LETTER TO THE EDITOR

Reversal of Thrombocytopenia in a Pregnant Woman After Changing Hemodiafiltration Membranes

To the Editor:

We would like to confirm the finding described recently by Dr Post1 by reporting another case in which switching to a polysulfone dialysis membrane from another manufacturer was sufficient to reverse thrombocytopenia in a pregnant dialyzed patient. In May 2010, we started a 28-year-old gravida 5 para 2 pregnant woman on a daily program (6 days a week) of 4 hours postdilution online hemodiafiltration (HDF)2 using a polyethersulfone membrane (SureLyzer; a biocompatible polysulfone membrane supplied by Nipro Europe [www.nipro-europe.com]). Our objective was a predialysis serum urea level <14 mmol/L. Chronic kidney disease had been diagnosed nearly 2 years prior, without renal histology available before the preterminal stage. She was 13 weeks pregnant when we started HDF. Two weeks after the start of treatment, the platelet count started to decrease (Fig 1). Preeclampsia and HELLP (hemolysis, elevated liver enzymes, and low platelet count occurring in association with preeclampsia) syndrome were excluded because of the absence of hypertension, edema, proteinuria, and abnormal liver enzyme levels and because of the onset early in pregnancy. Antiphospholipid and antplatelet antibodies were undetectable. Changing to a different biocompatible polysulfone membrane, FX100 (Fresenius [www.fresenius.com]), was followed by an increasing platelet count without a change in other HDF parameters. The patient completed her pregnancy successfully and gave birth at 36 weeks of gestation for urinalysis or urine culture in the 2 days before antibiotic prescription with absence of other cultures or recent prior hospitalization (cohort selection detailed in Fig S1). Men were excluded from the study to limit complicated UTIs. The primary study outcome was urinary tract infection (UTI), defined using insurance fee codes extending from 2005;20(11):2537–2444.

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References


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Figure 1. Platelet count as a function of time. Hemodiafiltration therapy was initiated at day 91; platelet levels began to decrease 2 weeks thereafter. Arrow indicates when the switch in membrane type was made.


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RESEARCH LETTERS

Hospital Admissions for Hyperkalemia With Trimethoprim-Sulfamethoxazole: A Cohort Study Using Health Care Database Codes for 393,039 Older Women With Urinary Tract Infections

To the Editor:

Trimethoprim-sulfamethoxazole (TMP-SMX) is an antibiotic used for a variety of infections, and it may cause hyperkalemia by blocking amiloride-sensitive sodium channels in the cortical collecting duct.1,2 The mechanism of action relates mainly to inhibition of sodium reabsorption and potassium excretion by TMP. The risk of TMP-induced hyperkalemia was described first in patients with AIDS receiving high doses of TMP-SMX for Pneumocystis jiroveci (formerly Pneumocystis carinii) pneumonia.2,4 Since then, hyperkalemia also has been described in patients with decreased kidney function treated using standard doses of TMP-SMX.2,3,7 Other factors also may have a role, including hypokalliemia, older age, and concurrent medications that impair renal potassium excretion, such as angiotensin-converting enzyme inhibitors.8

Case reports,9 smaller cohort studies,9 and, most recently, 2 nested case-control studies10,11 have shown an association between TMP-SMX and hyperkalemia. We conducted a study to extend previous observations of the biologically plausible risk of hyperkalemia with TMP-SMX compared with other common antibiotics. Ours was a retrospective population-based cohort study that linked several health care databases in Ontario, Canada, from January 1, 1997, to March 31, 2009 (databases and their validity detailed in Table S1). Ontario is Canada’s most populous province (39% of the national population) with more than 12 million residents, of whom 1.8 million are 65 years or older. The Ontario Drug Benefit database contains highly accurate records of all outpatient prescriptions dispensed to patients 65 years or older.12

We considered elderly women (aged ≥66 years) who received a single outpatient antibiotic prescription for a simple urinary tract infection (UTI), defined using insurance fee codes for urinary or urine culture in the 2 days before antibiotic prescription with absence of other cultures or recent prior hospitalization (cohort selection detailed in Fig S1). Men were excluded from the study to limit complicated UTIs. The patient’s index date was the day she filled the antibiotic prescription. Antibiotic drugs of interest were either TMP-SMX or any of 4 other antibiotics commonly used to treat UTIs in Ontario (ciprofloxacin, norfloxacin, nitrofurantoin, and amoxicillin). Only the first UTI was assessed for women who had multiple UTIs during the study period. The primary study outcome was hospital admission for hyperkalemia within 10 days of the index
Medication use in the preceding 120 days was compared with the 120 days before the index date that may have influenced the risk of hospitalization for hyperkalemia, chronic kidney disease, Charlson comorbidity score, socioeconomic status, number of different drugs prescribed in the preceding year, and medications used within the 120 days before the index date that may have influenced potassium concentrations (including agents that block the renin-angiotensin system, potassium-sparing diuretics, β-blockers, and nonsteroidal anti-inflammatory drugs).

The cohort consisted of 393,039 women. Baseline characteristics were similar regardless of the antibiotic prescribed (Table 1). The hospitalization rate for hyperkalemia per 100,000 patients was 51.4 in the TMP-SMX group, representing a 3.33-fold increased risk compared with amoxicillin (Table 2). No such association was observed with ciprofloxacin, norfloxacin, or nitrofurantoin. Only 2.6% of women admitted for hyperkalemia had an outpatient potassium level measured in the days after their TMP-SMX antibiotic prescription.

With this study, we extended clinical observations of the biologically plausible risk of hyperkalemia with TMP-SMX. A higher risk associated with TMP-SMX was evident at the population level. Only a small proportion of antibiotic prescriptions were deemed significant enough to result in hospitalization. Also, the risk compared with amoxicillin (Table 2). No such association was observed with ciprofloxacin, norfloxacin, or nitrofurantoin. Only 2.6% of women admitted for hyperkalemia had an outpatient potassium level measured in the days after their TMP-SMX antibiotic prescription.

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Table 2. Association Between Antibiotic Use and Hospital Admissions for Hyperkalemia

<table>
<thead>
<tr>
<th>Event Rate (/100,000 persons)</th>
<th>Odds Ratio (95% confidence interval)</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX</td>
<td>51.4</td>
<td>2.52 (1.00-6.35)</td>
<td>3.33 (1.32-8.42)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>16.9</td>
<td>0.83 (0.29-2.42)</td>
<td>0.81 (0.28-2.39)</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>8.5</td>
<td>0.42 (0.14-1.22)</td>
<td>0.52 (0.18-1.54)</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>9.6</td>
<td>0.47 (0.16-1.38)</td>
<td>0.51 (0.17-1.50)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>20.4</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
</tbody>
</table>

Abbreviation: TMP-SMX, trimethoprim-sulfamethoxazole.

hyperkalemia assessed using administrative database codes is a highly specific but insensitive measure. Thus, the absolute event rates presented in this study underestimate the true risk. The absolute risk would be higher if one were to consider outpatient hyperkalemia events ascertained through careful laboratory measurements, emergency department visits for hyperkalemia, or life-threatening hyperkalemia that resulted in sudden cardiac death before hospital admission. Also, we studied a relatively low-risk cohort of healthy older women. Absolute risks would be higher in elderly persons with increased comorbid conditions or predisposing factors for hyperkalemia. Finally, we acknowledge that only a minority of patients had baseline serum creatinine values. However, available values were similar across the 5 antibiotic groups. This supports an assertion that the groups were similar in the proportion of patients with baseline chronic kidney disease.

In conclusion, physicians should be cognizant of this potentially life-threatening side effect and should consider monitoring serum potassium levels after TMP-SMX prescription in older patients at risk of hyperkalemia.

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Supplementary Materials

Table S1: Data sources, Ontario Administrative and Drug Databases.

Figure S1: Cohort Study Design.

Note: The supplementary material accompanying this article (doi:10.1053/j.ajkd.2010.11.006) is available at www.ajkd.org.

References


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Serum Concentrations of Aluminum in Hemodialysis Patients

To the Editor:

In the past, the major sources of aluminum exposure were dialysate water, aluminum-containing phosphate binders, and