

Re: Continuous Low-dose Antibiotic Prophylaxis for Adults with Repeated Urinary Tract Infections (AnTIC): A Randomized, Open-label Trial

Fisher H, Oluboyede Y, Chadwick T, et al

Lancet Infect Dis 2018;18:957–68

Expert's summary:

In this randomized, open-label, parallel-group, superiority trial, the authors investigated the efficacy and safety of continuous low-dose antibiotic prophylaxis in adults with repeated urinary tract infections (UTIs) due to clean intermittent self-catheterization (CISC) [1]. After screening of 1743 patients from 51 UK National Health Service organizations, 404 patients (23%) were enrolled and received antibiotic prophylaxis (203 patients) or no prophylaxis (201 patients). For the primary outcome, the incidence of symptomatic antibiotic-treated UTIs over 12 mo was 1.3 cases per person-years (95% confidence interval [CI] 1.1–1.6) in the prophylaxis versus 2.6 cases per person-years (95% CI 2.3–2.9) in the control group, resulting in an incidence rate ratio of 0.52 (95% CI 0.44–0.61; $p < 0.0001$). The antibiotic prophylaxis was well tolerated: 22 minor adverse events related to antibiotic prophylaxis were reported, mainly gastrointestinal disturbance, skin rash, and *Candida* infection. Importantly, the resistance of urinary bacteria was higher in the prophylaxis versus the control group: nitrofurantoin 24% versus 9% ($p = 0.038$), trimethoprim 67% versus 33% ($p = 0.0003$), and cotrimoxazole 53% versus 24% ($p = 0.002$).

Expert's comments:

Repeated UTIs have a relevant negative impact on patients' quality of life, impose a substantial economic burden on every health care system, and remain one of the major challenges in urology. In particular, patients relying on CISC are at high risk of repeated UTIs, with an average prevalence of 25% estimated in European and American cohorts [1]. Although continuous low-dose antibiotic prophylaxis was very effective in the study by Fisher et al. [1], with a 48% reduction in UTI frequency, the significant increase in antibiotic resistance is alarming and might lead to the selection of multiresistant uropathogens, which could result in virtually untreatable infections. Thus, the benefits

of preventing UTIs have to be carefully balanced against harms from antibiotic resistance when considering continuous antibiotic prophylaxis. Moreover, the long-term implications are largely unknown. Taking into account these issues, well-tolerated therapeutic alternatives to antibiotics are urgently needed. Very promising results were found with intravesical bacteriophages, which showed favorable efficacy and safety profiles, so randomized controlled trials are warranted to further define the role of this potentially groundbreaking therapy [2,3]. In addition, treatments for voiding dysfunction aimed at making CISC redundant should be considered, such as neuromodulation approaches involving electrical stimulation of the tibial, pudendal, and sacral nerves. Finally, closed-loop optogenetic neuromodulation systems targeting specific neurons to control urinary tract function might completely revolutionize the field [4].

Conflicts of interest: The author has nothing to disclose.

References

- [1] Fisher H, Oluboyede Y, Chadwick T, et al. Continuous low-dose antibiotic prophylaxis for adults with repeated urinary tract infections (AnTIC): a randomized, open-label trial. *Lancet Infect Dis* 2018;18:957–68.
- [2] Sybesma W, Zbinden R, Chanishvili N, et al. Bacteriophages as potential treatment for urinary tract infections. *Front Microbiol* 2016;7:465.
- [3] Ujmajuridze A, Chanishvili N, Goderdzishvili M, et al. Adapted bacteriophages for treating urinary tract infections. *Front Microbiol* 2018;9:1832.
- [4] Kessler TM, Birder LA, Gomery P. Neuromodulation of urinary tract function. *N Engl J Med* 2019;380:2067–9.

Thomas M. Kessler*

Department of Neuro-Urology, Balgrist University Hospital, University of Zürich, Zürich, Switzerland

*Department of Neuro-Urology, Balgrist University Hospital, University of Zürich, Forchstrasse 340, Zürich 8008, Switzerland.
E-mail address: tkessler@gmx.ch.

<https://doi.org/10.1016/j.eururo.2019.05.018>

© 2019 European Association of Urology. Published by Elsevier B.V. All rights reserved.

