Reference

1. Chaudhry SI, Wang Y, Concato J, Gill TM, Krumholz HM. Patterns of weight change preceding hospitalization for heart failure. *Circulation*. 2007;116: 1549-1554.

Long-Term Effects of Dietary Sodium Intake on Cytokines and Neurohormonal Activation in Patients With Recently Compensated Congestive Heart Failure

Parrinello G, Di Pasquale P, Licata G, et al (Univ of Palermo, Italy; et al)
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Background.—A growing body of evidence suggests that the fluid accumulation plays a key role in the pathophysiology of heart failure (HF) and that the inflammatory and neurohormonal activation contribute strongly to the progression of this disorder.

Methods and Results.—The study evaluated the long-term effects of 2 different sodium diets on cytokines neurohormones, body hydration and clinical outcome in compensated HF outpatients (New York Heart Association Class II). A total of 173 patients (105 males, mean age 72.5 ± 7) recently hospitalized for worsening advanced HF and discharged in normal hydration and in clinical compensation were randomized in 2 groups (double blind). In Group 1, 86 patients received a moderate restriction in sodium (120 mmol to 2.8 g/day) plus oral furosemide (125 to 250 mg bid); in Group 2, 87 patients: received a low-sodium diet (80 mmol to 1.8 g/day) plus oral furosemide (125 to 250 mg bid). Both groups were followed for 12 months and the treatment was associated with a drink intake of 1000 mL daily. Neurohormonal (brain natriuretic peptide, aldosterone, plasma rennin activity) and cytokines values (tumor necrosis factor-α, interleukin-6) were significantly reduced with a significant increase of the anti-inflammatory cytokine interleukin-10 at 12 months in normal, $P < .0001$) than low-sodium group. The low-sodium diet showed a significant activation of neurohormones and cytokines and worsening the body hydration, whereas moderate sodium restriction maintained dry weigh and improved outcome in the long term.

Conclusions.—Our results appear to suggest a surprising efficacy of a new strategy to improve the chronic diuretic response by increasing Na intake and limiting fluid intake. This counterintuitive approach underlines the need for a better understanding of factors that regulate sodium and water handling in chronic congestive HF. A larger sample of patients and further studies are required to evaluate whether this is due to the high dose of diuretic used or the low-sodium diet (Fig 1).

▶ Fluid accumulation is prominent in the pathophysiology of congestive heart failure (CHF) and is associated with sodium retention. Traditionally, sodium restriction without limiting water intake has been an integral part of the

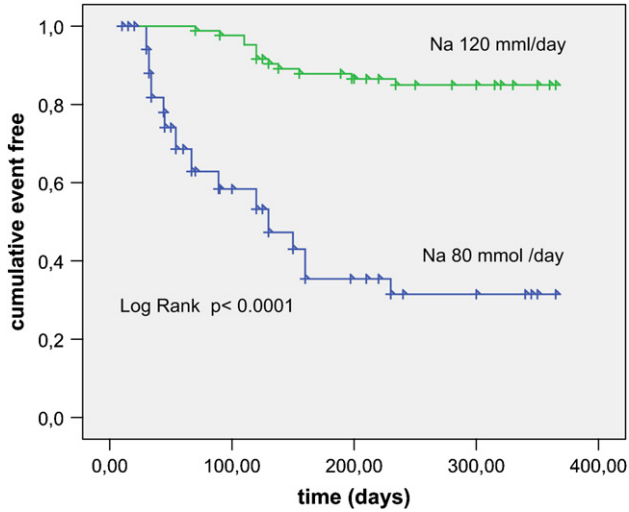

FIGURE 1.—Kaplan-Meier cumulative event curves for primary end point (hospital readmission) in the 2 groups during 1-year follow-up. Na 120 mmol (2.8 g)/day vs. Na 80 mmol (1.8 g)/day. (Reprinted from Parrinello G, Di Pasquale P, Licata G, et al. Long-term effects of dietary sodium intake on cytokines and neurohormonal activation in patients with recently compensated congestive heart failure. *J Card Fail*. 2009;15:864-873, with permission from Elsevier.)

management of the patient with CHF.[1,2] Paterna and colleagues[3] previously reported that a high dose furosemide plus small-volume intravenous hypertonic saline solution (120 mmol of sodium) in patients with refractory CHF achieved dry weight more rapidly, had a faster reduction in natriuretic peptide (BNP) levels, a shorter hospital stay, and lower readmission rates in the 30 day study period than patients given high dose furosemide and a low sodium intake (80 mmol of sodium). The fluid intake was restricted to 1000 ml/day in both groups. The authors postulated that the intravenous infusions of hypertonic saline mobilized extravascular fluid and increased the arterial blood volume, thus increasing renal blood flow and a diuresis.[3-5] They showed also that the hypertonic saline, high furosemide regimen was effective in reducing neurohormonal activation, including lowering plasma renin activity and aldosterone.[6,7] In CHF, proinflammatory cytokines (TNF-α, IL-6, and IL-1β) and chemokines (monocyte chemoattractant protein-1 and IL-8) as well as various adhesion molecules, all correlate with the severity of the disease. The present study is the first to evaluate the effects of 2 different sodium diets in medically treated, compensated CHF patients on neurohormonal and pro-inflammatory cytokine activity during a 12 month follow-up period. The 2.8 gm sodium/day diet is moderate restriction whereas the 1.8 gms/day diet is severe. This, together with fluid restriction to 1000 ml/day and 125-250 mg/day of furosemide resulted in lower neurohormonal activation in the moderate restrictive sodium diet than in the low sodium diet and markedly fewer rehospitalizations over the follow-up year. The explanation for these results is that the moderate sodium intake maintains an appropriate arterial blood volume that inhibits the

neurohormonal activation seen with the low sodium diet and improves renal and hormonal alterations[6-8] as well as reducing pro-inflammatory cytokines [52-53]. The findings of this counterintuitive approach highlight the need for better understanding of the mechanisms of regulating sodium and water in the patient with CHF.

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References

1. Yan RT, Liu PP. Narrative review: pharmacotherapy for chronic heart failure: evidence from recent clinical trials. *Ann Intern Med*. 2005;142:132-145.
2. Nohria A, Lewis E, Stevenson LW. Medical management of advanced heart failure. *JAMA*. 2002;287:628-640.
3. Paterna S, Pasquale PD, Parrinello G, et al. Changes in brain natriuretic peptide levels and bioelectrical impedance measurements after treatment with high-dose furosemide and hypertonic saline solution versus high-dose furosemide alone in refractory congestive heart failure. *J Am Coll Cardiol*. 2005;45:1997-2003.
4. Paterna S, Di Pasquale P, Parrinello G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution infusion in comparison with a high dose of furosemide as a bolus, in refractory congestive heart failure. *Eur J Heart Failure*. 2000;2:305-313.
5. Licata G, Di Pasquale P, Parrinelllo G, et al. Effects of high-dose furosemide and small-volume hypertonic saline solution in comparison with a high dose of furosemide as bolus in ractory congestive heart failure: long term effects. *Am Heart J*. 2003;145:459-466.
6. Rodeheffer RJ, Redfield MM. Congestive heart failure: diagnosis, evaluation, and surgical therapy. In: Murphy JG, ed. *Mayo Clinic Cardiology Review. Baltimore, MD: Lippincott Williams & Wilkins*; 2000:55-74.
7. Paterna S, Parrinello G, Cannizzaro S, et al. Medium term effects of different dosage of diuretic, sodium, and fluid administration on neurohormonal and clinical outcome in patients with recently compensated heart failure. *Am J Cardiol*. 2009;103:93-102.
8. Paterna S, Parrinello G, Fasullo S, Sarullo FM, Di Pasquale P. Normal sodium diet versus low sodium diet in compensated congestive heart failure: is sodium an old enemy or a new friend? *Clin Sci*. 2008;114:221-230.

Congestive Heart Failure Therapy and Technology

Application of Implantable Hemodynamic Monitoring in the Management of Patients With Diastolic Heart Failure: A Subgroup Analysis of the COMPASS-HF Trial.

Zile MR, Bourge RC, Benett TD, et al (Med Univ of South Carolina, Charleston, SC; Univ of Alabama at Birmingham; Medtronic, Inc., Minneapolis, MN; et al)
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Background.—Nearly half of all patients with chronic heart failure (HF) have a normal ejection fraction (EF), and abnormal diastolic function (ie, diastolic heart failure [DHF]). However, appropriate management of DHF patients remains a difficult and uncertain challenge.

Methods and Results.—The Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure (COMPASS-HF) trial was designed to evaluate whether an implantable hemodynamic