in acute HF patients presenting with congestion who are considered refractory to conventional intravenous bolus dosing of furosemide, 2) To compare the relative safety of these “more aggressive” diuretic regimens in patients with refractory HF, and 3) To determine clinical predictors of efficacy and safety endpoints when refractory diuretic regimens are implemented.

A retrospective cohort study will be conducted at the LA County + USC Medical Center, evaluating patients who initially received intravenous bolus furosemide therapy upon admission to the hospital and were escalated to one of the following “more aggressive” refractory diuretic regimens: 1) continuous infusion furosemide, 2) combination of furosemide plus another diuretic agent (i.e. metolazone), 3) switched to a more potent loop diuretic such as bumetanide, or 4) combination of any previous three regimens. Data will be extracted from the Intensive Cardiac Care Unit Eclipsys computer system and verified with the paper charts when necessary. Data to be collected that is related to the study objectives includes: baseline demographics, HF characteristics, clinical status on admission, daily laboratory values, hourly and daily urine output and daily weight changes, in-hospital diuretic and medication regimen, and patient outcomes (duration of ICCU stay, and patient disposition at discharge). The primary endpoint of the study is the comparison between treatment arms of the mean hourly urine output over 24 hours after initiation of the refractory diuretic regimen. Differences within each treatment arm will be compared using paired-sample *t*-tests. Mean differences across the four treatment arms will be analyzed by one-way analysis of variance. The potential interaction of concomitant intravenous vasoactive therapy (nitroglycerin, nitroprusside, nesiritide, and inotropes) to the refractory diuretic regimens will also be assessed as a pre-specified subgroup analysis. A multivariate analysis using linear regression will be performed to examine predictors of response if the current study finds differences in efficacy and/or safety endpoints between the refractory diuretic regimens on univariate analysis.

This study will provide important information regarding the safety and efficacy of various strategies used to overcome refractory diuresis in patients with acute decompensated HF, and will potentially provide the basis for developing a protocol to determine clinical predictors of efficacy and safety endpoints when refractory diuretic regimens are implemented.