Nephrology for Hospital Medicine: Do This, Don't Do That

RAGHAV WUSIRIKA, MD

ASSOCIATE PROFESSOR NEPHROLOGY AND HYPERTENSION

SEPTEMBER 23RD, 2022

Case 1

64 y/o with a history of non-ischemic cardiomyopathy with an EF of 10% who presents to the hospital with 10 days of progressive weight gain of 10 kg, edema and SOB. Her Cr has increased from a baseline of 1.75 to 3.5. Home medications include torsemide 100 mg bid, metolazone 2.5 mg daily and spironolactone 50 mg daily. You give her a dose of IV furosemide 160 mg with no increase in urine output.

What do you do next?

A) Change to IV bumex

B) Start a furosemide gtt

C) Add acetazolamide

D) Add an SGLT2 inhibitor

E) Add tolvaptan

G) Infuse hypertonic saline

What do you do next?

Change to IV bumex

Start a furosemide gtt

Add acetazolamide

Add an SGLT2 inhibitor

Add tolvaptan

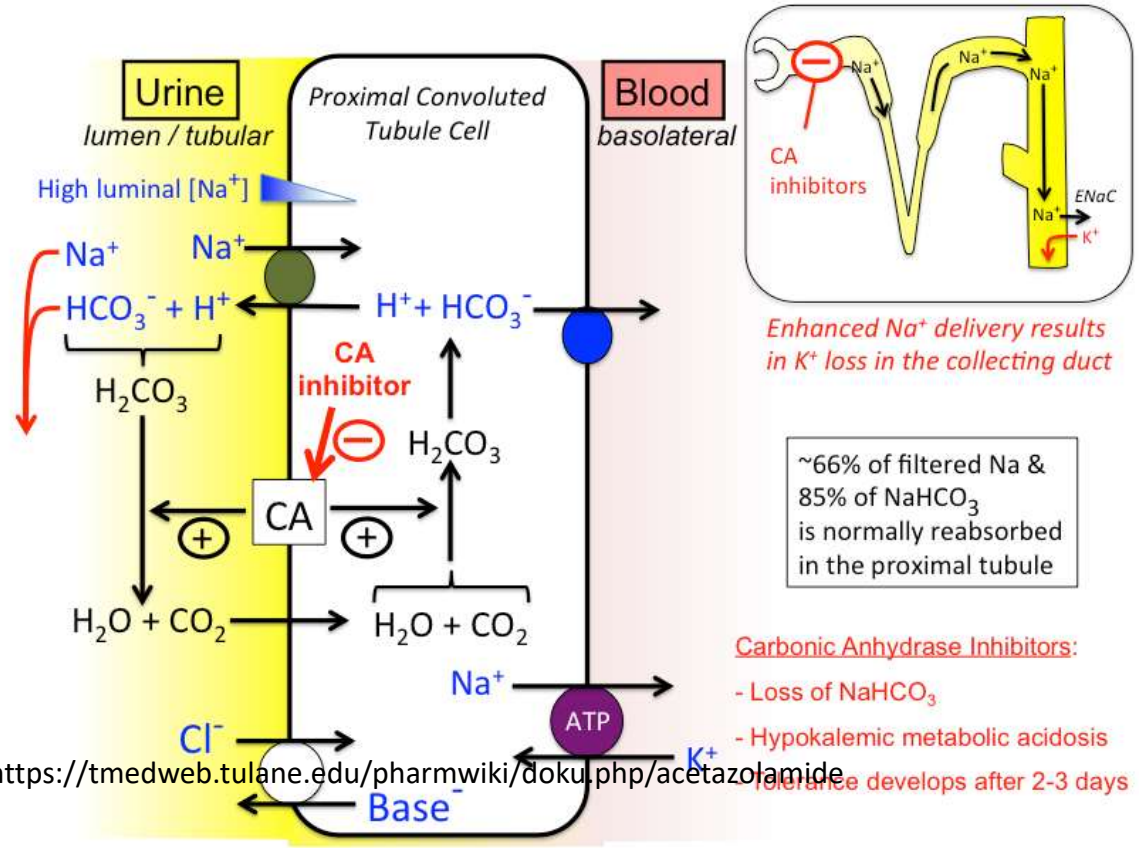
Infuse hypertonic saline

Acetazolamide blocks proximal Na resorption

Patient already has blocks in:

- loop of Henle
- DCT
- collecting duct

- SGLT2 inhibitors also work in the proximal tubule



https://tmedweb.tulane.edu/pharmwiki/doku.php/acetazolamide

Acetazolamide was more effective than placebo in ADVOR trial

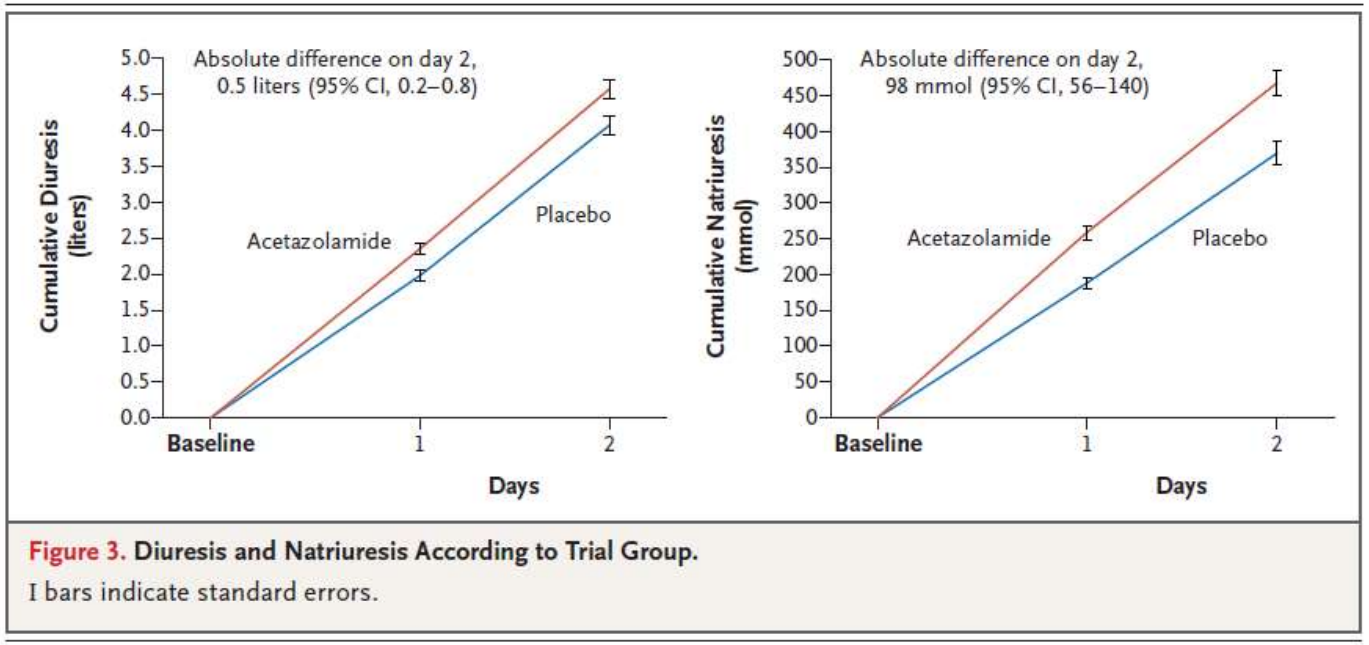


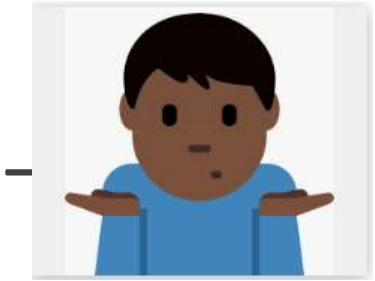
Figure 3. Diuresis and Natriuresis According to Trial Group.
I bars indicate standard errors.

Patients admitted for acute decompensated heart failure already being given loop but not thiazide yet

Dose of 500 mg IV daily

Mullens W, Dauw J, Martens P, Verbrugge FH, Nijst P, Meekers E, Tartaglia K, Chenot F, Moubayed S, Dierckx R, Blouard P, Troisfontaines P, Derthoo D, Smolders W, Bruckers L, Droogne W, Ter Maaten JM, Damman K, Lassus J, Mebazaa A, Filippatos G, Ruschitzka F, Dupont M; ADVOR Study Group. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload. N Engl J Med. 2022 Aug 27

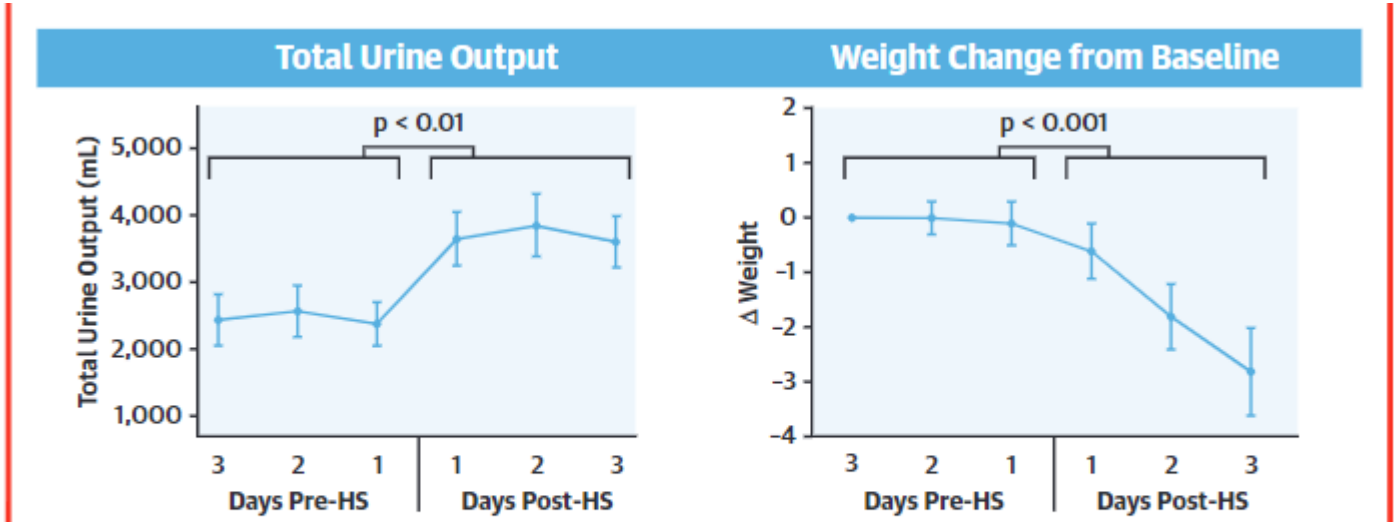
Hypertonic Saline -



Feels wrong to give Na to patients who are volume overloaded

There probably is some limited situations where this is reasonable

Dosed as 150 ml bolus at the same time as IV loop diuretic



Griffin, M. et al. J Am Coll Cardiol HF. 2020;8(3):199-208.

Patients receiving hypertonic saline (HS) had improved urine output and weight loss, without dangerous fluctuations in serum sodium or respiratory decompensation. There were no changes in the percentage of patients requiring supplemental oxygen, and fluctuations in serum sodium were within the acceptable range following administration of hypersonic saline. Both total urine output and weight loss improved.

Post treatment

You gave acetazolamide and the patients urine output started to increase. The patient is net negative 2L but her creatinine has increased from 3.5 to 4 and her BUN has increased from 80 to 150.

What do you do now?

A) Increase acetazolamide dose

B) No change

C) Hold diuretics

D) Hold diuretics and give back IVF

Diuretic induced AKI is reversible

Getting to euvolemia is a clinically important endpoint

Creatinine increases are acceptable to get this end point

If patients get to the point of needing dialysis to get to euvolemia, nothing you are going to do is going to change that

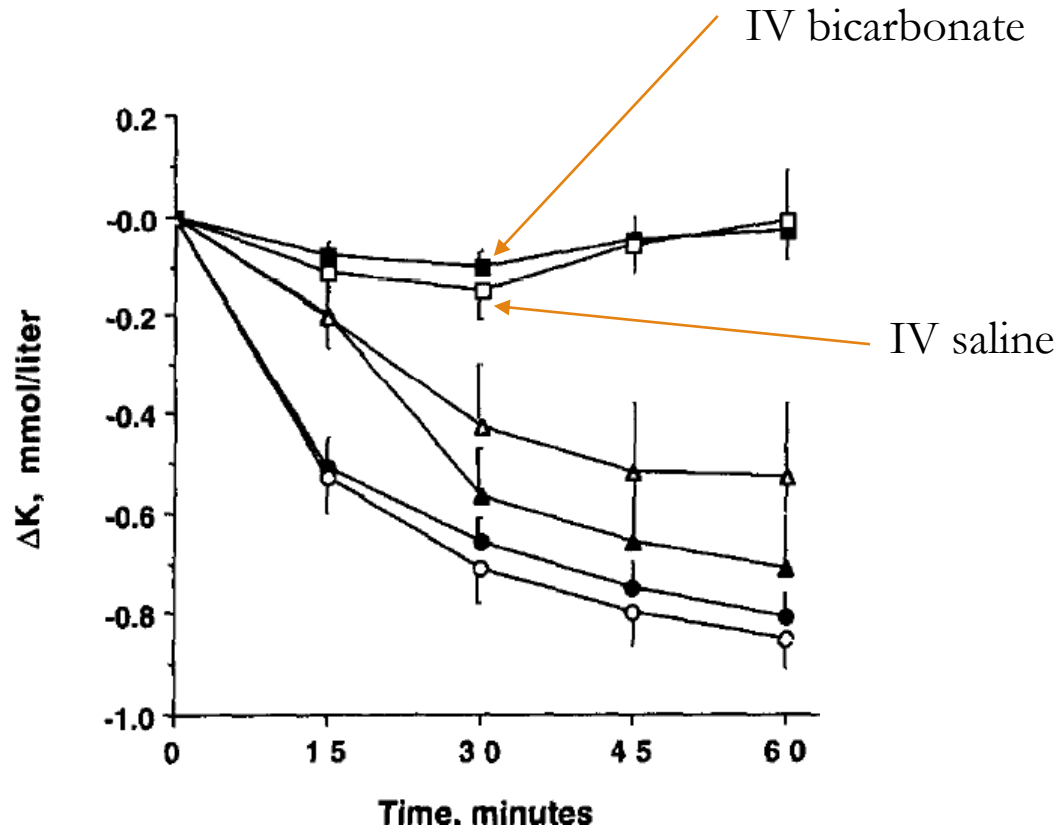
Azotemia $\neq$ Uremia

Case 2

A 45 y/o male ESRD patient comes to your hospital after missing 1 week of dialysis due to feeling unwell. He has some lower extremity edema but is on room air. His labs come back and his K is 6.2 and not hemolyzed. An EKG is done and shows peaked T-waves. After giving Ca, Insulin+glucose and albuterol what do you do next?

- A) IV bicarbonate
- B) Kayexalate
- C) Patriomer (Veltassa)
- D) Zirconium Cyclosilicate(Lokelma)

IV Bicarbonate: No better than NS in the only trial with ESRD patients



Allon M, Shanklin N. Effect of bicarbonate administration on plasma potassium in dialysis patients: interactions with insulin and albuterol. *Am J Kidney Dis.* 1996;28(4):508–514. doi:10.1016/s0272-6386(96)90460-6

Kayexalate may not work and has side effects

Kayexalate-

- Trades potassium for Na in the GI tract and excreted in the stool
- No studies to prove it's efficacy
- It has a known risk of bowel necrosis when given to patient's with an ileus

McGowan CE, Saha S, Chu G, Resnick MB, Moss SF. Intestinal Necrosis due to Sodium Polystyrene Sulfonate (Kayexelate). Southern medical journal. 2009;102(5):493-497.

Patriomer (Veltassa)

Also a resin that binds K in the GI tract

Less GI side effects than Kayexelate

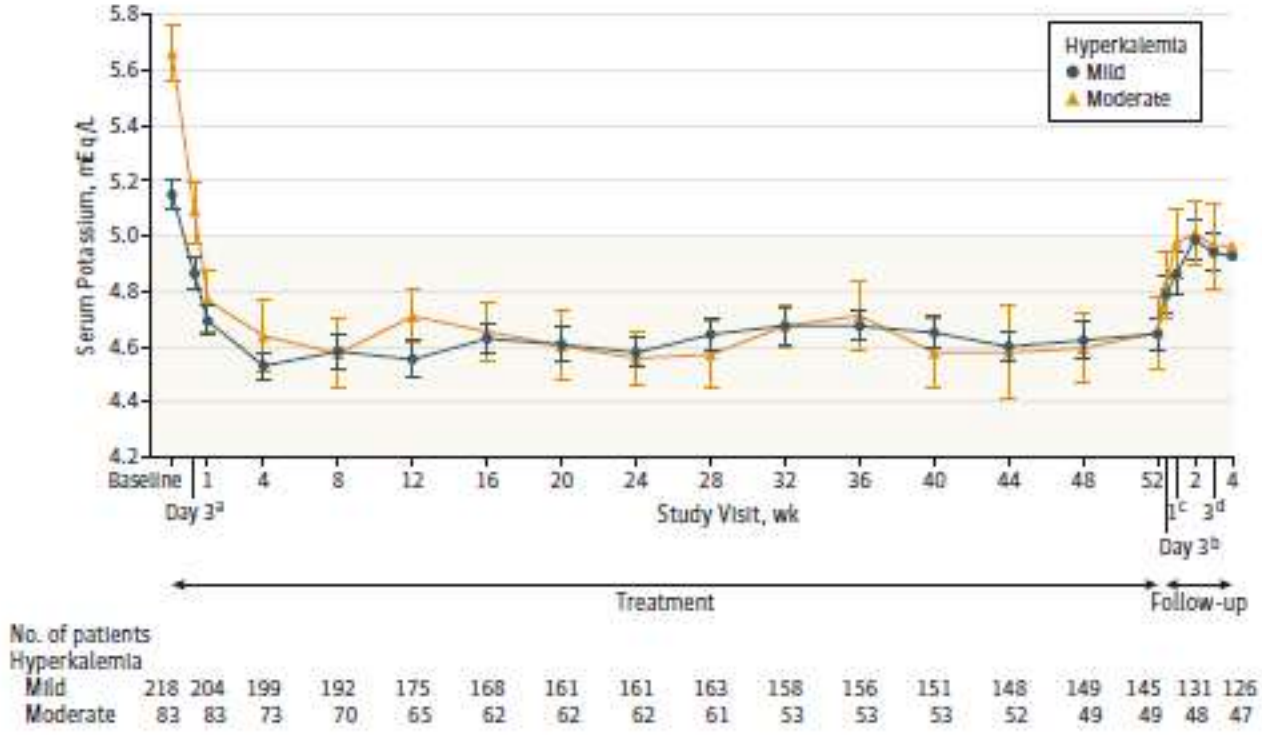
Studied for treatment of chronic hyperkalemia not acute lowering of hyperkalemia

- Takes days for full effect

Can lower serum K by 1 mmol/L

Patriomer (Veltassa)

Figure 3. Least Squares Mean (95% CI) Serum Potassium Levels Over 52 Weeks and During Posttreatment Follow-up In Patients With Mild or Moderate Hyperkalemia (Post Hoc Mixed-Effects Models for Repeated-Measures Analysis)



Bakris GL, Pitt B, Weir MR, et al. Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease: The AMETHYST-DN Randomized Clinical Trial [published correction appears in JAMA. 2015 Aug 18;314(7):731. Dosage error in article text]. *JAMA*. 2015;314(2):151–161. doi:10.1001/jama.2015.7446

Zirconium Cyclosilicate(Lokelma)

Zirconium is another binding resin which exchanges Na for K in the GI tract

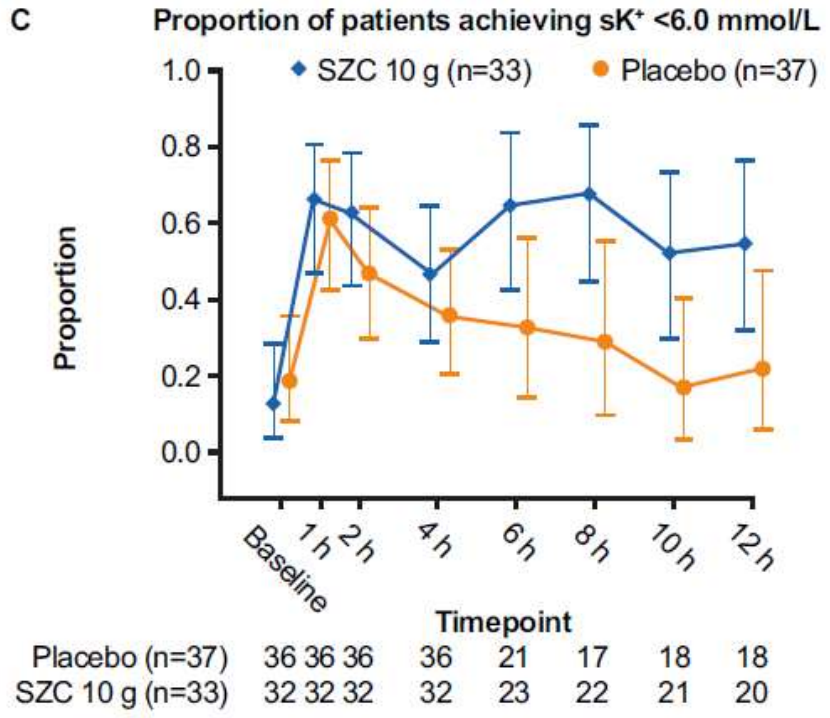
More specific for K than kayexelate or patriomer which also bind Ca, Mg, other medications

Dosed as 5gm-15g once to three times daily

Fishbane S, Ford M, Fukagawa M, et al. A Phase 3b, Randomized, Double-Blind, Placebo-Controlled Study of Sodium Zirconium Cyclosilicate for Reducing the Incidence of Predialysis Hyperkalemia. *J Am Soc Nephrol.* 2019;30(9):1723–1733. doi:10.1681/ASN.2019050450

Lokelma has an acute K lowering protocol

- 10 gm given orally 3 times over a 10 hour period (hours 1, 4, and 10)



Peacock WF, Rafique Z, Vishnevskiy K, Michelson E, Vishneva E, Zvereva T, Nahra R, Li D, Miller J. Emergency Potassium Normalization Treatment Including Sodium Zirconium Cyclosilicat
Phase II, Randomized, Double-blind, Placebo-controlled Study (ENERGIZE). Acad Emerg Med. 2020 Jun;27(6):475-486. doi: 10.1111/acem.13954. Epub 2020 Mar 28. PMID: 32149451;
PMC7318712.

Acute Hyperkalemia

Use Lokelma when able to do so

- Only major side effect is a Na load when used chronically

Avoid Kayexlate

Bicarb probably only works in patients who make urine

Case 3

A patient is transferred from an outside hospital with altered mental status. On arrival to the hospital you note that her creatinine has increased from 1.2 on admission 2 days ago to 3 today. She has not made more than 200 ml of urine in the past 12 hours. She is now having shortness of breath on 3L of oxygen with bibasilar crackles and 2+ LE edema.

Her labs from 2 days ago showed a urinalysis with a specific gravity of 1.045, negative for protein, blood, leukocyte esterase and nitrites. Urine studies are sent and her FeNa is 0.5%

What do you do now?

A) Bolus 1 L NS

B) start maintenance fluids at 100 ml/hr

C) Nothing

D) IV furosemide

FeNa can be misleading

- FeNa is most accurate in oliguria
- Only suggests that the kidney is sodium avid; not what the volume status is
- Can be low with ATN in following scenarios due to vasoconstriction
  - Contrast Nephropathy
  - CHF
  - Liver Disease
  - Burns
  - Calcineurin toxicity

Ignore the FeNa when it doesn't make clinical sense

If a patient looks volume overloaded, ignore the FeNa and diurese them

Clue to this case was a the Specific Gravity of 1.045 – likely from contrast, max urine osmolarity of humans is ~1.035

Summary

Acetazolamide and SGLT2 inhibitors can be used in refractory heart failure

Achieving euvolemia is more important than what the serum creatinine does

Lokelma can acutely lower potassium when dialysis is not available or delayed

FeNa can be misleading