Title: Evaluating Loop Diuretic Dose Requirements After Treatment with Sodium Glucose Co-transporter-2 Inhibitors with or without Sacubitril/Valsartan for Patients with Congestive Heart Failure

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Learning Objective:
At the conclusion of my presentation, the participants will be able to explain the impact of the introduction of sodium glucose co-transporter-2 (SGLT-2) inhibitors with or without sacubitril/valsartan on an individual's daily diuretic dose requirement over the course of a year.

Self-Assessment Question
Would you empirically reduce the doses of diuretics when initiating a SLGT-2 inhibitor with or without sacubitril/valsartan based on these results?

Background:
There is limited data on the effect of introducing sodium-glucose cotransporter-2 inhibitors and/or sacubitril/valsartan on the diuretic dose requirements for patients with heart failure with reduced or preserved ejection fraction.

Methods
A retrospective chart review was conducted to include patients 18 years and older diagnosed with heart failure (New York Heart Association Class II-IV), prescribed a loop diuretic who were initiated on a SGLT-2 inhibitor with or without sacubitril/valsartan. Exclusion criteria included a contraindication to sacubitril/valsartan or SGLT-2 inhibitors, severe renal impairment (eGFR < 20 mL/min/1.73 m^2), current pregnancy or breastfeeding, type 1 diabetes, a history of angioedema, or a left ventricular assist device. The primary outcome was to evaluate loop diuretic dose requirements (torsemide equivalents) after initiation of a SGLT-2 inhibitor with or without sacubitril/valsartan at 3, 6, and 12 months. Secondary outcomes assessed the frequency of heart failure related hospitalizations and mortality. Safety outcomes included reporting of changes in renal function or electrolyte imbalances. Descriptive statistics, paired Student-T tests and Wilcoxon rank tests were used where appropriate.

Results
A total of 116 patients were included in the analysis. There was a decrease in the average loop diuretic dose requirements of 1.2 mg ($p=0.146$), 3.1 mg ($p<0.001$) and 2 mg ($p<0.001$) from the baseline average of 27.3 (SD=19.4) and the 1st, 2nd and 3rd follow-up appointments respectively. Over the 1 year follow up, there were 20.7 heart failure related acute care visits and 2.6 deaths per 100 patient years. There was a

statistically significant increase in median serum creatinine level from 1.1 to 1.2 mg/dL (p=0.027) between baseline and 3 months. An increase in estimated glomerular filtration rate from 54 to 55 mL/min/1.73 m^2 from 3-12 months (p=0.036) was observed. There were no statistically significant electrolyte imbalances that occurred.

Conclusion(s)

There is limited data on the diuretic-sparing effect the combination of a SGLT-2 inhibitor and sacubitril/valsartan have on heart failure patients. These results suggest that initiation of the above therapies may lead to a reduction in loop diuretic dosing in as early as 1 month, with the most significant reduction seen at 3 months. Renal function initially declined, but overall, showed a net improvement. These results may support empiric reduction of loop diuretics in appropriate patients.