

New Treatment Strategies in Urinary Tract Infections

Florian ME Wagenlehner*

Department of Urology, Pediatric Urology and Andrology, University of Giessen, Giessen, Germany

Urinary Tract Infections (UTIs) are amongst the most prevalent bacterial infections, in the community as well as in the whole health-care system. Antimicrobial resistance of uropathogens is increasing worldwide [1-3]. Especially resistance of *E. coli* and other Enterobacteriaceae against trimethoprim/sulfamethoxazole, fluoroquinolones, 3rd generation cephalosporin, and even against carbapenems are of great concern. In addition the rates of resistance of non-fermentative Gram-negative bacteria, such as *Pseudomonas* spp. against fluoroquinolones and carbapenems have also increased [1-3]. Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* spp. (VRE) are less frequent uropathogens, but they play an important role in hygienic issues in patients with health care associated UTI (HAUTI) [4]. Surveillance studies in complicated UTI/ HAUTI are scarce. An ongoing, world-wide one day prevalence study monitoring infections explicitly in urological patients is the Global Prevalence Study of Infections in Urology (GPIU) performed by the European Section of Infections in Urology (ESIU) [5]. Since 2003 19,756 hospitalized patients were analyzed and in 1,866 of them HAUTI was reported. The resistance rates of most of the uropathogens against the antibiotics tested fluctuated usually around high average values without any significant trends of increase or decrease with Asia exhibiting the highest rates in general. The only antibiotic tested with an overall resistance rate below 10% was imipenem, representing the carbapenems. All other antibiotics had much higher overall resistance rates including so called broad-spectrum antibiotics like piperacillin/tazobactam, ciprofloxacin and gentamicin approaching 30 to 40% [6].

As the total antibiotic consumption in the community drives the selection pressure of antibiotic resistance, different strategies should be applied:

In benign, but very frequent infections, such as uncomplicated cystitis, strategies to avoid antibiotics either to treat acute episodes or to prevent recurrent episodes are currently investigated. Such strategies comprise antiinflammatory drugs, phytotherapeutics and immunostimulation. Approximately 40 to 60% of patients will profit of non-antibiotic treatment and therefore do not need antibiotics.

For antibiotic treatment of uncomplicated cystitis older antibiotics, such as fosfomycin, pivmecillinam and nitrofurantoin, have experienced a revival and are now included in many national and international guidelines [6,7]. Antibiotics with exclusive indication for this very frequent entity are also warranted in the future to be explored [6,7].

For the treatment of complicated UTI and HAUTI however, new antibiotics are urgently needed [8]. Analogues of substances of known antibiotic classes (fluoroquinolones, 3rd gen cephalosporins, betalactamase-inhibitors, monobactams, aminoglycosides, and tetracyclines) are developed further. Compounds directed against novel bacterial targets, such as aminoacyl-tRNA synthetase inhibitors, e.g. mupirocin, LpxC inhibitors, oligonucleotide therapeutics, peptidomimetics are currently investigated. However, new antibiotic substances can only become successful therapeutics for UTI, if they are largely eliminated by the kidneys in its active form.

Since bacterial growth and also antibacterial activity are very

much depending on the milieu, pharmacokinetic/pharmacodynamics considerations directed to the urinary tract should be investigated already in phase one studies for better profiling new substances selected for clinical development [9].

There are some new analogues of known antibiotic classes evaluated also for the treatment especially of complicated UTI. However, given the high administration rate of antibiotics for treatment of UTI, several non-antibiotic treatment strategies should be further explored, in order to reduce antibiotic consumption at least in benign, non-severe infections, such as uncomplicated cystitis [10].

References

1. (ECDC) (2011) Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. Stockholm.
2. (ECDC) (2011) Updated risk assessment on the spread of NDM and its variants within Europe. Stockholm.
3. ECDC/EMA (2009) ECDC/EMA joint technical report. The bacterial challenge: time to react. Stockholm.
4. Bjerkklund Johansen TE, Cek M, Naber K, Stratchounski L, Svendsen MV, et al. (2007) Prevalence of hospital-acquired urinary tract infections in urology departments. *Eur Urol* 51: 1100-1111.
5. Çek M, Tandoğdu Z, Naber K, Tenke P, Wagenlehner F, et al. (2013) Antibiotic prophylaxis in urology departments, 2005-2010. *Eur Urol* 63: 386-394.
6. Wagenlehner FME SG, Hoyme U, Fünfstück R, Hummers-Pradier E, Kaase M, et al. (2011) Epidemiology, diagnostics, therapy and management of uncomplicated bacterial community acquired urinary tract infections in adults. *Chemother Journal* 20: 158-68.
7. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, et al. (2011) International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 52: e103-20.
8. Wagenlehner FM, Weidner W, Perletti G, Naber KG (2010) Emerging drugs for bacterial urinary tract infections. *Expert Opin Emerg Drugs* 15: 375-397.
9. Wagenlehner FM, Wagenlehner C, Redman R, Weidner W, Naber KG (2009) Urinary bactericidal activity of Doripenem versus that of levofloxacin in patients with complicated urinary tract infections or pyelonephritis. *Antimicrob Agents Chemother* 53: 1567-1573.
10. Wagenlehner FM, Bartoletti R, Cek M, Grabe M, Kahlmeter G, et al. (2013) Antibiotic stewardship: a call for action by the urologic community. *Eur Urol* 64: 358-360.

*Corresponding author: Prof. Dr. med. Florian Martin Erich Wagenlehner, MD, PhD, Department of Urology, Pediatric Urology and Andrology, Justus-Liebig-University of Giessen, Giessen, Germany, Tel: +49/641 98544516; Fax: +49/641 98544509; E-mail: Wagenlehner@AOL.com

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