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February 2020 ~ Resource #360201

Loop Diuretic Use in Heart Failure

The chart below provides practical information on the use of loop diuretics in heart failure, presented in a "frequently asked questions" format. For information on loop diuretics use for other indications, and for other diuretics' dosing, kinetics, cost, and place in therapy, see our chart, *Comparison of Commonly Used Diuretics*. For information on diuretic use in acute heart failure, see our chart, *Acute Heart Failure: FAQs*.

Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; NYHA = New York Heart Association

Clinical Question	Pertinent Information or Resources
What is the **role** of loop diuretics in the treatment of heart failure?	• Loop diuretics are recommended for all volume overloaded patients with NYHA class II to IV heart failure to improve **symptoms**, **exercise tolerance**, and efficacy of other heart failure medications (e.g., beta-blockers).[2] • A thiazide could be used instead of a loop for patients with mild fluid retention and hypertension, for blood pressure control.[2] • Unlike potassium-sparing diuretics (e.g., spironolactone, eplerenone), loop diuretics have not been shown to reduce the risk of death.[2,3]

How do loop diuretics **compare**?	• **Bioavailability**: bumetanide and torsemide have better bioavailability (i.e., less erratic absorption) than furosemide, so some patients will respond better to them than to furosemide.[2]
	  • Furosemide bioavailability is about 50% (range 10% to 90%).[4,8]
	  • Torsemide and bumetanide bioavailability is >80% to 90%.
	• **Cost**: furosemide is the least expensive loop diuretic
	• **Efficacy**: torsemide benefits over furosemide in regard to heart failure hospitalization and improvement in NYHA functional class have not been proven at equivalent doses [Evidence level A-2].[6,7] There is not much data with bumetanide in heart failure.

What is the role of ethacrynic acid?	• Ethacrynic acid is rarely used because:
	  • data on ethacrynic acid in heart failure is lacking.
	  • it may be more ototoxic than other loops.[13]
	  • it is the most expensive loop diuretic (U.S.: ~$9.98/each 25 mg tablet;[a] Canada: $1.04/each 25 mg tablet[a]).
	• Ethacrynic acid does not contain a sulfa group and is a possible alternative in sulfonamide-allergic patients. For more information on use of loop diuretics in these patients, see our chart, *Sulfa Drugs and the Sulfa-Allergic Patient*.

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Clinical Question	**Pertinent Information or Resources**
How do you **dose** loop diuretics in the treatment of heart failure?	--For information on diuretic use in **acute** heart failure, see our chart, *Acute Heart Failure: FAQs*.-- **General concepts**: • High sodium intake and NSAID use reduces diuretic efficacy.[2] • In heart failure with **preserved** ejection fraction, diuretics must be dosed cautiously because preload reduction can cause reduced cardiac output with hypotension and renal impairment.[9] • Start with a low dose, and increase to achieve target weight (e.g., a 0.5 to 1 kg weight loss daily to goal) and symptoms.[2,10] Titrate to eliminate clinical signs/symptoms of fluid overload without causing hypotension or renal insufficiency, or limiting the up-titration of disease-modifying agents (e.g., ACEIs, ARBs, potassium-sparing diuretics).[1,2] • Not all patients will need a daily scheduled dose.[2] Consider transitioning to as-needed use once patients are stable and receiving optimized guideline-directed medical therapy (i.e., beta-blockers and inhibitors of the renin-angiotensin system), without signs of fluid retention [Evidence level B-1].[1] • Patients can self-titrate dose based on daily weights.[2] Customize our patient education handout, *Heart Failure Meds and More*, with your patient's diuretic dose and instructions. • Giving furosemide or bumetanide twice daily might improve efficacy.[2] But first, try increasing the once-daily dose to the maximum single dose (or where there's no further diuresis); diuresis depends on how high the loop concentration gets in the urine.[11] • If furosemide or bumetanide is given twice daily, give the second dose in the afternoon to minimize nocturia.[2] • Check renal function and electrolytes at baseline and one to two weeks after initiation or dosage increase.[10] **Dosing of loops for chronic heart failure**: • Furosemide: initial 20 to 40 mg once or twice daily; max total daily dose 240 mg (600 mg in renal impairment).[2,10,11] • Bumetanide: initial 0.5 to 1 mg once or twice daily; max total daily dose 10 mg.[2,11] • Torsemide: initial 10 to 20 mg once daily; max total daily dose 200 mg.[2,11]

What are some considerations when **switching loop diuretics**?
 	
Continued…
	General considerations
	• Furosemide is the most commonly used loop diuretic.[2] A switch to bumetanide or torsemide could be considered for patients:
	  • who require hospitalization for acute heart failure despite furosemide use.[8]
	  • who are not achieving good symptomatic control despite optimization of guideline-directed medical therapy and furosemide.[7]
	  • who may have impaired furosemide absorption due to splanchnic congestion.[8]

More. . .

Clinical Question	**Pertinent Information or Resources**
Considerations when **switching loop diuretics**, continued	• Consider switching to torsemide rather than bumetanide; torsemide has a longer duration of action and more evidence in heart failure.[2,6,7] Dosing considerations: • Bumetanide 0.5 to 1 mg orally = furosemide 40 mg orally[5] • Torsemide 10 to 20 mg orally = furosemide 40 mg orally[5] • Oral furosemide bioavailability is only about 50%.[4] • Ethacrynic acid 50 mg orally ~ furosemide 40 mg orally[14]
Can other diuretics be **combined** with loops to improve response?	• Switching from furosemide to bumetanide or torsemide may be preferable to adding a thiazide to improve response, as combining diuretics increases the risk of electrolyte disturbances.[2,8] • Consider adding spironolactone or eplerenone before trying a thiazide; spironolactone and eplerenone provide some diuresis, offset potassium loss, and improve outcomes, particularly in heart failure with reduced ejection fraction.[2,11] • If a thiazide is added, it is not necessary to time the thiazide so that it is given prior to the loop.[12] (For example, there is no proof that giving the thiazide 30 minutes before the loop provides better diuresis.) • Contrary to popular belief, thiazides can be effective if CrCl is <30 mL/min.[8] Metolazone may be most effective.[13]

a. U.S. cost is wholesale average cost. U.S. medication pricing by Elsevier, accessed January 2020. Canadian cost is wholesale.

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Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*****	1. High-quality RCT 2. SR/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*****	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
RCT = randomized controlled trial; **SR** = systematic review
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. http://www.aafp.org/afp/2004/0201/p548.pdf.]

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