

Treatment of Urinary Tract Infections and Antibiotic Stewardship

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Abstract

Urinary tract infections affect >30% of people around the world. Empirical treatments are currently used for several infections, but appropriate criteria for the rational use of antibiotics should be focused to prevent bacterial resistance phenomena and the increased risk of difficult to-treat infections. Relevant information concerning risk factors and different levels of severity as well as appropriate microbiological interpretation of pathogens have been included and discussed. Moreover, the optimal clinical approach to asymptomatic bacteriuria and recurrent infection episodes has been evaluated, with appropriate suggestions for antibiotic treatment. The prevalence of antibiotic resistance is worsening, probably because of the increasing number of multidrug-resistant bacterial strains and the indiscriminate use of broad-spectrum antibiotics and empirical treatments, inducing increased treatment costs and hospitalizations. Antibiotic stewardship should be introduced in clinical practice to avoid the risk of infection episodes in which the urologist cannot risk systemic inflammatory response syndrome or sepsis. For these reasons, adequate indications for the rational use of antibiotic treatment have been described and discussed, including when and how empirical treatments should be used in current clinical practice.

Patient summary: The prevalence of antibiotic resistance is worsening likely because of the increasing number of multidrug-resistant bacterial strains and the indiscriminate use of broad-spectrum antibiotics. Antibiotic stewardship should be introduced in clinical practice to avoid the risk of infection episodes in which the urologist cannot risk systemic inflammatory response syndrome or sepsis.

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1. Introduction

Urinary tract infections (UTIs) are one of the most common causes (>20%) of outpatient visits to general practitioners. The total cost of treatment of UTIs in the United States is

similar to costs for angina pectoris and Crohn's disease. Women are more frequently affected by UTIs than men due to risk factors such as age, urethral length, marital status and frequency of sexual intercourse, alterations in menstrual cycle, concomitant bowel diseases, and lower genitourinary

tract morphodynamic alterations; however, idiopathic recurrent infections have also been described nonpregnant premenopausal women. In any case, women more often undergo antibiotic treatment for UTIs than men.

Epidemiologic studies indicate that approximately 33% of women will have at least one UTI episode during their lifetime when antibiotic treatment will be necessary [1]. Episodes of recurrence within 6 mo of the first event will occur in 20–50% of cases [2,3]. Each episode of UTI is normally characterized by symptoms for 6.1 d, reduction of daily activities for 2.4 d, and absence from work for 1.2 d [4]. UTI should be considered a social problem that reduces the patient's quality of life and interferes with relational and occupational activities.

2. Classification of urinary tract infections

Different levels of severity, the presence of risk factors, and appropriate microbiological classification of pathogens must be considered as relevant elements in the classification and characterization of UTIs.

2.1. Clinical presentation

The clinical situation is classified as cystitis, pyelonephritis, and urosepsis. Asymptomatic bacteriuria is not considered as an infection but is a risk factor for UTI in certain circumstances. Urethritis and male accessory gland infections (male *adnexitis*; eg, prostatitis) are not included in this paper because clinical presentations are diverse.

2.2. Level of severity

Concerning the clinical presentation of the three UTI entities discussed, the following severity grades can be considered: Pyelonephritis is always more severe than cystitis, and urosepsis is always more severe than the former two. In addition, pyelonephritis can present as a mild and moderate infection, which usually can be treated by oral antimicrobials in an outpatient setting, or as a severe infection with systemic reactions like nausea and vomiting and usually requires initial parenteral therapy and hospitalization. For urosepsis, the severity grading in general use for sepsis—sepsis, severe sepsis, and septic shock—can be adapted.

2.3. Classification according to risk factors

Conventional definitions of UTI are based on the two main categories: complicated and uncomplicated.

Complicated UTIs are defined as cases with abnormal anatomy and/or function of the urinary tract, the presence of concomitant diseases that are able to interfere with host's physiologic defense mechanisms, and/or failed previous medical treatments. These conditions are summarized in Table 1 [5]. The category of complicated UTI is very heterogeneous and not always clear. All other cases are commonly described as uncomplicated and can be treated successfully with appropriate antibiotics only.

Table 1 – Factors suggesting complicated urinary tract infection

Factors
Permanent indwelling catheter or intermittent catheterization
Postvoid urine volume >100 ml
Obstructive uropathy, neurogenic bladder, urolithiasis, and/or cancer
Vesicoureteral reflux or other functional alterations
Anatomic alteration of the urinary tract (orthotopic and heterotopic neobladder)
Chemotherapy and/or radiotherapy
Perioperative urinary tract infection
Renal insufficiency and transplant, immunodeficiency, diabetes mellitus
Adapted with permission from the European Association of Urology [5].

2.3.1. Risk factors: ORENUC

The classification of UTIs according to the ORENUC system provides more detailed differentiation of the underlying risk factors. The letter O indicates episodic UTI events in women of premenopausal age with no known risk factors. The letter R refers to risk factors such as the use of contraceptive devices, hormonal cycle alterations, or the presence of controlled diabetes mellitus that increase the risk of developing recurrent episodes of infection. The letter E indicates other extraurogenital risk factors including pregnancy, uncontrolled diabetes mellitus, immunodeficiency or immunosuppression, concomitant connective tissue diseases, preterm childbirth, and difficult to-treat UTIs in men. Nephropathies (for N) are favorable conditions for the development of UTIs and represent a substantial limitation to the use of antibiotics. Moreover, urologic (for U) factors such as urinary tract obstruction, intermittent or short-term urinary catheterization, asymptomatic bacteriuria (ABU), neurogenic bladder, and clean-contaminated surgical procedures may need elimination to obtain successful antibiotic treatments. The presence of permanent catheterization (for C) due to unsolved urinary obstruction or difficult-to-control neurogenic bladder is the last and most important risk factor to consider [5]. Some recent studies demonstrated the presence of bacterial biofilm colonies as early as 24 h after catheter insertion.

2.4. Microbiological characterization of pathogens

Escherichia coli (70–95% of cases) and *Staphylococcus saprophyticus* (5–10%) represent the essential causative bacteria in uncomplicated UTIs. Some *Enterobacteriaceae* such as *Proteus mirabilis* and *Klebsiella* spp are isolated occasionally. Although *E coli* also remains the most frequent pathogen in complicated UTIs, the microbiological spectrum includes other gram-negative bacteria, such as *Citrobacter* spp, *Enterobacter* spp, *Pseudomonas aeruginosa*, and some gram-positive bacteria such as *Enterococcus* spp and *Staphylococcus* spp [5].

New adjunctive elements such as the identification of uropathogenic *E coli* (UPEC) and the host–microorganism interaction are becoming relevant in the clinical interpretation of UTIs and should be properly evaluated to improve the results of antibiotic treatments.

In particular, bacterial biofilm production, intracellular bacterial colonization, and the quality of the host immune

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