CLINICAL VIGNETTE

Sodium Restriction as a Cause of Hyperkalemia

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Case

A 68-year-old male cardiologist presents to nephrology for evaluation of persistent hyperkalemia for more than 5 years. He notes his potassium levels have ranged from 5.0 to 6.1, and he has been followed by a community nephrologist since the abnormality was first noted on a routine chemistry panel 5 years ago. His prior workup included normal levels of aldosterone and renin. He has never taken an ACE inhibitor and does not use NSAIDS. The GFR, as calculated by the MDRD equation from outside lab records, was persistently in the range of 72 to 81ml/min. Outside urinary sodium levels were consistently below 20 meq/L.

When pressed about his diet, he reported being followed by a dietitian quite closely and that he was well-versed about foods high in potassium, which he has been consciously avoiding. He also stated he is on a very rigid sodium restriction at approximately 500 mg to 1 gram daily. The patient emphasizes this diet has adversely affected his overall nutrition and that he lost about 15 to 20 pounds in the past 5 years. He has been taking daily kayexalate, which resulted in chronic diarrhea, to control his potassium levels. He denies taking any herbal medications or over-the-counter supplements.

Analysis of the prior outside labs did not indicate acidemia associated with his episodes of hyperkalemia. There was no history of diabetes with hgba1c levels of 4.8 to 5.1 with no fasting sugars noted to be above 100. There was no prior history of urinary obstruction, sickle cell disease, or chronic tubulointerstitial disease. His renal ultrasound was unremarkable.

We were suspicious that the hyperkalemia may be secondary to the severe dietary sodium restriction. Therefore to test this hypothesis, we had the patient increase his sodium intake in a stepwise manner, initially from 1 gram/day, then increasing by a gram/day each week with weekly potassium checks. The serum potassium levels progressively decreased as the sodium intake increased.

| Sodium Intake mg/day	Serum Potassium meq/L
500	5.8
1000	4.8
2000	4.1
3000	4.0

Discussion

The differential for hyperkalemia is broad and typically involves either impaired urinary potassium excretion or transcellular shift. Impaired urinary excretion occurs through multiple mechanisms. These include hypoaldosteronism, medications, advanced renal failure, voltage-dependent potassium secretory defect due to impaired sodium reabsorption in the cortical collecting tubule, and low distal sodium delivery resulting from any states characterized by reduced effective circulating volume.

The patient was not taking the typical medications that cause hyperkalemia such as non-steroidal anti-inflammatory drugs, ACEI or ARB, potassium sparing diuretics, or trimethoprim. In vitro hemolysis can often lead to a spuriously elevated potassium level, which will be evident by the reddish serum due to the release of hemoglobin from red cells.[1] Our patient had no evidence of in vitro hemolysis, nor did he have any evidence of in vivo hemolysis as his hematocrit and LDH level were within the normal range. On further analysis of the patient's hyperkalemia, the pH levels were consistently within the normal range, ruling out acidemia leading to transcellular shift. His GFR as calculated by the MDRD equation was at no time in the range of 15 mL/min or lower where hyperkalemia is typically seen. The patient had normal plasma aldosterone and renin levels which would argue against a hypoaldosterone or pseudohypoaldosterone state. The low urinary sodium concentration (urine $[Na^+]$ < 20 meq/L) also excluded hypoaldosteronism and voltage-dependent potassium secretory defect due to impaired sodium reabsorption in the cortical collecting tubule as the causes of his hyperkalemia.[2]

Our hypothesis was that the hyperkalemia was due to the severe dietary sodium restriction leading to diminished effective circulating volume. The diminished effective

circulating volume will in turn lead to avid proximal sodium reabsorption and resultant decreased distal delivery of sodium. The decrease in the distal delivery of sodium will result in less reabsorption of sodium and consequent decreased potassium secretion in the cortical collecting tubule, thereby resulting in hyperkalemia. The persistently low urinary sodium concentration (urine $[Na^+] < 20$ meq/L) is reflective of the decreased distal sodium delivery in our patient. We tested our hypothesis by following potassium levels after stepwise increase of sodium intake. The serum potassium level progressively decreased as the sodium intake increased, supporting decreased distal delivery of sodium as the cause of the hyperkalemia.

Figure 1. The nephron is the functional unit of the kidney. The point of emphasis in Figure 1 is the collecting duct (CD) where the reabsorption of positively charged sodium (Na^+) leads to a negatively charged tubular lumen, which promotes secretion of potatssium (K^+). A decrease in the distal delivery of Na+ could theoretically lead to reduced potassium secretion and resultant hyperkalemia.
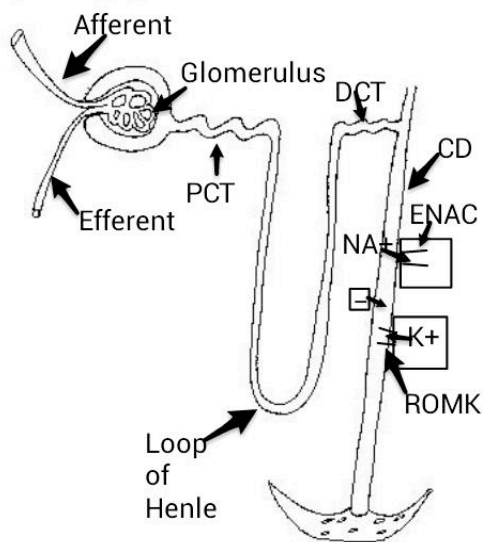
Nephron

REFERENCES

1. Giebisch G. Renal potassium transport: mechanisms and regulation. Am J Physiol. 1998 May;274(5 Pt 2):F817-33. Review. PubMed PMID: 9612319.
2. Lehnhardt A, Kemper MJ. Pathogenesis, diagnosis and management of hyperkalemia. Pediatr Nephrol. 2011 Mar;26(3):377-84. doi: 10.1007/s00467-010-1699-3. Epub 2010 Dec 22. Review. PubMed PMID: 21181208; PubMed Central PMCID: PMC3061004.