

Treatment of Acute Decompensated Heart Failure: Systematic Literature Review

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Abstract

This review is aiming to discuss treatment of acute decompensated heart failure, the presented review was conducted by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. were searched up to November 2018 for published and unpublished studies and without language restrictions, if several studies had similar findings, we randomly selected one or two to avoid repetitive results. On the basis of findings and The results of these clinical experiments showed the treatment of acute decompensated heart failure. On the basis of the findings and results, this review found Rolofilin, an adenosine A1 receptor antagonist, serelaxin, recombinant human relaxation 2, diuretic.

Keywords: Treatment; Acute; Decompensated Heart Failure

Introduction

Decompensated acute heart failure is responsible for over a million treatments annually in the United States. It is the most common reason for hospital admission among patients over 65 years old [1]. Intravenous loop diuretics are an essential component of current treatment and are administered to approximately 90% of patients who are hospitalized with heart failure [2]. Despite decades of clinical experience with these agents, prospective data to guide the use of loop diuretics are sparse, and current guidelines are based primarily on expert opinion [3,4]. As a result, clinical practice varies widely with regard to both the mode of administration and the dosing.

High doses of loop diuretics are indicative of the severity of the disease but have side effects such as activation of renin-angiotensin and the sympathetic nervous system, electrolyte disturbances and worsening of kidney function. Scientific studies have established a relationship between high doses of diuretics and harmful clinical outcomes, including kidney failure, Heart failure, death [5-7].

But there is uncertainty about the doses, and the optimal management situation. Pharmacokinetic and pharmacodynamics data indicate that there are potential benefits to continuous infusion compared to intermittent bolus. Although many small studies assessed the role of continuous diuretics infusion in patients with heart failure, they lacked the ability to address clinical questions [8,9].

Preexisting chronic kidney disease and worsening renal function are common in patients hospitalized with acute heart failure and are associated with poor outcomes [10,11]. Multiple factors are responsible for this association [11,12], including coexisting conditions, less use of effective therapies in patients with renal dysfunction than in patients without renal dysfunction, and inadequate treatment of volume overload because of a suboptimal response to diuretics or concern regarding diuretic toxicity [11,13].

Adenosine is an important intermediary in the kidneys for both impaired kidney function, diuretic resistance, glomerular filtration rate (GFR) and stimulating renal release. Also, activation of A₁ receptors enhances the absorption of proximal tubular sodium [14,15]. In patients with heart failure, A₁ receptor antagonists may maintain GFR, enhance sodium excretion and improve the response of diuretics.

Previous studies involving patients with heart failure have shown that co-administration of A₁-receptor antagonists and loop diuretics enhances diuresis while maintaining or improving renal function [16,17]. In the PROTECT (Placebo-Controlled Randomized Study of the Selective A₁ Adenosine Receptor Antagonist Rolofylline for Patients Hospitalized with Acute Decompensated Heart Failure and Volume Overload to Assess Treatment Effect on Congestion and Renal Function) pilot study, a dose-finding study [18], rolofylline at a dose of 10, 20, or 30 mg or placebo was administered daily for up to 3 days in patients with acute heart failure, underlying renal dysfunction, and volume overload. As compared with patients who received placebo, patients who received the 30-mg dose of rolofylline had greater relief of dyspnea and less worsening of renal function, with a trend toward fewer deaths or readmissions for heart or renal failure. The present phase 3 PROTECT trial was designed to confirm these findings [19].

Admission to hospital for heart failure portends an increased risk of poor outcomes, with a 5 - 15-times increase in the risk of death compared with ambulatory patients and a mortality rate of 10 - 20% in the 6 months after hospital discharge [20,21]. Although hospital admission could simply herald disease progression, this event and the related interventions might also directly contribute to poor outcomes through increased neurohormonal and inflammatory activation, hemodynamic compromise and consequent end-organ damage [20,22]. Drugs that prevent or treat these factors might favorably affect the clinical course and prognosis of these patients, even if given for a short time during the acute episode. Serelaxin is recombinant human relaxin-2, a naturally occurring peptide that regulates maternal adaptations to pregnancy [23] with several effects potentially relevant to the treatment of acute heart failure, including increased arterial compliance, cardiac output, and renal blood flow [24,25]. Pre-RELAX-AHF [26] a phase 2, dose finding study with 234 patients, suggested beneficial effects of serelaxin on both dyspnea and post-discharge clinical outcomes in patients admitted for acute heart failure, with evidence of congestion, normal-to-raised blood pressure, and mild-to-moderate renal dysfunction. The RELAX in Acute Heart Failure (RELAXAHF) trial was done in the same targeted patient population to evaluate the effects of serelaxin on dyspnea relief and post-discharge clinical efficacy outcomes, as well as its safety and tolerability [27].

Methods

This review was conducted in November 2018 in accordance with the preferred reporting lines for systematic reviews and metrics for the Meta-Analysis Announcement (PRISMA) for systematic reviews. All subjects related to treatment of acute decompensated heart failure were reviewed, such as Rolofilin, adenosine A₁ receptor antagonists, serlaxine, recombinant human relaxation 2, diuretic.

To reach the goal, Medline, Embase, Web of Science, Science Direct, and Google Scholar were searched for research, articles, and reports published over the past 15 years.

Search completed without language restrictions. Data were extracted from the study year, study design and major results of diabetes. Selected studies were summarized and unproductive studies were excluded. The data specified is shown in table 1.

Author and year	Sample	Management	Key point
Barry M, 2010 [28]	2033 patients were randomly assigned	rolofylline, an adenosine A ₁ -receptor antagonist	Rolofylline did not have a favorable effect with respect to the primary clinical composite end point, nor did it improve renal function or 60-day outcomes. It does not show promise in the treatment of acute heart failure with renal dysfunction.
John R, 2013 [29]	1161 patients were randomly assigned	Serelaxin, recombinant human relaxin-2,	Treatment of acute heart failure with serelaxin was associated with dyspnoea relief and improvement in other clinical outcomes, but had no effect on readmission to hospital. Serelaxin treatment was well tolerated and safe, supported by the reduced 180-day mortality.
Michael F, 2011 [30]	308 patients	Diuretic	Among patients with acute decompensated heart failure, there were no significant differences in patients' global assessment of symptoms or in the change in renal function when diuretic therapy was administered by bolus as compared with continuous infusion or at a high dose as compared with a low dose

Table 1: Results from sequencing studies.

Inclusion criteria

Inclusion criteria were decompensated heart failure: acute, treatment.

Exclusion criteria

Irrelevant articles not related to the aim of this review and articles that did not meet the inclusion criteria in this review.

Data extraction and analysis

Information relating to each of the systematic review question elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of. treatment of acute decompensated heart failure.

Results and Discussion

Rolofylline, as compared with placebo, did not provide a benefit with respect to the primary end point (odds ratio, 0.92; 95% confidence interval, 0.78 to 1.09; P = 0.35). Persistent renal impairment developed in 15.0% of patients in the rolofylline group and in 13.7% of patients in the placebo group (P = 0.44). By 60 days, death or readmission for cardiovascular or renal causes had occurred in similar proportions of patients assigned to rolofylline and placebo (30.7% and 31.9%, respectively; P = 0.86). Adverse-event rates were similar overall; however, only patients in the rolofylline group had seizures, a known potential adverse effect of A₁-receptor antagonists [28].

Clinical trials were conducted on 1161 patients randomized to Serelaxin (n = 581) or placebo (n = 580). The results of Serelaxin GDIC in improving primary VAS AUC dyspnea endpoint (448 mm x h, 95% CI 120 - 775; p = 0.007), but did not affect other primary endpoint (Likert scale; placebo, 150 patients [26%]; Serelaxin, 156 [27%]; P = 0.70).

There are no reported significant effects of secondary endings of CVD or hospitalization for heart failure or renal failure (placebo, 75 events [Kaplan Meyer estimate for 60 days, 13.0%]; Serelaxin, 76 events [13.2%]; Risk ratio [HR] 1.02 [0.74 - 1.41], p = 0.89) or live days outside the hospital until day 60 (placebo, 47.7 [SD 12.1] days; serelaxin, 48.3 [11.6]; p = 0.37). There were significant reductions in other pre-determined endpoints, including fewer deaths per day 180 (placebo, 65 deaths; serelaxin, 42; HR 0.63, 95% CI 0.42-0.93; p = 0.019) This is due to the treatment with Cerelaxin [29].

There was no significant difference in global patient assessment of symptoms in comparing swallowing with infusion (mean AUC, 4236 ± 1440 and 4373 ± 1404 , respectively; $P = 0.47$) or in the mean change in the creatinine level (0.05 ± 0.3 mg per deciliter [4.4 ± 26.5 per liter] and 0.07 ± 0.3 mg per dL [6.2 ± 26.5 per liter], respectively; $P = 0.45$). In There was no significant difference in global patient assessment of symptoms in comparing swallowing with infusion (mean AUC, 4236 ± 1440 and 4373 ± 1404 , respectively; $P = 0.47$) or in the mean change in the creatinine level (0.05 ± 0.3 mg per deciliter [4.4 ± 26.5 per liter] and 0.07 ± 0.3 mg per dL [6.2 ± 26.5 1 l per liter], respectively; $P = 0.45$) [30].

The clinical and economic burdens of heart failure are well described. Over the past 25 years, advancement of treatment has improved symptoms, quality of life and increased survival among patients with chronic heart failure. In contrast, new treatments have consistently failed to improve outcomes for patients with heart failure as well as patients with chronic kidney disease or impaired kidney function at high risk [28].

There is a slight improvement in respiratory measures, associated with significant reductions in early progressive heart failure events, signs and symptoms of congestion, and the initial length of hospital stay as a result of RELAX-AHF. However, there was no improvement in hospital readmission for heart failure or kidney failure. A 37% decrease in cardiovascular deaths and all causes was observed in patients treated with serelaxin and blood pressure was moderately reduced and was well tolerated with no marked distinction in the pro-SMD and lower rate of renal adverse events compared to placebo [29].

There is little potential data to guide the decision making process regarding the use of these factors. No statistically significant differences were found in the global patient evaluation of symptoms or change in creatinine level from baseline to 72 hours when administration of diuretic treatment by swallowing compared to continuous infusion or with a low dose strategy compared to a high dose strategy [30].

Conclusion

The results of these clinical experiments showed the treatment of acute decompensated heart failure. On the basis of the findings and results, this review found Rolofilin, an adenosine A₁ receptor antagonist, serlaxine, recombinant human relaxation 2, diuretic.

Conflict of Interest

The authors of this article hasn't receive and support for this work and it was completely self-funded.

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