# Use of Diuretics in the Treatment of Heart Failure in Older Adults

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**KEYWORDS**

• Heart failure • Diuretics • Fluid congestion • Elderly patients

**KEY POINTS**

- Diuretic therapy remains a cornerstone of heart failure (HF) therapy.
- In the treatment of volume-overloaded patients, diuretics clearly improve symptoms and quality of life.
- Despite the acceptance of diuretic therapy for the treatment of symptoms, considerable debate has ensued for many decades about the impact of this class of agent on mortality, cardiac function, and disease progression.
- Accordingly, diuretics should be used judiciously in patients with HF, at the minimum effective dose, with careful monitoring of electrolyte balance, and continued only if there is a demonstrable ongoing clinical need.
- Aldosterone receptor antagonists (ARAs) should be distinguished from both loop and thiazide-type diuretics in that outcomes data support their routine use in advanced systolic HF and in patients after myocardial infarction with clinical HF symptoms and a left ventricular ejection fraction less than 40%.
- ARAs also can be considered for use in patients with diastolic HF and a normal ejection fraction.

Most therapies used in the contemporary management of heart failure (HF) have been rigorously evaluated in large-scale clinical trials to assess their beneficial effects on quality of life and prognosis. Such therapies include angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers, β-adrenergic-blockers, and aldosterone receptor antagonists (ARAs). Diuretics are the most commonly prescribed class of drugs in patients with HF and in the short term they remain the most effective treatment for relief from fluid congestion. Diuretic therapy in the patient with HF often is as much an art as a science. Moreover, as a class of drugs, diuretics are fairly heterogeneous in their effects. Diuretic therapy in HF always should be accompanied by dietary sodium restriction. Important considerations in defining diuretic effect include issues of dose amount, frequency of dosing, concomitant medications, blood pressure, and, most importantly, the degree to which cardiac function is compromised. Diuretic combinations are often quite effective in the more advanced stages of HF. Diuretic-related electrolyte side effects are common and require ongoing vigilance both to detect their occurrence as well as to track their correction.

Diuretics are tools of considerable therapeutic importance. First, they effectively reduce blood pressure, while at the same time decreasing the morbidity and mortality associated with

This is an updated version of an article that appeared in *Heart Failure Clinics*, Volume 3, Issue 4.
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Heart Failure Clin 13 (2017) 503–512
http://dx.doi.org/10.1016/j.hfc.2017.02.006

hypertension. The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Hypertension continues to recommend diuretics as first-line therapy for the treatment of hypertension.[1] In addition, they remain an important component of HF therapy, in that they improve the symptoms of congestion, which typify the more advanced stages of HF.[2–6] This article reviews the mode of action of the various diuretic classes and the physiologic adaptations that follow and sets up the basis for their use in the treatment of volume-retaining states, particularly as applies to the elderly. In addition, the article reviews the common side effects related to diuretics.

## OVERVIEW

Guideline-promulgating committees have positioned diuretics as necessary adjuncts in the medical therapy for HF when symptoms of volume overload exist.[2–6] Diuretics are typically used first for the acute relief of congestion and thereafter for achieving and maintaining a target or ''dry'' weight. Diuretic doses are typically higher in the case of congestion relief and can generally be scaled back in the chronic treatment phase of HF. Diuretic therapy typically results in rapid improvement of dyspnea and increased exercise tolerance.[7] No controlled randomized trials have assessed the effect on symptoms or survival of thiazide and loop diuretics, and they should always be administered in combination with ACE inhibitors and β-blockers if tolerated.

The relation of systolic to diastolic HF is clearly shifted toward diastolic HF in elderly patients, especially in women.[8] Mortality increases with systolic dysfunction in elderly patients compared with younger patients with HF.[9] Mortality is less with diastolic dysfunction, but still higher compared with elderly individuals without HF.[10] In addition, morbidity is increased both with diastolic and systolic HF in elderly patients. Drug therapy for systolic HF in elderly patients is similar to younger patients, although guideline recommendations for drug therapy are based in most cases on studies conducted in younger patients with systolic HF. However, when administering drug therapy for systolic HF in the elderly, clinicians should be mindful of the physiologic decrease in renal function with age and the more frequent renal impairment that occurs in elderly patients receiving diuretics for HF management.[11] In addition, loop diuretic treatment of any patient with HF always should be at the lowest effective dose. This is particularly so in the elderly patient with HF because the hypercalciuria, produced in a dose-dependent manner by loop diuretics,[12] increases the bone-fracture rate, a clinical finding also observed with thiazide-type diuretics.[13]

## TREATMENT ALGORITHM FOR DIURETIC USE IN HEART FAILURE

A diuretic treatment algorithm for the treatment of HF can become extremely complicated. No one such algorithm can ever meet the treatment needs of all patients, particularly elderly patients. In cases involving the elderly, negative effects of excessive diuresis on blood pressure and renal function often have an impact on decisions related to diuretic dose and frequency. **Table 1** offers some guidance on the order of medication choice and the basis for such choices. Loop diuretics offer short-term benefits in HF because of symptomatic relief. However, in the long term, they have the potential to adversely influence outcome due to electrolyte changes or excessive neurohumoral activation.[14–16] Consequently, in the long term, diuretic withdrawal or dosage reduction is desirable.[17] Diuretic withdrawal (or interruption) is facilitated by adherence to a low-sodium (low-$Na^+$) diet. Such withdrawal is typically better tolerated in patients requiring lower diuretic doses, a patient subset characterized by having both smaller ventricles and a higher left ventricular ejection fraction.[17]

## INDIVIDUAL CLASSES OF DIURETICS

Interclass and intraclass differences exist for all diuretic classes. The diuretic classes of note include carbonic anhydrase inhibitors, loop and distal tubular diuretics, and potassium ($K^+$)-sparing agents.[16]

### *Carbonic Anhydrase Inhibitors*

Acetazolamide is the only carbonic anhydrase inhibitor with relevant diuretic effects. Acetazolamide is readily absorbed and undergoes renal elimination predominantly by tubular secretion. Its administration is ordinarily accompanied by a brisk alkaline diuresis. Although carbonic anhydrase inhibitors are proximal tubular diuretics (where the bulk of $Na^+$ reabsorption occurs), their net diuretic effect is modest, because $Na^+$ reabsorption in more distal nephron segments offsets proximal $Na^+$ losses. Acetazolamide use is constrained by both its transient action as well as the development of metabolic acidosis with its prolonged administration. Alternatively, acetazolamide (250–500 mg daily) can correct the metabolic or contraction alkalosis that on occasion occurs with aggressive thiazide or loop diuretic therapy.[18]