A Case of Trimethoprim-Sulfamethoxazole Induced Life-Threatening Hyperkalemia

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Learning Objectives

- Recognize that hyperkalemia is a side-effect of standard dose trimethoprim-sulfamethoxazole (TMP-SMX) therapy.
- Recognize the risk factors for severe hyperkalemia with TMP-SMX use.

Patient Presentation

Initial Clinic Presentation:
- 62 yo WF with hypertension on triamterene
- Presents to clinic with URI symptoms
- Prescribed TMP-SMX DS, one po BID
- CMP normal, potassium of 4.1

Hospital Presentation:
- Presents to ED five days later
- Has severe generalized muscle weakness with difficulty standing and dizziness

Physical Exam:
- Vital signs: T: 96 HR: 38 BP: 66/34 RR: 24
- capillary refill >3 sec

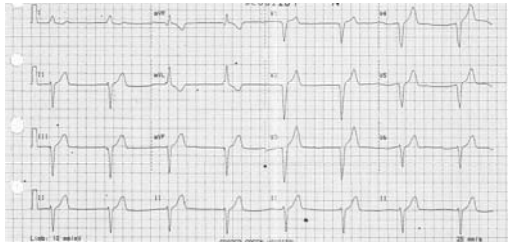
Laboratory Data:

130	106	34	Lactate 7.2
7.1	11	1.9	pH: 7.26, PCO_2: 24, PO_2: 88

Treatment:
- Hyperkalemia was treated with calcium, insulin/dextrose, bicarbonate, and kayexalate

Outcome:
- Symptoms resolved & vital signs normalized within 4 hrs
- She was discharged in good condition 2 days later

EKG



Bradycardia with ventricular rate of 46 bpm, tall peaked T waves, no discernable P waves, and QRS prolongation at 134 ms

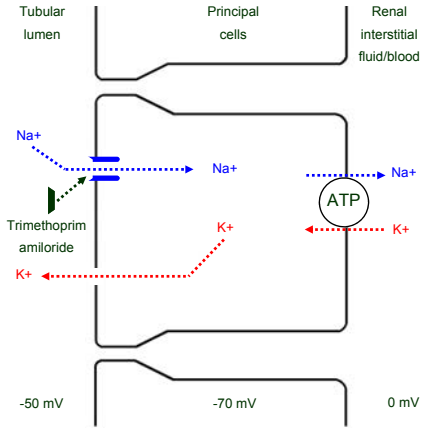
Introduction

- Although TMP-SMX has been widely used as an antibacterial agent since the 1970's, hyperkalemia was not appreciated as a side effect until the 1990's[1].
- Hyperkalemia continues to be an underappreciated but potentially life-threatening side effect of this heavily prescribed medication.

Discussion

- Most healthy patients treated with TMP-SMX have a clinically insignificant rise of about 0.4 mmol/L in their level of potassium[4].
- However, hospitalized patients and patients with certain risk factors often have a more robust increase in serum potassium (mean 1.21 mmol/L) and are at risk for clinically significant severe hyperkalemia[5].

Mechanism of TMP-SMX Induced Hyperkalemia



Collecting tubules of nephron

The trimethoprim component of TMP-SMX has actions similar to the potassium sparing diuretic amiloride in the nephron. Trimethoprim blocks the amiloride-sensitive sodium channel on the apical membrane of the cortical collecting tubule. The decreased sodium entry into the principal cell reduces the transepithelial voltage. The reduction in transepithelial voltage decreases the net driving force for diffusion of potassium from the principal cell to the tubular lumen. The net effect is an inhibition of sodium reabsorption and potassium excretion from the nephron[2,3]. In vitro studies have shown TMP's presence in the distal tubule reduces potassium secretion by 59%[2].

Risk Factors for Severe Hyperkalemia

- Renal dysfunction
- Increasing age (most likely due to a decrease in GFR)
- Concomitant use of other medications that increase serum potassium levels (Ace-I, K-sparing diuretics, potassium supplementation)[5,6]

Our patient was older and taking triamterene which made her susceptible to severe hyperkalemia.

Take Home Points

1. In most patients, standard dose TMP-SMX increases serum potassium which peaks after 5 days of therapy.
2. The increase in serum potassium is clinically insignificant in most patients, but can cause severe hyperkalemia in some patients.
3. Factors that predispose to severe hyperkalemia:
   - Renal dysfunction
   - Increasing age
   - Concomitant use of medications that increase serum potassium levels

References

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2. Muto S, Tsuruoka S, Miyata Y, Fujimura A, Kusano E: Effect of Trimethoprim-Sulfamethoxazole on Na+ and K+ Transport Properties in the Rabbit Cortical Collecting Duct Perfused in vitro. Nephron Physiology 2006;102:p51-60.
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4. Alappan R, Perazella MA, Buller GK: Hyperkalemia in hospitalized patients treated with trimethoprim-sulfamethoxazole. Ann Intern Med 1996;124:316–320.
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