

# Current approach to diuretic resistance in heart failure

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## Abstract

Diuretics are one of the main drugs for heart failure, which is the leading cause of morbidity and mortality. It contributes to the reduction of symptoms and hospitalizations. However, diuretic resistance is seen in 20-30% of patients with heart failure. Various parameters such as weight loss, congestion status, urine output, urine sodium excretion is evaluated in determining diuretic resistance. Treatments such as restriction of salt and fluid intake, discontinuation of nonsteroidal anti-inflammatory drugs, increasing diuretic dose and frequency, combination of diuretics from different classes, hypertonic saline infusion or dopamine infusion are used in diuretic resistance.

## Introduction

Heart failure is seen in 1% of patients over 65 years old [1]. Heart failure is one of the leading causes of morbidity and mortality. Diuretics are among the main drugs used in this disease with high morbidity and mortality rates [1-2]. However, 20-30% of patients with heart failure have diuretic resistance. Diuretics reduce congestion and reduce hospitalizations [1]. Therefore, we present the current approach to diuretic resistance in heart failure in this article.

## Mechanisms of diuretic resistance

Low systemic blood pressure, high blood urea nitrogen, ischemic heart failure and diabetes are predictors of diuretic resistance. Diuretics are ineffective in case of venous edema, lymphatic edema, and shifting of the intravascular volume to the third space. No sodium and fluid restriction, hepatic cirrhosis, hypoalbuminemia, nephrotic syndrome, insufficient absorption, insufficient dosage of the drug, low frequency of drug intake, drug nonadherence, decreased diuretic secretion, insufficient kidney to the drug, use of nonsteroidal anti-inflammatory drugs, increased renin angiotensin aldosterone system activation causes diuretic resistance [1,3].

## Definition of diuretic resistance

1 mg bumetanide, 20 mg torsemide and 40 mg furosemide are equivalent. Congestion persists despite using furosemide over 80 mg, weight change <2.7 kg despite 40 mg furosemide or equivalent diuretic, urine output <1400 ml/day despite using 40 mg furosemide or equivalent diuretic, fractional excretion of sodium in basal <0.2%, a urinary sodium concentration / urinary furosemide concentration ratio of <2 mmol / mg or a urinary sodium amount of <90 mmol despite 160 mg furosemide twice in 3 days is defined as diuretic resistance [4,5].

## Treatment

### Initial measures

Daily sodium intake should be below 100 mEq/day. Nonsteroidal anti-inflammatory therapy should be discontinued. The frequency and dosage of loop diuretics should be increased [1,5-7].

In hospitalized patients, 80 mg intravenous loop diuretic or intravenous loop diuretic is started at 2.5 times the oral dose at home.

Urine sodium strategy (emergency pathway) for evaluating the diuretic response or urine output strategy (established pathway) can be used [2,5-7].

Spot urine sodium is checked 1-2 hours after the diuretic is started in the emergency pathway. If urine sodium is >50-70 mmol/l, urine sodium assessment is repeated after each dose. Current doses are repeated every 6-12 hours [2,5-7].

In the established pathway, urine output is evaluated 2-6 hours after the diuretic is started. If the urine output is above 150 ml/hour, the current doses are repeated every 6-12 hours [2,5-7].

If spot urine sodium is <50-70 mmol/l or urine output is <150 ml / hour, twice the previous dose is administered intravenous loop diuretic. In insufficient diuretic response, up to 300 mg of furosemide and equivalent loop diuretics are repeated. Combination therapy is started in case of insufficient diuretic response. The first choice in combination therapy is to add a thiazide diuretic to the loop diuretic. The second preference in combination therapy is to add acetazolamide, amiloride or spironolactone to the loop diuretic [2,5-7].

## Advanced measures

Hypertonic saline infusion improves diuresis and renal function while shortening hospitalization. The addition of dopamine infusion to low dose intravenous furosemide provides urine output similar to high dose diuretic [5-7].

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