

Acetazolamide Therapy in Patients with Heart Failure: A Meta analysis

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Background: Acute heart failure (AHF) is a sudden worsening of chronic HF necessitating hospitalization. It involves complex pathophysiology including activation of multiple pathways (inflammatory, neurohumoral, immune) in multiple organs leading to unfavorable short and long-term prognosis. Impaired diuretic response caused by sodium reabsorption is associated with increased rehospitalization and mortality. Since a large amount of sodium is reabsorbed in the proximal tubule, acetazolamide induces natriuresis and may facilitate further diuresis. We performed this meta-analysis to assess the effects of acetazolamide therapy on natriuresis and clinical symptoms of congestion including rales and dyspnea.

Methods: A literature search was conducted using EMBASE, MEDLINE, and Google Scholar Database from inception through 17th April 2023 to identify studies evaluating the use of acetazolamide in AHF. Search terms included 'acetazolamide' and 'acute heart failure'. Additional relevant articles were evaluated using references of included articles. Eligible studies were randomized clinical trials, published in English, that assessed the effects of addition of acetazolamide to standard diuretic therapy as compared to placebo on natriuresis at 24-48 hours and decongestion. Study quality was assessed by Cochrane risk of bias tool. RevMan 5.4 was used for the analyses. Study results were analyzed using a random effects model. I² statistics were applied to assess the between-study heterogeneity.

Results: Three eligible RCTs of 66 screened studies enrolled a total of 284 heart failure patients who received Acetazolamide in addition to their background diuretics treatment. Of the excluded 63 studies, 33 were reviews, 16 study design was not RCT, two duplicate studies, 6 studies had other outcomes of interest and seven studies compared acetazolamide with other diuretics. Most studies compared acetazolamide with other add on diuretics including spironolactone, metolazone, etc. One study was identified by cross reference and one study Verbrugge et al 2014 that met all the criteria could not be included since it reported natriuretic effects in with standard error without sample size. The results showed that when compared to a placebo, Acetazolamide significantly increased natriuresis at the end of 24 to 48 hours, with a standardized mean difference (SMD) of 0.40 (95% CI, 0.24 to 0.57, p value <0.00001, I²=0). Two of three studies evaluated the effect of addition of Acetazolamide on clinical symptoms of HF, including dyspnea and rales. However, in this 259 patients, addition of Acetazolamide did not demonstrate a significant improvement in dyspnea or rales compared to standard treatment, with an OR of 1.34 (95% CI, 0.37 to 4.91, p = 0.66 I²=70). Cochrane risk of bias showed low risk for two studies and low to moderate for one study with uncertainty in allocation.

Conclusions: Our study demonstrates a significant increase in natriuresis but no improvements in clinical symptoms of congestion with use of acetazolamide among HF patients. Multiple strategies to overcome diuretic resistance are being explored to improve in-hospital AHF.