

Hyperkalemia in an Elderly Patient Receiving Standard Doses of Trimethoprim Sulfamethoxazole— Case Report and Brief Review of the Literature

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Trimethoprim sulfamethoxazole (Tpm-Smx) is a commonly used antimicrobial drug in the treatment of respiratory tract and urinary tract infections.

Tpm-Smx has been in clinical use since 1968.¹ It may induce an isolated elevation of serum creatinine (pseudorenal failure), interstitial nephritis with acute renal failure²⁻⁴ and mild hyperkalemia when used in patients with acquired immunodeficiency syndrome (AIDS).⁵ There have been rare case reports of dangerous hyperkalemia in patients receiving high doses of cotrimoxazole.⁶ Recently, three elderly patients were reported to have developed hyperkalemia with standard doses of Tpm-Smx.⁷

In this article we present the case history of a patient who developed moderate hyperkalemia while on regular dose Tpm-Smx and also a brief review of the literature on this topic to increase the awareness of this potentially lethal complication which may be under-recognized.

Case Report

An 89-year-old female fractured both her left hip and left humerus after a fall in her apartment. She underwent surgery and while an in-patient developed a symptomatic lower urinary tract infection caused by *Escherichia coli*, sensitive to both Tpm-Smx and ampicillin.

Her serum chemistries on admission were Na 135 mmol/L, K 3.8 mmol/L, Cl 103 mmol/L, total CO₂ 23.4 mmol/L, blood urea nitrogen (BUN) 5.1 mmol/L and creatinine 90 µmol/L. Urinalysis on admission was normal. She was started on Tpm-Smx orally, one tablet twice a day. Each tablet consisted of trimethoprim 160 mg and sulfamethoxazole 800 mg.

On the fourth day on Tpm-Smx her serum potassium increased to 5.8 mmol/L. This could not be explained on clinical grounds as she was not diabetic or hypertensive nor did she have renal failure. The patient was not on any known medication that might alter the potassium

metabolism or homeostasis; there was no change in her diet and she was not dehydrated.

Her serum chemistries were repeated on the sixth day and were as follows: Na 139 mmol/L, K 6.4 mmol/L, Cl 104 mmol/L, BUN 8.7 mmol/L, CO₂ 22.5 mmol/L, creatinine 170 µmol/L. Urinalysis was unremarkable, there was no peripheral eosinophilia and clinically she continued to be afebrile and had no skin rashes. An electro-cardiogram showed elevated and peaked T-waves.

Tpm-Smx was discontinued and the patient was given kayexalate orally (30 g once) and 10 U of regular insulin in an intravenous drip of 500 mL dextrose 10%, infused over five hours. Serum potassium fell to 5.3 mmol/L and serum creatinine decreased to 120 µmol/L. During the week following discontinuation of Tpm-Smx, her serum potassium stabilized at 5.0 mmol/L and serum creatinine at 90 µmol/L. The clinical course of potassium and creatinine are demonstrated in Figure 1.

Discussion

Our patient had mild acute renal failure and moderate hyperkalemia caused by Tpm-Smx. Hyperkalemia is not

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FIGURE 1. Relation of serum potassium, creatinine and trimethoprim-sulfamethoxazole in patient. The serum potassium rose from a low-normal 3.6 mmol/L to 5.8 mmol/L after only two days of Tpm-Smx. On the contrary, the creatinine was slower to rise. The potassium peaked at 6.4 mmol/L. Both potassium and creatinine levels rapidly normalized with discontinuation of Tpm-Smx.

generally recognized as a complication of Tmp-Smx. Disorders of potassium metabolism have been described in patients receiving high doses of trimethoprim (20 mg/kg/day).^{8,9} Medina and colleagues found mild hyperkalemia (potassium level of 5.1 to 6.1 mmol/L) in 53% of patients with AIDS taking trimethoprim-dapsone and 20% in those taking Tmp-Smx.⁵ Serum potassium levels increased significantly in patients with AIDS who were treated with high doses of Tmp-Smx therapy, typically reaching a moderately high level nine to 10 days after initiation of therapy and this was associated with mild increase in blood urea nitrogen and serum creatinine.¹⁰

Our patient is an example of a common problem in today's clinical practice. Tmp-Smx is commonly prescribed for treatment of uncomplicated urinary tract infection and respiratory tract infections, usually for a course of seven to 10 days.

In this elderly patient, serum potassium had increased by day four of initiation of treatment. On day six it reached a potentially dangerous level, requiring intervention. The potassium was 6.4 mmol/L and concurrently serum creatinine almost doubled over the baseline level. The BUN increased mildly. There was no explanation for this except for the Tmp-Smx treatment. After discontinuation of Tmp-Smx the serum potassium, creatinine and BUN normalized in the next three days.

Tmp-Smx interferes with renal potassium excretion by a mechanism similar to that of amiloride and blocks apical membrane sodium channels in the mammalian distal nephron. As a consequence, the transepithelial voltage is reduced and potassium secretion is inhibited, which leads to hyperkalemia.⁸ The drug also interferes with creatinine secretion into the renal tubules¹¹ which may explain concomitant increased levels of creatinine with potassium. This negative effect on creatinine clearance is not due to a reduction in the glomerular filtration but an isolated defect in tubular excretion.¹² In these cases, the elevation of serum creatinine occurs without a significant concomitant increase in serum BUN or any other sign of renal disease. Tmp-Smx can, however, also cause global renal dysfunction secondary to an interstitial nephritis.¹⁻³

In conclusion, Tmp-Smx may lead to a potentially lethal hyperkalemia, even if used in the standard doses, particularly in the elderly patients who may have pre-

existing renal dysfunction or reduced glomerular function due to the process of aging¹³ and who often develop dehydration when acutely ill.¹⁴ The hyperkalemia usually appears during the first few days of treatment so serum potassium must be checked. If creatinine or potassium are increased significantly, then Tmp-Smx should be discontinued.

Additional data is needed to evaluate closely the age-associated decrease of glomerular filtration rate and the risk for dose-dependent, potentially fatal complications of this drug, particularly in the elderly patient.

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