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Potential novel therapy in acute decompensated heart failure with volume overload

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Article type: Therapy (Clinical Trial)

Rankings: *Methods* 5/5, *Usefulness* 3.5/5

Introduction

Background

Acute decompensated heart failure is a prevalent condition associated with major morbidity and mortality and results in numerous emergency department visits and hospital admissions.

Objectives

Determine if acetazolamide can improve the efficiency of loop diuretics and enhance decongestion in patients with acute decompensated heart failure.

Methods

Design

The ADVOR trial is a multicenter, parallel-group, double-blind, randomized, placebo-controlled trial. Randomization was stratified by LVEF ($\leq 40\%$ or $> 40\%$) and trial site.

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Setting

Recruitment between November 2018 and January 2022 at 27 sites across Belgium.

Subjects

Adults admitted for heart failure with signs of fluid overload (edema, pleural effusion or ascites) and elevated NT-proBNP or BNP. Patients were required to be on maintenance oral diuretic therapy and to have had their left ventricular ejection fraction (LVEF) assessed in the previous year.

Intervention

Following randomization, patients received a 500 mg bolus of acetazolamide or placebo once a day in addition to intravenous loop diuretics.

Outcomes

Primary outcome was the proportion of patients with successful decongestion within 3 days after randomization. The congestion score used is a composite of the degree of edema, pleural effusion and ascites.

Results

A total of 2915 patients were evaluated, of whom 519 were randomized to the acetazolamide (259 patients) or placebo (260 patients) group. The primary outcome of decongestion within 3 days occurred in 108/256 patients (42.2%) in the treatment group and in 79/259 (30.5%) in the placebo group (Risk ratio 1.46; 95% CI 1.17–1.82; $P < 0.001$). Treatment was less effective in patients receiving a higher home maintenance loop diuretic dose.

The secondary outcome of death from any cause or rehospitalization for heart failure during the 3-month follow-up occurred in 76/256 patients (29.7%) in the acetazolamide group and in 72/259 patients (27.8%) in the placebo group (Risk ratio 1.07; 95% CI 0.78–1.48; NS). The duration of hospital stay was 8.8 days (95% CI 8.0–9.5) in the treatment group and 9.9 days (95% CI 9.1–10.8; NS) in the placebo group.

Adverse events frequency was similar in the two groups, and metabolic acidosis did not occur in any patient.

Appraisal

Strengths

- Targets a clinically relevant question
- Robust study design
- Randomization with stratification according to the LVEF

Limitations

- The majority of patients were Caucasian, limiting the generalizability of the results
- The primary outcome (decongestion) is not patient-centered
- The congestion score is infrequently used in clinical practice
- The congestion score depends on subjective clinical examination and is not a validated tool
- Patients with newly diagnosed heart failure were excluded
- Patients treated with SGLT2 inhibitors were excluded
- The power of the study does not allow us to conclude on the absence of adverse effects

Context

Loop diuretics are the mainstay of decongestant therapy and are used as a monotherapy in approximately 70% of patients presenting with acute decompensated heart failure [1, 2]. However, as shown in the Diuretic Optimization Strategies Evaluation (DOSE) trial, few patients achieve complete decongestion after 72 h of loop diuretic treatment [3]. In practice, local internal medicine experts suggest adding hydrochlorothiazide or metolazone for patients resistant to high-dose IV furosemide. Combination therapy with acetazolamide is rarely prescribed for patients admitted with acute decompensated heart failure.

Bottom line

This study adds evidence on diuretic combination strategies to treat decompensated heart failure. The addition of acetazolamide to standard therapy in carefully selected admitted patients increases the odds of having a successful decongestion. Emergency department physicians are unlikely to use combination therapy or acetazolamide in the initial management of acute decompensated heart failure.

Declarations

Conflict of interest None to declare.

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