We divide antibiotics causing hyperkalemia into two different categories:

1. **Well known:** Trimethoprim-sulfamethoxazole (TMP-SMX), Penicillin G, Azoles, Amphotericin B and Pentamidine

2. **Rarely described:** Erythromycin, Daptomycin

**Trimethoprim-sulfamethoxazole (TMP-SMX)**

Trimethoprim-sulfamethoxazole is the most common mentioned antibiotic causing hyperkalemia in medical literature. Trimethoprim is structurally similar to amiloride, a potassium-sparing diuretic. It competitively inhibits the sodium channels of the epithelium in the distal nephron, thereby impairing renal potassium excretion by approximately 40%. (7,8) The incidence and severity of hyperkalemia may greater when the dosing of the trimethoprim component exceeds 5 mg/kg/day. (8,9) However, there are reports of occurring hyperkalemia with standard dose TMP-SMX (10,11), especially in elderly patients, even in the presence of a normal serum creatinine level. (12,13) The literature has long reported the occurrence of TMP-SMX-induced hyperkalemia in patients with acquired immunodeficiency syndrome (14,15) and patients with end stage renal disease (15).

Patients treated with standard-dose trimethoprim-sulfamethoxazole should be monitored closely for the development of hyperkalemia, especially if they have concurrent renal insufficiency. (15,16) Occasionally,
hyperkalemia might be additive in conjunction to other drugs, especially angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blocker (ARBs) and potassium sparing diuretics (PSDs). (12,13,17-21, 31)

**Penicillin G**

Penicillin G is administered as the potassium or sodium salt. Penicillin G contains 0.33 mmol of sodium or 1.7 mmol of potassium per million units. There are case reports of cardiac arrest following penicillin-induced hyperkalemia (22-25)

**Azoles**

Azole antifungals may interfere with the biosynthesis of adrenal steroids and therefore can predispose patients to aldosterone deficiency. (26,27) They are not equivalent in potassium imbalance. Among azoles, voriconazole (28-30), fluconazole (31-34), itraconazole (35,36) can cause hyperkalemia. Although it is unclear whether hyperkalemia can be induced by voriconazole alone (28), however, few cases of voriconazole-induced hyperkalemia have been reported, following high serum voriconazole level due by drug-drug interactions. (29,30)

**Amphotericin B**

Although hypokalemia is a commonly reported side effects of both conventional amphotericin B deoxycholate and its lipid formulations, however, hyperkalemia, which is sometimes could be fatal is also reported. (37,38)

**Pentamidine**

Pentamidine is alternative antibiotic treatment of patients with acquired immunodeficiency syndrome (AIDS) complicated with Pneumocystis carinii infection. Hyperkalemia is a well-known side effect of pentamidine and there several reports available. (39-43)

**Erythromycin**

Ericson et al. conducted a large retrospective cohort study on infants exposed to ≥1 dose of erythromycin and observed that the most common laboratory adverse event during exposure to erythromycin was hyperkalemia. (44)

**Daptomycin**

Daptomycin is mainly used for treatment of resistant gram-positive cocci, including staphylococcal and enterococcal infections. The mechanism of daptomycin-induced hyperkalemia is due to rhabdomyolysis, a known side effect of daptomycin. (45,46)

In conclusion, it is important to investigate the causes of hyperkalemia. Although antibiotics can be responsible, however, might be more than one cause are detectable at the same time. Patients under treatment with above antibiotics—mostly TMP/SMX—especially in conjunction with ACEIs, ARBs and PSDs should be monitored closely for serum potassium level.

---

**Table 1: Antibiotic-induced hyperkalemia**

<table>
<thead>
<tr>
<th>Main Mechanism</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defective aldosterone signaling</td>
<td>Azoles</td>
</tr>
<tr>
<td>Defective distal electrogenic sodium reabsorption</td>
<td>Trimethoprim, Pentamidine</td>
</tr>
<tr>
<td>Cellular K+ translocation</td>
<td>Amphotericin B (conventional and lipid formulations)</td>
</tr>
<tr>
<td>Exogenous K+ load</td>
<td>Penicillin G (intravenous), Daptomycin</td>
</tr>
</tbody>
</table>

---

**References**

12. Matthew A. Weir, David N. Juurlink, Tara Gomes, Muhammad Mamdani, Daniel G. Hackam, Arsh K. Jain and Amit X. Garg. Beta-Blockers, Trimethoprim-


34. Santhana Krishnan SG, Cobbins RK. Reversible acute adrenal insufficiency caused by fluconazole in a critically ill patient. Postgrad Med J. 2006; 82: e23. [PMC free article] [PubMed] [Google Scholar]


******