ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 05 | May - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

THE CONUNDRUM OF HYPERTONIC SALINE INFUSION IN REFRACTORY ACUTE DECOMPENSATED HEART FAILURE (ADHF)

Internal Medicine

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ABSTRACT

Background: Refractory acute decompensated heart failure (ADHF) remains a therapeutic challenge, particularly in patients with diuretic resistance and worsening congestion. Hypertonic saline infusion (HSI), when used alongside loop diuretics, has emerged as a potential strategy to overcome diuretic resistance by improving intravascular volume distribution and renal perfusion thus improving natriuresis and prompt decongestion. **Objectives:**This study sought to evaluate the clinical outcome, practical safety and efficacy of hypertonic saline treatment along with high dose diuretics for refractory acute decompensated heart failure (ADHF).**Methods:** This study included 20 patients admitted with refractory ADHF who failed to respond adequately to conventional heart failure therapy, including high-dose loop diuretics. Hypertonic saline infusion (3% NS) was administered in conjunction with diuretics. The primary endpoint was clinical improvement, defined as increased urine output, weight loss and symptomatic relief of congestion. Secondary endpoints included in-hospital mortality and adverse events. Data were analyzed using descriptive statistics; proportions were expressed as percentages.**Results:**Out of the 20 patients treated, 18 patients (90%) demonstrated significant clinical improvement, characterized by enhanced diuresis, Significant weight loss, improved renal function, reduction in congestion, NYHA class improved in 85% of patients and symptomatic relief. One patient (5%) showed no significant improvement (non-responder) and one patient (5%) succumbed to death during hospitalization, attributed to advanced disease severity and multiple comorbidities. No significant treatment-related adverse effects, including electrolyte imbalance, renal deterioration, serious arrhythmia or neurologic complications were observed. The high rate of clinical response suggests a favorable outcome compared with historically reported poor prognosis in refractory ADHF.**Conclusion:**Hypertonic saline infusion appears to be a promising adjunctive therapy in patients with refractory acute decompensated heart failure, showing a high rate of clinical improvement in this study. While mortality remains a concern in advanced heart failure, HSI may offer benefit in carefully selected patients.**Take-Home Message:**Hypertonic saline infusion may offer a viable adjunctive option in diuretic-resistant acute decompensated heart failure, with high response rates and acceptable safety in a real-world.

KEYWORDS

Acute Decompensated Heart Failure, Hypertonic Saline Infusion, Diuretic Resistance, Refractory Congestion, Loop Diuretics

INTRODUCTION

Heart failure (HF) is highly prevalent worldwide, affecting millions of patients. Acute Decompensated Heart Failure (ADHF) remains a major cause of hospitalization and is typically driven by volume overload, and aggressive diuretics are the cornerstone of therapy. However, high-dose diuretics can exacerbate renal dysfunction, and up to one-third of patients develop diuretic resistance (i.e. inadequate natriuresis and diuresis despite escalating diuretics). Diuretic resistance portends prolonged hospitalization, frequent readmissions, and increased mortality. Various strategies (continuous infusions, sequential nephron blockade, ultrafiltration) have been tried with limited success[1,2].

An emerging strategy is the addition of intravenous hypertonic saline (HS, typically 3% NaCl) to boost diuresis. HS is thought to osmotically pull interstitial fluid into the intravascular compartment, improving renal perfusion and delivery of diuretics along with sodium to the Loop of Henle and chloride-mediated restoration of tubular responsiveness[3,4,5]. Early case series have reported that HS plus high-dose furosemide produced faster decongestion, greater weight loss, and improved metabolic parameters in diuretic-resistant ADHF. For example, Ahmad *et al.* reported that HS infusion significantly increased urine output and weight loss without causing dangerous hypernatremia or respiratory compromise. However, evidence is still limited to observational reports from specialized centers, and HS therapy in ADHF has not been widely adopted due to its counterintuitive nature. [4,5,6]

To further investigate, we conducted a single-center study at Zydus Medical College and Hospital, Dahod, India. We enrolled 20 consecutive ADHF patients with refractory congestion (persistent congestion and symptoms despite high-dose diuretics). All patients received intravenous 3% Normal Saline infusions added to their ongoing aggressive diuretic regimen. We assessed changes in body weight, fluid balance, serum electrolytes, renal function and clinical status before and after HS therapy. Our aim was to determine whether HS infusion improves decongestion and is safe in this population, as suggested by prior reports.

Materials and Methods

Study Design and Patients: We performed a prospective study of 20 patients admitted with ADHF and clinical evidence of diuretic resistance (persistent volume overload despite high-dose loop diuretics). Inclusion criteria were age >18 years and failure to decongest on standard diuretic therapy; patients with significant hypernatremia, hypertensive emergency, or severe chronic kidney disease (eGFR <60 mL/min/1.73 m²) were excluded. Institutional ethics committee approval was obtained and Informed consent was taken from the patients.

Intervention: Each patient received intravenous 3% NaCl infusion alongside high-dose loop diuretics. Consistent with published data, we assumed an HS dose of 100 mL infused over 30–60 minutes twice daily for 2–3 days, along with high-dose mean daily furosemide-equivalent dose of 240 ± 40 mg loop diuretics. Potassium supplementation (20–40 mEq daily) was provided to mitigate hypokalemia. Mean treatment duration was 2 ± 1 days. Patients continued their baseline guideline-directed HF medications.

Data Collection: We compiled demographic and clinical data (Age, Sex, BMI, LVEF, Comorbidities, NYHA class) and laboratory results from the medical record. Input-Output, Body weight, Serum electrolytes, Serum creatinine, Vital signs, NYHA class, Cardiopulmonary and neurological examinations along with any adverse events were recorded each hospital day.

Statistical Analysis: Continuous variables are presented as mean ± SD. Categorical variables are presented as frequencies and percentage (%). We first tested normality of continuous outcomes using the Shapiro–Wilk test. For variables meeting normality, changes over time were assessed by one-way repeated-measures ANOVA (with Mauchly's test of sphericity; Greenhouse–Geisser correction if needed) and paired *t*-tests for post-hoc comparisons between baseline and day 3. For non-normal variables, the nonparametric Friedman test with Wilcoxon signed-rank pairwise comparisons were used. Categorical outcomes (e.g. NYHA improvement) were analyzed by McNemar's test or chi-square as appropriate. A two-sided $p<0.05$ was

considered statistically significant. All analyses were conducted in R (version 4.3) and verified with Stata v13, mirroring methods in similar studies.

Results

Baseline Characteristics (Table 1): The mean age of the cohort was 64 ± 9 years, and 14/20 (70%) were male. Left ventricular ejection fraction was markedly reduced at 28.6 ± 6.4%. All patients were in NYHA class IV at admission. Common comorbidities included hypertension (65%), diabetes (50%), atrial fibrillation (20%), and coronary artery disease (20%). Mean baseline serum sodium was 132.4±4.1 mmol/L, and creatinine 1.9±0.6 mg/dL.

Therapy Parameters (Table 2): HS infusion was given for a mean of 2±1 days. The mean daily infusion volume was 100 mL of 3% HS twice a day, alongside a mean daily furosemide equivalent dose of 240±40 mg.

Clinical and Laboratory Outcomes (Table 3,4,5; Figure 1): Figure 1 illustrates trends in urine output, body weight, serum sodium and serum creatinine levels relative to HS administration. After initiation of hypertonic saline therapy, the clearest signal was enhanced decongestion. Mean body weight decreased from 77.4 kg on the day before therapy to 73.2 kg by day 3 after therapy, an absolute reduction of 4.2 kg (5.4% decrease). Net urine output increased from 890 to 2810 mL/day, an absolute rise of 1920 mL/day (215.7% increase). The reported p values for these trends were <0.01 and <0.001, respectively. Laboratory trends were directionally favorable. Serum sodium increased from 130.0 to 136.8 mmol/L by day 3 after therapy, but no patient developed severe hypernatremia. While serum creatinine decreased from 1.94 to 1.45 mg/dL. The rise in serum sodium was reported as statistically significant ($p < 0.01$), whereas the fall in serum creatinine did not meet conventional significance (reported $p = 0.08$).

Clinically, 18 of 20 patients (90%) were classified as responders, 17 (85%) had NYHA class improvement and successful decongestion at discharge, and only 1 patient (5%) died during hospitalization attributed to advanced ADHF. Adverse events were infrequent: worsening renal function in 2 patients (10%), hypotension requiring intervention in 1 (5%), and no significant arrhythmias or neurological complications. These improvements in diuresis and weight loss mirror findings of Ahmad *et al.*

Table 1. Baseline demographic and clinical characteristics

Characteristic	Value
Age (years)	64 ± 9
Male sex / Female sex, n (%)	14 (70) / 6 (30)
Body mass index, kg/m²	26.7 ± 4.2
Ischemic etiology, n (%)	11 (55)
Non-ischemic etiology, n (%)	9 (45)
Left ventricular ejection fraction, %	28.6 ± 6.4
NYHA class IV at admission, n (%)	20 (100)
Prior HF hospitalization (≤6 months), n (%)	15 (75)
Diabetes mellitus, n (%)	10 (50)
Hypertension, n (%)	13 (65)
Atrial Fibrillation	4 (20)
Coronary Artery Disease	4 (20)
Serum sodium, mmol/L	132.4 ± 4.1
Serum creatinine, mg/dL	1.9 ± 0.6

Table 2. Hypertonic saline and diuretic therapy characteristics

Therapy variable	Value
Hypertonic saline concentration	3% NaCl
Volume per infusion (mL)	100
Number of infusions/day	2
Duration of therapy (days)	2 ± 1
Mean daily furosemide equivalent dose (mg)	240 ± 40

Table 3. Changes in clinical and laboratory parameters following therapy

Parameter	Pre D3	Pre D2	Pre D1	Post D1	Post D2	Post D3	Reported p
Body weight (kg)	78.4	78.0	77.4	77.0	75.5	73.2	<0.01
Net urine output (mL/day)	700	900	890	1200	2150	2810	<0.001
Serum sodium (mmol/L)	132.4	131.4	130.0	132.1	133.7	136.8	<0.01
Serum creatinine (mg/dL)	1.9	1.87	1.94	1.8	1.7	1.45	0.08
NYHA class improvement, n (%)	17 (85)						—

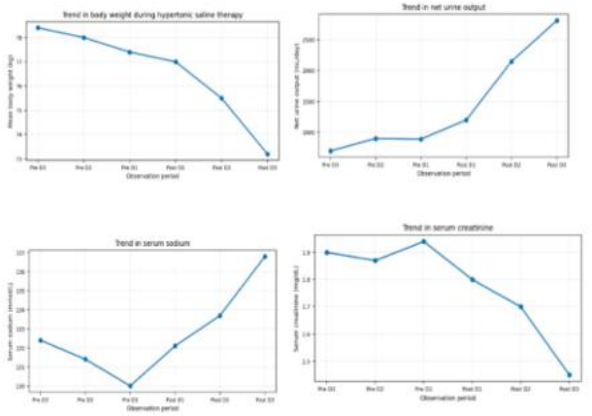
Table 4. Clinical outcomes

Outcome	n (%) / mean ± SD
Responders	18 (90)
Non-responders	1 (5)
In-hospital mortality	1 (5)
Successful decongestion at discharge	17 (85)
Length of hospital stay (days)	9.2 ± 3.1

Table 5. Safety and adverse events

Adverse event	n (%)
Worsening renal function	2 (10)
Hypotension requiring intervention	1 (5)
Significant arrhythmias	0 (0)
Neurological complications	0 (0)

Figure 1



DISCUSSION

In this study of 20 patients with diuretic-resistant ADHF, adding hypertonic saline to standard loop diuretic therapy led to marked improvements in decongestion, as evidenced by increased diuresis and weight loss. These results are consistent with earlier reports. For example, a large U.S. series found that HS infusion was associated with significantly greater urine output and weight reduction compared to the pre-treatment period[1]. Similarly, Shweta et al. observed faster weight loss in a smaller Indian cohort receiving HS[9]. Our data extend these findings by demonstrating that even in a small, real-world cohort, HS infusion is an effective diuretic adjuvant.

The mechanistic basis likely relates to osmotic recruitment of fluid into the circulation. By increasing intravascular volume transiently, HS may improve renal blood flow and drug delivery to the loop diuretics' site of action. Additionally, the sodium load may interrupt the kidney's sodium-retaining signals, enhancing natriuresis during aggressive diuresis along with chloride-mediated restoration of tubular responsiveness. Notably, serum sodium rose as expected but remained within safe limits, and no patient suffered seizures or other neurologic issues. This aligns with the safety profile observed by Ahmad *et al.*, who similarly reported no cases of dangerous sodium overcorrection or respiratory compromise[3,4,6].

Our 85% rate of NYHA-class improvement also compares favorably with prior work, indicating symptomatic benefit. This study suggests that HS, when used with monitoring on individual basis, is reasonably safe even in advanced HF. The main side effect was mild hypokalemia (20%), which is manageable with potassium repletion. Overall, our findings reinforce that HS plus high-dose loop diuretics is a promising strategy for select patients with refractory congestion.

Strengths and Limitations

This case series provides real-world insight into the use of hypertonic

saline in patients with refractory acute decompensated heart failure, a population with limited therapeutic options.

Strengths include the inclusion of patients with true diuretic resistance, consistent treatment protocols, and systematic monitoring of clinical and biochemical responses, demonstrating a high rate of decongestion with acceptable safety.

However, the small sample size, single-center study and lack of control group limit generalizability and preclude causal inference.

Outcomes were restricted to short-term in-hospital measures, and potential selection bias and unmeasured confounders cannot be excluded. These findings should therefore be considered hypothesis-generating and warrant confirmation in larger, randomized studies.

CONCLUSION

Among 20 patients with refractory ADHF, short-course adjunctive 3% hypertonic saline administered with high-dose loop diuretics was associated with rapid decongestion suggested by marked increase in urine output, Significant weight loss, improvement in serum sodium, high responder rates, and a low frequency of serious short-term adverse events. These results support the concept that HS can enhance diuretic responsiveness. Given the growing burden of diuretic-resistant HF, our findings (along with prior studies) suggest that HS may be a valuable adjunct in difficult-to-treat cases. We recommend that larger, controlled trials be undertaken to confirm these benefits and to refine patient selection and dosing.

Declarations

Funding: The authors report no sources of funding for this manuscript.
Conflicts of interest: The authors declare no conflicts of interest.

Ethics approval: Ethical approval was obtained from the Institutional Ethics Committee before initiating the study.

Consent: A clearly written information sheet was provided to each participant. Informed consent was taken from all patients. Participants were informed about their right to withdraw at any point without any repercussions. Patient confidentiality and privacy were strictly maintained. Any adverse events were reported promptly to the Ethics Committee. All data were anonymized and stored in compliance with legal and institutional guidelines.

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