Pilot Study of Loop Diuretics Among Individuals Receiving Hemodialysis

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Background & Methods

Patients receiving maintenance hemodialysis (HD) are more at risk to develop cardiovascular diseases, leading to increased mortality rates. Volume-related factors such as volume overload, large interdialytic weight gains (IDWGs), and higher ultrafiltration (UF) rates correlate with cardiovascular risk factors, among other modifiable contributors to cardiovascular complications such as hypertension, arterial stiffness, left ventricular hypertrophy, and heart failure. Reversing fluid overload has been shown to improve blood pressure and cardiac remodeling. Lower IDWGs and UF rates are associated with lower rates of intradialytic hypotension and less myocardial ischemia on cardiac imaging. Oral loop diuretics are one potential strategy to increase urine output and reduce volume-associated complications in HD patients. Observational data show associations between loop diuretic use and lower IDWGs, less intradialytic hypotension, and fewer hospitalizations.

Objectives:

Primary: to generate pilot data on the short-term and longer-term efficacy, safety, tolerability, and acceptability of furosemide in patients with HD-dependent kidney failure

Exploratory: to generate data on the short-term and longer-term clinical outcomes in patients with HD-dependent kidney failure receiving furosemide

Methods: 18-week open-label pilot feasibility study of escalating doses of oral furosemide. Study outcomes include short-term and longer-term acceptability, adherence, tolerability, and safety.

Study Design

Single center, open-label, non-randomized pilot study to test whether oral furosemide is safe and effective at increasing urine volume in HD patients. The study will consist of 2 periods:

Period 1 (6-week dose escalation): All participants will receive escalating doses of furosemide as tolerated, and we will examine the short-term safety, tolerability, and efficacy of furosemide. The maximum potential furosemide dose is 160mg BID.

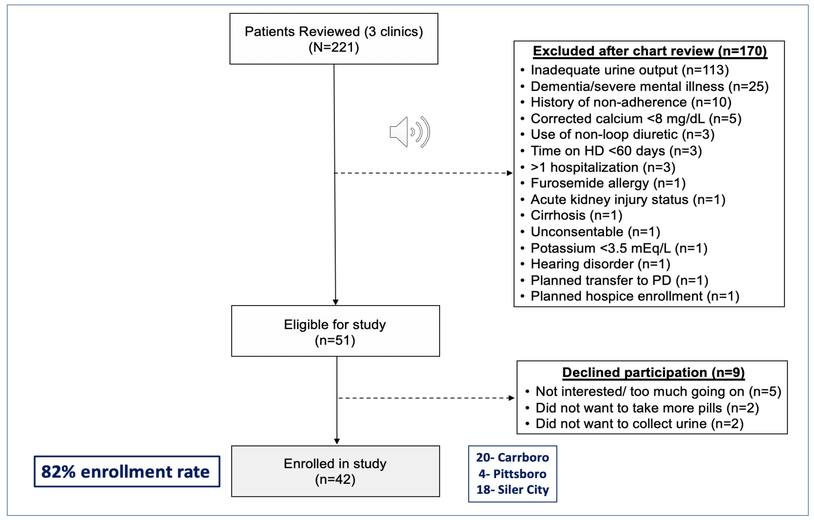
Period 2 (subsequent 12-week follow-up): All participants will continue the maximally tolerated period 1 furosemide dose, and we will examine the acceptability of and adherence to furosemide and the longer-term safety and efficacy of furosemide.

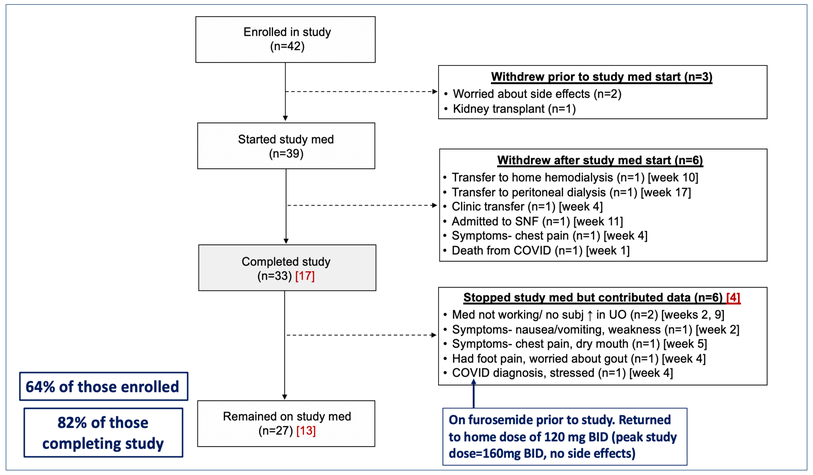
Results

UNC Research Team Activities

- Receive blood samples from clinic nurses and 24-hour urine collection containers from patients
- Process blood serum & 24-hour urine samples
- Conduct 7 hearing assessments and 13 symptom assessments with participants
- Prescribe and deliver furosemide

Study Participant Flowcharts





Baseline Characteristics

Characteristic	Value* (N=39)	Characteristic	Value* (N=39)
Age (y)	65 +/- 12; (29-85)	Diabetes	17 (44)
Female	10 (26)	Heart Failure	16 (41)
Race		Coronary Artery Disease	17 (44)
White	14 (36)	Hypertension	35 (90)
Black	23 (59)	Cancer	5 (13)
Other	2 (5)	ESKD Cause	
Hispanic	6 (15)	Diabetes	17 (44)
Dialysis Vintage (y)	2.3 +/- 2.0; (0.3-10)	Hypertension	16 (41)
Hx of Kidney Tx	0	Other	6 (15)
ACE/ARB	13 (33)	Diuretic	22 (56)
CCB	21 (54)	Other Antihypertensive	8 (21)
BB	27 (69)	Catheter Vascular Access	7 (18)
Vasodilator	2 (5)		

Baseline Furosemide Status

Pre-Study Dose [furosemide equivalent]	N=39
Not taking Loop Diuretic	**17 (44%)**
Taking Loop Diuretic	**22 (56%)**
Furosemide 20mg BID on non-HD days	1
Furosemide 40mg qday	2
Furosemide 40mg BID on non-HD days	1
Furosemide 80mg qday on non-HD days	2
Furosemide 80mg qday	3
Furosemide 80mg BID on non-HD days	4
Furosemide 80mg BID	2
Furosmide 120mg BID	1
Bumetanide 2mg [80mg] qday on non-HD days	1
Bumetanide 2mg [80mg] BID on non-HD days	1
Bumetanide 2mg [80mg] BID	1
Bumetanide 4mg [160mg] BID	1
Torsemide 40mg [80mg] qday	1
Torsemide 80mg [160mg] qday on non-HD days	1

* 14 dose variation among those taking loop diuretic at baseline

Discussion & Conclusion

Results to-date: We enrolled 42 HD patients from 3 NC clinics. To date, we have finished data collection at 2 clinics (n= 24 patients). Of those 24 patients, 16 (67%) completed the study. Study withdrawal reasons included side effect worries (n=3) and clinic transfer (n=5). Of the 16 completing the study, 13 (81%) remained on furosemide at study end.

Conclusion: Data collection is ongoing. We will use the results to inform the design and justification of a larger trial testing the clinical efficacy of loop diuretics in hemodialysis-dependent patients.

References

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