Trimethoprim reduced dysuria in women with symptoms of urinary tract infection but negative urine dipstick test results

Richards D, Toop L, Chambers S, Fletcher L. Response to antibiotics of women with symptoms of urinary tract infection but negative dipstick urine test results: double blind randomised controlled trial. BMJ. 2005;331:143.

Clinical impact ratings: GIM/FP/GP

Question
Are antibiotics effective for treatment of women with symptoms of urinary tract infection but negative results on urine dipstick testing?

Methods
Design: Randomized controlled trial.
Allocation: Concealed.*
Blinding: Blinded (patients, health care providers, data collectors, and (outcome assessors)†).
Follow-up period: 3 and 7 days.
Setting: General practices in Christchurch, New Zealand.

Patients: 66 women who were 16 to 50 years of age and presented with a history of dysuria and frequency and had a negative dipstick test for both leukocytes and nitrates. 7 women were excluded after randomization because they did not meet the age criteria. Exclusion criteria were pregnancy, complicated urinary tract infection including symptoms of pyelonephritis, known allergy to trimethoprim, or proven urinary tract infection or treatment for presumed urinary tract infection in the past month.

Intervention: 26 women were allocated to trimethoprim, 300 mg, for 3 days, and 33 were allocated to placebo.

Outcomes: Resolution of dysuria at 3 and 7 days and median time to resolution of dysuria (based on symptom diaries or a structured telephone questionnaire). Secondary outcomes were resolution of other symptoms.

Patient follow-up: 59 women (89%) completed the structured telephone questionnaire at 7 days (mean age 36 y).

Main results
Among the 48 women (81%) who reported dysuria on day 1, fewer women in the trimethoprim group than in the placebo group still had dysuria on day 3 and day 7 (Table). Women in the trimethoprim group had a shorter median time to resolution of dysuria (3 vs 5 d, P = 0.002). Among the 22 women reporting feverishness or shivers at baseline, fewer women in the trimethoprim group had these symptoms at 3 days, but the groups did not differ at 7 days (Table); women in the trimethoprim group had a shorter median time to resolution of feverishness or shivers (2 vs 6 d, P = 0.02). Among women reporting baseline symptoms of frequency (n = 55), blood in urine (n = 8), itching (n = 22), abdominal pain (n = 47), or low-back pain (n = 31), the trimethoprim and placebo groups did not differ for continued presence of the specific symptom at 3 or 7 days or for median time to resolution of symptoms.

Conclusion
In women with symptoms of urinary tract infection but negative urine dipstick results for both nitrates and leukocytes, trimethoprim for 3 days reduced dysuria at 7 days.

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*See Glossary.
†Information provided by author.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Placebo</th>
<th>Trimethoprim</th>
<th>NNT (CI)</th>
<th>RRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria at 3 d</td>
<td>48</td>
<td>24%</td>
<td>74%</td>
<td>68% (35 to 86)</td>
</tr>
<tr>
<td>Dysuria at 7 d</td>
<td>48</td>
<td>10%</td>
<td>41%</td>
<td>77% (20 to 94)</td>
</tr>
<tr>
<td>Feverishness or shivers at 3 d</td>
<td>22</td>
<td>0</td>
<td>45%</td>
<td>100% (37 to 100)</td>
</tr>
<tr>
<td>Feverishness or shivers at 7 d</td>
<td>22</td>
<td>0</td>
<td>36%</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.
*Number of women with the symptom on day 1.
†Based on Fisher exact test as reported in original article.

Commentary
The prevalence of urinary symptoms in women 40 to 60 years of age is about 30%, and the yearly incidence is 10% (1). To offer antibiotic treatment to a large proportion of symptomatic women regardless of urine findings would have staggering effects in terms of side effects and induction of resistance. This is why we should carefully examine the implications of the study by Richards and colleagues.

The methodology and reporting of the study are excellent. However, a major question exists about external validity in that only about 20% of eligible persons were recruited. Such a group willing to take antibiotics might include more persons likely to have bacterial urinary tract infections (e.g., persons who have had urinary tract infections in the past). The sensitivity and negative predictive value of the dipstick urine test vary and may be higher than in the present study (2).

The authors were careful to point out that their results should not influence practice until confirmed by further studies. A similar study should examine the overall response to antibiotic treatment, as well as the value of clinical symptoms and signs and their combination (3-5) and of laboratory tests (e.g., dipstick examination of a second urine sample or microscopic examination) to predict response to antibiotics.

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References