**PULSE**: Hypertonic Saline in Diuretic Resistance

**Title:** Not Just for Neurology: The Use of Hypertonic Saline for Diuretic Resistance in Decompensated Heart Failure

**Objectives:**

1. Define the criteria needed for diagnosis of diuretic resistance.
2. Describe the proposed mechanisms of diuretic resistance and current management options.
3. Discuss current literature that assesses the use of hypertonic saline in diuretic resistance.

**Abstract: (300 words)**

Heart failure is a chronic condition that involves the heart's inability to supply oxygenated blood to meet body requirements due to worsened function. This can lead to fluid overload, dyspnea, and decrease in functional status, all worsening a patient's quality of life. The 2022 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for management of heart failure discuss recommendations regarding fluid overload. In the guidelines, the preferred diuretic in the heart failure patient population is loop diuretics. If an inadequate response is noted with loop diuretics alone, the guidelines do suggest the addition of thiazide diuretics to augment diuresis.

Diuretic resistance is a complication in patients with heart failure on chronic loop diuretic therapy with inadequate response. If left unaddressed, this can increase patients' risk for readmissions due to fluid overload, worsening renal dysfunction, and even death. Per AHA, diuretic resistance is diagnosed one of two ways: failure to increase urine sodium excretion by at least 90 mmol over 3 days despite furosemide equivalent doses of 160 mg twice daily, or a urine sodium output of less than 50 mmol based on a spot urine sample 1-2 hours after dose of diuretic.

There are several proposed mechanisms that facilitate diuretic resistance. Some of these include the pharmacokinetics of loop diuretics, a sodium intake that exceeds the amount of sodium lost to natriuresis, and enhanced reabsorption downstream of the loop of Henle. Hypertonic saline has been proposed as an agent to combat diuretic resistance. The rationale behind utilizing this hypertonic fluid is that it can provide chloride repletion which when low, sodium retention is increased. Additionally, the use of hypertonic saline is thought to pull volume from intravascular spaces without depleting intravascular volume to help combat diuretic resistance. The purpose of this presentation is to review current literature regarding the use of hypertonic saline for diuretic resistance and assess possible clinical applications for use.

**Sources:**

1. What is heart failure? www.heart.org. June 13, 2023. Accessed April 22, 2024. https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure

2. Heart failure signs and symptoms. www.heart.org. June 13, 2023. Accessed April 22, 2024. https://www.heart.org/en/health-topics/heart-failure/warning-signs-of-heart-failure.
3. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee of clinical practice guidelines. *Circulation.* Apr 2022;145(18):e895-e1032.
4. Wilcox CS, Testani JM, Pitt B. Pathophysiology of diuretic resistance and its implications for the management of chronic heart failure. *Hypertension*. Aug 2020;76:1045-1054.
5. Hoorn EJ, Ellison DH. Diuretic resistance. *Am J Kidney Dis*. 2017;69(1):136-142.
6. Hollenberg SM, Warner Stevenson L, Ahmad T, et al. 2019 ACC expert consensus decision pathway on risk assessment, management, and clinical trajectory of patients hospitalized with heart failure. *J Am Coll Cardiol*. Oct 2019;74(15):1966-2011
7. Felker GM, Ellison DH, Mullens W, et al. Diuretic therapy for patients with heart failure. *J Am Coll Cardiol*. 2020;75(10):1178-1195
8. Miller WL. Fluid volume overload and congestion in heart failure. *Circulation: Heart Failure*. Aug 2016;9(8):e002922
9. Houston BA, Kalathiya RJ, Kim DA, et al. Volume overload in heart failure: an evidence-based review of strategies for treatment and prevention. *Mayo Clin Proc*. Sept 2015;90(9):1247-1261.
10. Farkas J. Hyperdiuresis: using hypertonic saline to facilitate diuresis. www.pulmcrit.org. Dec 9, 2019. Accessed April 20, 2024. https://emcrit.org/pulmcrit/pulmcrit-hyperdiuresis-using-hypertonic-saline-to-facilitate-diuresis/.
11. Cox ZL, Hung R, Lenihan DJ, et al. Diuretic strategies for loop diuretic resistance in acute heart failure: the 3T trial. *JACC: Heart Failure*. March 2020;8(3):157-168.
12. Felker GM, Kerry LL, Bull DA, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med*. 2011;364:797-805.
13. Gandhi S, Mosleh W, Myers RBH. Hypertonic saline with furosemide for the treatment of acute congestive heart failure: a systematic review and meta-analysis. *Internal Journal of Cardiology.* 2014;173:139-145.
14. Paterna S, Di Gaudio F, La Rocca V, et al. Hypertonic saline in conjunction with high-dose furosemide improves dose-response curves in worsening refractory congestive heart failure. *Adv Ther*. October 2015;32:971-982.
15. Griffin M, Soufer A, Goljo E, et al. Real-world use of hypertonic saline in refractory acute decompensated heart failure: a U.S. center's experience. *JACC*. March 2020;8(3):199-208.
16. Liu C, Peng Z, Gao X, et al. Simultaneous use of hypertonic saline and IV furosemide for fluid overload: a systematic review and meta-analysis. *Critical Care Medicine*. Nov 2021;49(11):e1163-e1175.

17. Safiejko K, Smereka J, Pruc M, et al. Efficacy and safety of hypertonic saline solutions fluid resuscitation on hypovolemic shock: a systematic review and meta-analysis of randomized control trials. *Cardiol J.* 2022;29(6):966-977
18. Ha Baek S, Hwan Jo Y, Ahn S, et al. Risk of overcorrection in rapid intermittent bolus vs slow continuous infusion therapies of hypertonic saline for patients with symptomatic hyponatremia: the SALSA randomized clinical trial. *JAMA Intern Med*. 2021;181(1):81-92.
19. Metheny NA, Moritz ML. Administration of 3% sodium chloride via a peripheral vein: a literature review. *Journal of Infusion Nursing*. 2021;44(2):94-102.

**Knowledge Check Questions:**

1. Which part of the nephron is NOT considered to have a role in the proposed mechanisms for diuretic resistance due to enhanced reabsorption?
    a. Proximal convoluted tubule
    b. Loop of Henle
    c. Distal convoluted tubule
    d. Collecting duct
2. The use of HSS with concomitant loop diuretics has been shown in literature to improve which outcomes? Select all that apply.
    a. Respiratory status
    b. Improvement to renal function
    c. Fluid and weight loss
    d. Functional status
    e. Readmission rate due to heart failure
3. Which patient would it be most appropriate to utilize HSS in for diuretic resistance?
    a. A 32-year-old female with an EF of 62%, SCr of 0.9, and serum Na+ of 139 mEq/L with no edema.
    b. A 56-year-old male with an EF of 50%, SCr of 2.5, and serum Na+ 126 mEq/L with 3+ pitting edema.
    c. A 60-year-old female with an EF of 40%, SCr of 1.1, and serum Na+ of 141 mEq/L with 2+ pitting edema.
    d. A 64-year-old male with an EF of 33%, SCr of 1.8, and serum Na+ of 129 mEq/L with 3+ pitting edema.
    e. A 71-year-old male with an EF of 27%, SCr of 1.3, and serum Na+ of 137 mEq/L with 1+ pitting edema.