Critical Review Form

Therapy

Treatment of the Oliguric Patient with a New Sodium-Exchange Resin and Sorbitol, *NEJM* 1961; 264:111-115

Objective: **To evaluate "the new sodium-exchange resin for the treatment and prophylaxis of hyperkalemia in the patient with severe oliguria, and with the use of sorbitol as an adjunct to resin therapy." (p. 112)**

Methods: **Ten oliguric (<400 mL urine/day) patients at an unstated hospital (Peter Bent Brigham Hospital in Boston?) over an unspecified period of time were observed while treating or preventing hyperkalemia. No inclusion/exclusion criteria were reported and patients were not randomized. Patients were analyzed in one of three groups: Group 1 oral sorbitol alone, Group 2 oral kayexalate plus sorbitol, Group 3 rectal kayexalate plus sorbitol.**

All patients were permitted 500-700 mL of fluid daily in the form of intravenous D_5W or Karo syrup with ginger ale orally. No other medications or therapies were reported or controlled for. The experimental therapy consisted of Kayexalate 5 grams QID as a maintenance dose until the serum potassium had reached a low normal level. In addition, sorbitol 70% syrup in doses of 10-20 mL were given every two hours until a satisfactory diarrhea was produced. If the goal was to acutely lower potassium levels then 15 grams of kayexalate was given QID. If oral medications could not be tolerated (vomiting or paralytic ileus), then kayexalate and sorbitol were given as a retention enema (200 mL of 25% sorbitol plus 40 grams of resin) every 6 hours as needed.

Serum sodium and potassium were determined using the Baird atomic flame photometer while the serum carbon dioxide combining power was measured with a Thomas Van Slyke manometer.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No, therefore significant potential for *selection bias* with unequal prognostic characteristics between groups, and other unmeasured confounding variables.
2.	Was randomization concealed (blinded)?	No. Clinicians, patients, family members, and outcome assessors were not blinded to the treatment allocation area.
3.	Were patients analyzed in the groups to which they were randomized?	There was no randomization. Hence, an intention-to-treat analysis is not meaningful.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Uncertain. This is a big flaw in this study. No demographic characteristics were provided for these patients to judge prognostic equivalence between groups. Were they matched by age, gender, race, and etiology of oliguria? How many were on dialysis? What was the chronicity of renal dysfunction? What was the creatinine clearance? How much kayexalate/sorbitol did each subject receive? Did they receive other agents that might reduce potassium levels (see PGY IV paper)? How long did they follow patients and how did they determine this length of follow-up?
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes so a *co-intervention bias* was possible.
2.	Were clinicians aware of group allocation?	Yes.
3.	Were outcome assessors aware of group allocation?	Yes.

4.	Was follow-up complete?	No loss to follow-up is reported.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• Mean reduction of serum potassium from Day 0 to Day 5 was - PO kayexalate + sorbitol: 1.4 mEq/L (range 1.1 – 1.9) [N=5] - PO sorbitol: 1.7 mEq/L (range 0.5 – 3.4) [N=3] - Recal kayexalate + sorbitol: 2.5 mEq/L (range 1.8 – 3.3) [N=2] • Oral kayexalate + sorbitol increases serum sodium by a mean of 9 mEq/L while oral sorbitol reduces serum sodium (mean 2 mEq/L). • Oral kayexalate + sorbitol does not change carbon dioxide while oral sorbitol reduces carbon dioxide (mean 1.2 mEq/L). • The stool volume from one patient is reported after kayexalate plus sorbitol: 2L Day 1, 1.1 L Day 2, 2.5 L Day 3, <1 L every day thereafter.
	How precise was the estimate of the treatment effect?	Unknown. No confidence intervals are provided.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	

1.	Were the study patients similar to my patient?	No. These patients are oliguric patients of unknown age without clear history of ECG changes or co-morbid illness burden. Extrapolating these patients to the general ED population is who we usually treat with kayexalate for hyperkalemia (African-American, dialysis patients with chronic diabetic or hypertensive kidney disease) may lack external validity.
2.	Were all clinically important outcomes considered?	No patient-oriented outcomes were presented. Were hyperkalemia-related fatalities avoided? Did patients feel better with a potassium of 5.2 mEq/L rather than 6.6 mEq/L? Or did they feel worse because of the diarrhea?
3.	Are the likely treatment benefits worth the potential harm and costs?	Based upon the limitations highlighted below one cannot make any confident conclusions based on this study.

Limitations

1) **No randomization or blinding, hence there is significant potential for bias secondary to unmeasured confounding variables.**
2) **No description of patient population (including inclusion/exclusion criteria) so impossible to judge external validity for the emergency department setting in 2011.**
3) **No confidence intervals or tests for statistical significance.**
4) **No *a priori* or *post hoc* power calculation so there is a significant potential for Type I or Type II errors.**
5) **No patient-centric outcomes. Does a potassium of 6.0 mEq/L matter if the patient doesn't feel it and no adverse events occur? Particularly when the trade-off is 5 days of diarrhea?**

Bottom Line

Non-randomized, likely underpowered, poorly described pilot trial suggesting that oral sorbitol alone may reduce serum potassium in oliguric patients better than kayexalate plus sorbitol. Larger trials that control for etiology, severity and duration of renal dysfunction in ED-relevant patients with hyperkalemia are needed. Such trials should also assess patient-centric outcomes since hyperkalemia is often well-tolerated in chronic renal dysfunction while the side effects, of kayexalate plus sorbitol (diarrhea) are quite unpleasant.