Citation: Baek SH, 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 Jan 1;181(1):81-92.

Methodology (*Study design)*:
Prospective, open-label randomized Clinical Trial performed in 3 general hospitals in Korea. The study included 178 patients older than 18 years of age, with moderately severe to severe symptoms and glucose corrected sodium of 125 of less (avg. 118mmol/L) . **Primary outcome**: was the incidence of overcorrection defined as an increase in sNa >12mmol/L in first 24 or 18mmol/L in 48 hrs. **Secondary outcomes**: included efficacy and safety; whether symptoms remained at 24 and 48 hours after treatment with hypertonic saline, first time to an increase in sNa of 5 mmol/L, time from treatment initiation to achievement of sNa greater than 130mmol/L, time to achieving sNa of 5 to 9 mmol/L within 24 hours and sNa of 10 to 17 mmol/L or 130 mmol/L or greater within 48 hours; length of hospital stay; incidence of additional treatment; incidence of ODS

RESULTS:

- For ITT analysis, overcorrection occurred in 15 of 87 (17.2%) patients in the RIB group and 22 of 91 (24.2%) patients in the SCI group (absolute risk difference, −6.9% [95% CI, −18.8% to 4.9%]; P = .26

- For PP analysis, overcorrection occurred in 14 of 72 (19.4%) patients in the RIB group and 19 of 73 (26.0%) patients in the SCI group (absolute risk difference, −6.6% [95% CI, −20.2% to 7.0%]; P = .35)

- There were no differences in any of the secondary outcomes except need for relowering treatments (sNa overcorrected). The RIB group needed less relowering management treatment than the SCI group 41.4% vs 57.1% absolute risk difference, −15.8% [CI, −30.3% to −1.3%]. The RIB group also requires more “additional treatments” 90.8% vs. 74.7% (absolute risk difference, 16.1% [95% CI, 5.3%-26.9%]

Strengths:
No large-scale RCT comparing the efficacy and safety of RIB and SCI with hypertonic saline had been conducted, this was the first clinical trial albeit moderate in size. There was fairly even distribution of 4 major etiologic patient populations (diuretics, SIADH, adrenal insufficiency and decreased extracellular fluid volume due to non-renal loss). Authors did per-protocol (those who completed study) as well as ITT analysis as almost 20% were lost or excluded.

Weaknesses:
Applicability to our patient population uncertain (Korean and BMI’s 22.5). Did not describe how they measures symptoms. High loss of initially enrolled patients (17.2 RIB and 19.7%SCI) they attributed to non-familiarity with bolus treatments.Next, they used a non-patient-centered primary outcome, overcorrection which was suppose to serve a surrogate marker for osmotic demyelination syndrome (ODS). In reality, there was no incidence of ODS in the study, so it is difficult to qualify the clinical significance is. Finally, allocation sequence was not hidden, leading to the potential for selection bias.

My Clinical Bottom Line:
Both RIB and SIC appear to be effective and safe with a difference in the overcorrection risk that favors RIB (less relowering treatment) and tended to have a better efficacy in achieving sNa within 1 hour than SCI. RIB is therefore may be preferred treatment of symptomatic hyponatremi