

Antimicrobial treatment did not reduce complications of urinary tract infection in diabetes and asymptomatic bacteriuria

Harding GK, Zhanel GG, Nicolle LE, Cheang M. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. *N Engl J Med.* 2002;347:1576-83.

QUESTION

In women with diabetes and asymptomatic bacteriuria, does antimicrobial treatment decrease complications of urinary tract infection (UTI)?

DESIGN

Randomized {allocation concealed*}†, blinded {clinicians, patients, data collectors, outcome assessors, and data analysts}†,* placebo-controlled trial with 3-year follow-up (mean follow-up 27 mo). Clinicians and patients were blinded only for the first 6 weeks of the study.

SETTING

Endocrinology clinics in Winnipeg, Manitoba, Canada.

PATIENTS

108 women ≥ 17 years of age with diabetes who had 2 consecutive positive urine cultures ($\geq 10^5$ colony-forming units [CFU] of a urinary pathogen/mL) within a 2-week period and remained asymptomatic. Exclusion criteria included pregnancy and serum creatinine level $> 200 \mu\text{mol/L}$. Follow-up was 97% (105 women) at 1 month and 45% (49 women) at 3 years.

INTERVENTION

Women were allocated to trimethoprim-sulfamethoxazole, 160 mg and 800 mg, respectively, orally twice per day ($n = 55$; 49 women received antimicrobial therapy for 14

d, and 6 received antimicrobial therapy for 3 d) or matching placebo ($n = 50$). Women who were allergic to trimethoprim-sulfamethoxazole or who were infected with resistant organisms received ciprofloxacin, 250 mg orally twice per day.

MAIN OUTCOME MEASURES

Rates of symptomatic UTI and time to first episode of symptomatic UTI. Definite symptomatic lower UTI was defined by acute onset of symptoms of irritation of the lower tract in the absence of fever or costovertebral-angle pain or tenderness and in the presence of a positive urine culture ($\geq 10^3$ CFU of a urinary pathogen/mL). Definite pyelonephritis was defined by the presence of costovertebral-angle pain or tenderness and a positive urine culture ($\geq 10^4$ CFU of a urinary pathogen/mL) with or without systemic symptoms.

MAIN RESULTS

Analysis was by intention to treat. At a mean follow-up of 27 months, the proportion of patients having ≥ 1 episode of symptomatic UTI did not differ between the antimicrobial

therapy and placebo groups (Table). Also, the antimicrobial therapy and placebo groups did not differ for the time to a first symptomatic UTI episode ($P = 0.67$ by the log-rank test) or for rates of any symptomatic UTI (0.93 and 1.10/1000 d of follow-up, respectively, $P = 0.42$), pyelonephritis (0.13 and 0.28/1000 d of follow-up, respectively, $P = 0.13$), cystitis (0.80 and 0.83/1000 d of follow-up, respectively, $P = 0.89$), or hospitalization for UTI (0.06 and 0.10/1000 d of follow-up, respectively, $P = 0.36$).

CONCLUSION

In women with diabetes and asymptomatic bacteriuria, antimicrobial treatment did not reduce complications related to urinary tract infection.

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*See Glossary.

†Information provided by author.

Antimicrobial therapy vs placebo for ≥ 1 episode of symptomatic urinary tract infection at mean 27-month follow-up†

| Antimicrobial therapy | Placebo | RRI (95% CI) | NNH |
|-----------------------|---------|------------------|-----------------|
| 42% | 40% | 4.5% (-34 to 67) | Not significant |

‡Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article.

COMMENTARY

Consensus guidelines recommend periodic screening for microalbuminuria in patients with diabetes (1). The most convenient screening test for patients involves determination of the albumin-to-creatinine ratio in the absence of a UTI. Because of this screening practice, clinicians will identify a proportion of women with diabetes and asymptomatic bacteriuria. Experts have also advocated screening for UTI in women with diabetes believing that early diagnosis and treatment will prevent the serious morbidity associated with symptomatic infections (2). A key question therefore arises: Can preemptive antibiotic therapy prevent serious morbidity in women with diabetes and asymptomatic bacteriuria? The study by Harding and colleagues did not find this approach beneficial.

More symptomatic UTIs occurred in the subset of patients with 2 risk factors: glycosuria (showing poor glycemic control) and neuropathy. Glycosuria may predispose patients to UTI by serving as a growth factor for microbes (2), and neuropathy may be associated with abnormal urinary tract motility (such as delayed bladder emptying). Further studies should elucidate how these risk factors lead to symptomatic

urinary tract infections. Furthermore, the stage is set for a randomized trial of screening for asymptomatic bacteriuria limited to patients with glycosuria and neuropathy (at high risk for symptomatic UTI).

While awaiting further evidence, clinicians should aim to reduce glycosuria and neuropathy in patients with diabetes through tighter glycemic control. Also, clinicians should discuss preemptive antibiotic treatment with diabetic women who have asymptomatic bacteriuria and glycosuria, neuropathy, or serum creatinine $> 200 \mu\text{mol/dL}$. Clinicians will have to judge who has glycosuria and neuropathy since this study did not define a cutpoint for the former or diagnostic criteria for the latter.

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References

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