

The Potential Therapeutic Effect of Hypertonic Saline Solution (HSS) for the Management of Refractory Acute Decompensated Heart Failure (ADHF)

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Abstract:

Patients with acute decompensated heart failure (ADHF) have high rates of mortality and morbidity despite recent improvements in diagnosis and treatment. Still patients with significant heart failure and especially with NYHA class III - IV HF and low blood pressure with or without hyponatremia and renal failure are considered severe patients with reduced response to standard treatment with high mortality rates and high re-hospitalizations as they are associated with worse prognosis. Several works and meta-analysis have shown the importance and benefit of treatment with the infusion of hypertonic saline solution (HSS) in these patients and in different conditions of cardiovascular collapse. Current evidence indicates that the infusion of hypertonic solution in heart failure patients can provide clinical and hemodynamic improvement. The investigators are testing the hypothesis that the infusion of hypertonic solution in association with diuretics may prevent the occurrence of renal dysfunction in patients with ADHF and can reduce the re-hospitalizations rate. Our experience in treating several patients has been successful and has shown significant improvement in symptoms and weight loss and improvement in renal function, due to the small size of the sample we were unable to perform a controlled study. We hypothesize that HSS, treatment should be adopted practically and a treatment protocol should be built in patients with intractable ADHF, especially with hypotension, hyponatremia with/without renal failure and overloaded.

Keywords: heart failure; hypertonic saline; diuretics; hyponatremia; renal failure

Introduction

Acute decompensated heart failure (ADHF), with an incidence of 1-2%, is a clinical syndrome with significant morbidity and mortality despite therapeutic advancements and ongoing clinical trials [1]. A recent therapeutic approach to patients with ADHF includes combination therapy with hypertonic saline solution (HSS) and furosemide, based on the hypothesis that resistance to loop diuretics occurs because of achievement of plateau in water and sodium excretion in patients receiving long-term loop diuretic therapy [2]. The proposed treatment is not known among most physicians and institutions, and is not performed routinely or standardly, in addition there is no uniform protocol that describes the methods of treatment. Some studies, case reports and meta-analyses have researched the topic, most of them have proven the effectiveness of the treatment, to the best of our knowledge there are no large double blind randomized controlled studies. In previous years they were published some initial studies, that were followed by a series of small studies: in 2000, 2003, 2005, and culminated with 2011's SMAC-HF study [3]. SMAC-HF was a single center randomized blinded-study

(N=1927) comparing HSS with furosemide and a moderate sodium diet (120 mmol or 2760 mg) versus furosemide alone and a low sodium diet (80 mmol equivalent or 1840 mg). The HSS group had a shorter hospitalization (3.5 vs 5.5 days), improved NYHA class, lower readmission rate (~19% vs ~34%), and reduced CV mortality (~13% vs ~24%) [3]. The earliest work was an exploratory study from 1999 about treating heart failure with 150 ml of hypertonic saline (NaCl 1.4-4.6%) according to serum sodium values plus 250 mg IV furosemide twice a day [4]. They showed that this strange concoction was both safe and tolerated. The rationale behind this combination was to overcome diuretic resistance by using the HSS to draw water from the interstitial compartment, thus improving effective arterial blood volume and renal blood flow and counter the deleterious effects of furosemide by suppressing rather than activating the RAAS.

Recently the use of HSS was proposed as a treatment for refractory heart failure associated with high dose diuretic therapy, with promising results [5]. Most of the data were generally from patients with cardiogenic shock resulting from right ventricular infarction [6]. Another report also evaluated the use of hypertonic saline as an adjunct therapy in an ADHF

patients and indicated that HSS had positive effects on renal function [7]. Other experimental models HSS improved myocardial contractility [8]. The proposed mechanisms included volume expansion by hypertonic saline as a resuscitation fluid leading to the mobilization of fluid to the intravascular compartment followed by increased urine output (Figure 1). Additional effects include enhanced myocardial contractility, peripheral vasodilatation, improved neuro-hormonal profile, and increased renal blood flow. It is also hypothesized that the sodium chloride increase sensed by the macula densa may also play a role in increased diuresis. A meta-analysis was conducted to evaluate the efficiency of combination HSS plus furosemide therapy in patients with ADHF in terms of mortality, readmissions, length of hospital stay, kidney function, urine output, body weight, and B-type natriuretic peptide (BNP) [9]. 14 studies-four observational and ten randomized studies (total 3398 patients)-were included in the meta-analysis whose results demonstrate the superiority of combination HSS plus furosemide therapy over furosemide alone in terms of kidney function preservation (mean creatinine difference - 0.33 mg/dL; $P < 0.00001$), improved diuresis (mean difference [MD] 581.94 mL/24 h; $P < 0.00001$) and natriuresis (MD 57.19; $P < 0.00001$), weight loss (MD 0.99 kg; $P < 0.00001$), duration of hospital stay (MD - 2.72

days; $P < 0.00001$), readmissions (relative risk 0.63; $P = 0.01$), and mortality (relative risk 0.55; $P < 0.00001$). However, no difference in BNP levels was detected (MD 19.88 pg/mL; $P = 0.50$) (1). Despite the heterogeneity and possible risk of bias among the studies, results appear promising on multiple aspects. Other interesting study by Wan Y et al [10]. Demonstrated that periodical HSS with furosemide administration, combined with serious water restriction and a normal sodium diet, significantly reduces the hospitalization time, readmission rate, and mortality in patients with NYHA class III HF. In a cohort of severely ill refractory ADHF patients, there were no adverse electrolyte or respiratory safety signals associated with HSS administration [3]. Furthermore, HSS was associated with increased fluid and weight loss, as well as improvement in kidney function, one limitation of the study that the sample was small. These findings suggest additional rigorous study of HSS in the setting of ADHF is warranted. **These surprising results from this unconventional treatment caught my attention. Maybe sodium was like beta-blockers in heart failure, a treatment that was contraindicated for years before someone give it a chance and now has become an evidence-based treatment widely recommended.**

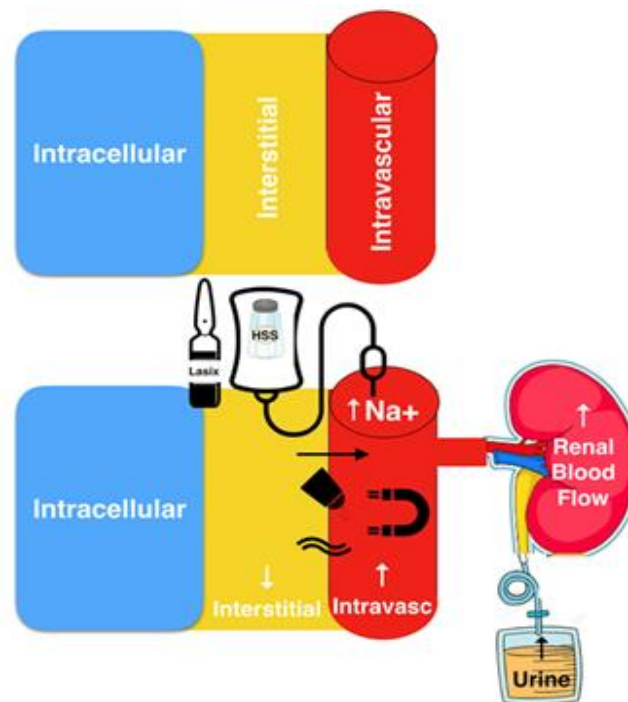


Figure 1. Hypertonic saline (HSS) rapidly increases the plasma sodium concentration and plasma osmolality, which in theory mobilizes fluid into the vascular compartment and increases renal blood flow followed by the excretion in the urine enhanced by diuretics.

Conclusion

We hypothesize that HSS administration exerted a beneficial effect on the patient's myocardial contractility and improved his cardiac output and blood pressure, therefore HSS may be an alternative therapeutic option for the initial management of ADHF, despite the heterogeneity and possible risk of bias among the studies, results appear promising on multiple aspects. In summary, we need stronger evidence to better understand the effects of HSS therapy the optimal dose and duration of treatment. A future adequately powered, multi-centre, placebo controlled, randomized, double dummy, blinded trial also is needed to assess the benefit of hypertonic saline in patients with renal dysfunction, in diverse patient populations.

References

1. Covic A, Copur S, Tapoi L, et al. (2020). Efficiency of Hypertonic Saline in the Management of Decompensated Heart Failure: A Systematic Review and Meta-Analysis of Clinical Studies. *Am J Cardiovasc Drugs*.
2. Griffin M, Soufer A, Goljo E, et al. (2020). Real World Use of Hypertonic Saline in Refractory Acute Decompensated Heart Failure: A U.S. Center's Experience. *JACC Heart Fail.* 8(3):199-208
3. Smith CE, Piamjariyakul U, Wick JA, et al. (2014). Multidisciplinary group clinic appointments: the Self-Management and Care of Heart Failure (SMAC-HF) trial. *Circ Heart Fail.* 7(6):888-894.

4. Paterna S, Parrinello G, Amato P, et al. (1999). Tolerability and efficacy of high-dose furosemide and small-volume hypertonic saline solution in refractory congestive heart failure. *Adv Ther.* 16(5):219-228.
5. Licata G, Di Pasquale P, Parrinello G, et al. (2003). Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as bolus in refractory congestive heart failure: long-term effects. *Am Heart J.* 145(3):459-466.
6. Ramirez JA, Serrano Júnior CV, et al. (1992). Acute hemodynamic effects of hypertonic (7.5%) saline infusion in patients with cardiogenic shock due to right ventricular infarction. *Circ Shock.* 37(3):220-225.
7. Issa VS, Bacal F, Mangini S, et al. (2007). Hypertonic saline solution for renal failure prevention in patients with decompensated heart failure. *Arq Bras Cardiol.* 89(4):251-255.
8. Kien ND, Reitan JA, White DA, Wu CH, Eisele JH. (1991). Cardiac contractility and blood flow distribution following resuscitation with 7.5% hypertonic saline in anesthetized dogs. *Circ Shock.* 35(2):109-116.
9. Gandhi S, Mosleh W, Myers RB. (2014). Hypertonic saline with furosemide for the treatment of acute congestive heart failure: a systematic review and meta-analysis. *Int J Cardiol.* 173(2):139-145.
10. Wan Y, Li L, Niu H, et al. (2017). Impact of Compound Hypertonic Saline Solution on Decompensated Heart Failure. *Int Heart J.* 58(4):601-607.



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