CORRESPONDENCE

Clinical Practice Guideline: Uncomplicated Bacterial Community-acquired Urinary Tract Infection in Adults—Epidemiology, Diagnosis, Treatment, and Prevention

by Dr. med. Jennifer Kranz, Dr. Stefanie Schmidt, Dr. Cordula Lebert, Dr. med. Laila Schneidewind, PD Dr. med. Guido Schmiemann, and Prof. Dr. med. Florian Wagenlehner in issue 50/2017

Guidelines for Interpretation Required.

The new S3 guideline emphasizes the importance of pivmecillinam and nitroxolin in the empirical treatment of uncomplicated cystitis (1). We welcome this recommendation because both substances are effective for a relevant range of pathogens, have very good pharmacodynamics and pharmacokinetics, and can contribute to reducing resistance selection pressure. However, diagnostic-clinical microbiology is faced with a dilemma, because clinical thresholds to interpret resistance tests for these substances are available to a limited degree only. The CLSI guideline includes only breakpoints for mecillinam (the active substance of the prodrug pivmecillinam) for testing for *Escherichia coli* (2). EUCAST, however, provides breakpoints for mecillinam for testing for *E. coli*, *Klebsiella* sp, and *Proteus mirabilis*. EUCAST breakpoints for nitroxoline currently exist only for *E. coli* (3). Other pathogens of urinary tract infections (for example, *Enterobacter* sp, *Citrobacter* sp, *Staphylococcus* sp, and *Enterococcus* sp) have not been considered. The problem is aggravated by the fact that mecillinam and nitroxoline are—with one exception—not included in the standard test panels of automated sensitivity testing.

As a result, mecillinam and nitroxoline can be tested to a restricted degree only, and microbiological laboratories can therefore provide only inadequate support to clinicians in terms of the targeted treatment of cystitis with pivmecillinam or nitroxoline.

This dilemma can be resolved in future only if interpretation guidelines are implemented for resistance testing of mecillinam and nitroxoline to all relevant pathogens, and if these substances are included in commercial test panels for automated resistance testing. It would be highly desirable for the German national antimicrobial susceptibility testing committee (NAK, www.nak-deutschland.org) to come up with suggestions for how to deal with lacking thresholds until international regulations become available. DOI: 10.3238/arztebl.2018.0191a

References

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Prof. Dr. med. Frieder Schaumburg
Prof. Dr. med. Karsten Becker
Institut für Medizinische Mikrobiologie
Universitätsklinikum Münster
Frieder.Schaumburg@ukmuenster.de

Prof. Dr. Sören G. Gatermann
Institut für Hygiene und Mikrobiologie
Ruhr-Universität Bochum

Conflict of interest statement

Professor Gatermann has received honoraria for preparing scientific conferences and physical resources for a research project of Beckman Coulter and bioMérieux that he initiated. Professor Schaumburg and Professor Becker declare that no conflict of interest exists.

Urine Culture is the Crucial Basis

The authors of the interdisciplinary S3 guidelines for the prevention and management of uncomplicated bacterial community-acquired urinary tract infections in adult patients urge “careful use of antibiotics” in view of the observed resistance trends. They point out that in their recommendations they especially considered aspects of rational antibiotic use (“antibiotic stewardship”) (1). The basis for targeted and forward-looking antibiotic use lies in rigorous microbiological diagnostics (i. e. the identification of the causative pathogen and determination of an antibiotic resistance profile). In this context, it is surprising that the guideline authors do not think urinary culture is required in women with clear-cut clinical signs and symptoms of an uncomplicated, non-recurrent or therapy-refractory cystitis. They base their recommendation on economic reasons and considerations of practicability in routine clinical practice. However, for example, in a seven-day therapy with nitrofurantoin, the results of a culture can be of clinical relevance. Furthermore, in Table S1 of the guideline, trimethoprim is recommended only when (according to the local resistance situation), $\leq 20\%$ of the *E. coli* isolates are categorized as resistant to trimethoprim. The responsible clinician, however, will only have recourse to reliable data on the local resistance situation if urine culture is done routinely. Since urine culture continues to be the basis of a sound antibiotic treatment of urinary tract infections, I advocate that urine should also be cultured in the case of community-acquired urinary tract infections. Joint interdisciplinary efforts are needed to overcome financial and organizational obstacles.

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Prof. Dr. med. Jonathan Jantsch

Institut für Klinische Mikrobiologie und Hygiene
Universitätsklinikum Regensburg
jonathan.jantsch@ukr.de

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In Reply:

Uncomplicated urinary tract infections are among the most common bacterial infections. They often trigger a visit to the doctor and therefore contribute crucially to outpatient prescription of antibiotics (1).

The gold standard in diagnosing an uncomplicated urinary tract infection according to the updated AWMF (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften*, Association of the Scientific Medical Societies in Germany) S3 guideline is the combination of clinical symptoms and urinalysis to determine even low numbers of pathogens, their differentiation, and susceptibility testing. Unfortunately, in routine clinical practice, this gold standard is often not implemented. Reasons given by doctors are a lack of practicality as well as the fact that it does not make financial sense because the test results become available only after (successful) treatment. In the context of updating the guideline we therefore attempted to develop instruments that at least prevent unnecessary antibiotic prescribing. By using the validated ACSS (Acute Cystitis Symptom Score) questionnaire, the diagnosis of uncomplicated cystitis can be made with a high degree of certainty on the basis of clinical criteria; the severity of the symptoms can be assessed; the course of the infection can be observed; and the effect of the treatment can be measured.

Regular investigations to determine resistance are obviously—as Professor Jantsch correctly comments—essential as they provide the basis for calculated antibiotic treatment. In contrast to the first edition of the guideline, a series of cross-sectional studies to capture the resistance situation in the outpatient setting

has become available. This enables a clearly differentiated picture of the resistance situation in uncomplicated infections. Resistance to nitrofurantoin is currently so low that testing would not lead to a change in treatment. The authors of the updated AWMF S3 guideline would welcome attempts to overcome financial and organizational obstacles, whose results should be published.

We unequivocally agree with the comments of Schaumburg, Gattermann, and Becker. Guidelines for the interpretation of resistance tests of mecillinam and nitroxoline to all relevant pathogens should be implemented, and these substances should be included in commercial testing panels. This is a declared objective of the guideline. It should be mentioned here that *Enterobacter* sp, *Citrobacter* sp, *Staphylococcus* sp, and *Enterococcus* sp are not relevant in uncomplicated urinary tract infections. The focus should be on the most common pathogens causing uncomplicated cystitis.

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Dr. med. Jennifer Kranz, FEBU

Klinik für Urologie und Kinderurologie
St. Antonius-Hospital
Akademisches Lehrkrankenhaus der RWTH Aachen
Eschweiler
jennifer.kranz@sah-eschweiler.de

Dr. Stefanie Schmidt

Dr. Cordula Lebert

Dr. med. Laila Schneidewind

PD Dr. med. Guido Schmiemann

Prof. Dr. med. Florian Wagenlehner

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Erratum

In the clinical snapshot “Angioedema Two Weeks After the Initial Administration of an ACE Inhibitor” by Dr. med. Barbara Bellmann and Iris Deppe in issue 9, page 142, the term “hypokalemia” was incorrectly used where it should have said “hyperkalemia.” The corrected sentence reads: “Angioedema is an occasional side effect of ACE inhibitors and angiotensin II receptor blockers, along with irritative cough and hyperkalemia.”

MWR