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## **Antibiotic and non-antibiotic treatment of urinary tract infections in the era of growing antimicrobial resistance**

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### **Abstract**

Urinary tract infection is one of the most common indications for prescribing antibiotics among otherwise healthy patients. The lifetime risk of having urinary tract infection among the female population reaches up to 50%. Empirical antibiotic therapy is the first line of treatment in uncomplicated cases. Bacterial resistant to antibiotics is constantly increasing and it is resulting in the evolvement of multidrug-resistant pathogens but also causes a limitation in empirical treatment options. Due to growing antimicrobial resistance, local antimicrobial susceptibility patterns should always be considered especially when empirical treatment is introduced. The article shows the ongoing need for updates in local resistance patterns. Recommendations for the empirical treatment should be constantly verified with reference to the local antimicrobial resistance status. Non-antibiotic preparations may be useful only in the prevention of urinary tract infections.

**Key words: urinary infection, antibiotics, antibiotic resistance**

## **Introduction**

Urinary tract infection (UTI) is one of the most common indications for prescribing antibiotics among otherwise healthy patients. [1] A lifetime risk of having UTI among the female population exceeds 50%. [2] The most familiar symptoms of UTI are urgency, frequency, and dysuria. Some of the risk factors of UTI are sexual activity, general health status, diabetes, pregnancy, and history of UTI. [3] Uncomplicated UTIs can be divided into asymptomatic bacteriuria, uncomplicated cysts, and uncomplicated pyelonephritis. However, asymptomatic bacteriuria is an indication for treatment only during pregnancy and prior to urological procedures. *Escherichia coli* is the most common microbial factor responsible for UTI. It causes more than 80% of the infections, with the other species being occasionally *Enterobacteriaceae*, such as *Proteus mirabilis* and *Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*. [1] Other bacterial species are rarely isolated. Empirical antibiotic therapy is the first line of treatment in uncomplicated cases. Usually, ciprofloxacin, ampicillin, and trimethoprim/sulfamethoxazole are used in this indication.

## **Antibiotic resistance**

Bacterial resistance to antibiotics is constantly increasing and it is resulting in the evolution of multidrug resistance pathogens (MDR) but also causes a limitation in empirical treatment options. Due to growing antimicrobial resistance, local antimicrobial susceptibility patterns should always be considered especially when empirical treatment is introduced. In Poland, many studies have been conducted to assess local susceptibility of bacteria causing UTI. In one of those studies conducted by Miotla et al. *Escherichia coli* was responsible for 65.5% positive urine cultures, followed by *Enterococcus faecalis* with 12.2%, *Klebsiella pneumoniae* 4.7%, and *Proteus mirabilis* 4.2%. Resistance rates for ampicillin, ciprofloxacin, and the trimethoprim/sulfamethoxazole combination were found to be very high which led to a conclusion that they should not be used in a standard empirical treatment regime. Cephalexin and cefuroxime were promising alternatives in the study. [3]

## **Antibiotic treatment**

Currently recommended first-line treatment antibiotics are nitrofurantoin, trimethoprim/sulfamethoxazole, and fosfomycin trometamol. Nitrofurantoin is considered a drug of the first choice due to the fact that it is equally effective as trimethoprim/sulfamethoxazole and has a similar incidence of adverse effects while having much lower resistance rates in many regions. Fosfomycin has a very good safety profile, it causes only minor side effects and has the lowest resistance rates of all above-mentioned antibiotics.

## **Non-antibiotic treatment**

There are herbal products that are considered to be effective in both the prevention and treatment of UTI. One of those products, Canephron N (Bionorica, Germany) is a drug made of century herbs, lovage roots, and rosemary leaves. It has a very good diuretic, spasmolytic, anti-inflammatory, antibacterial, and nephroprotective properties. It is a safe product with no serious side effects. [4] Canephron N was compared to treatment of UTI with fosfomycin trometamol in a large study conducted by Wagenlehner et al. This double-blinded, multicenter, non-inferiority study showed that only 16.5% of patients with UTI symptoms that were treated with Canephron N required additional antibiotic. Hence, in the fosfomycin group, 10.2% required a different antimicrobial drug. [5]

Another non-antibiotic product which is used by patients during UTI symptoms occurrence is cranberry extract. However, cranberries are only recommended in the prevention of UTI, not in the treatment. What is more, in the newest Cochrane Review, the authors found that cranberry juice/extract has no benefit in UTI prevention because it does not decrease the number of UTIs, even when used systematically. [6]

The increased risk of UTI is also associated with the reduction of vaginal microbiota especially *Lactobacillus* spp. colonies. Due to that fact, vaginal probiotics are considered as an option in the treatment and prevention of UTI. Probiotics were compared to antibiotics in a double-blinded study conducted on 252 female patients by Beerepoot et al. In this study patients with rUTI received either capsules containing 10<sup>9</sup> colony-forming units of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 or trimethoprim-sulfamethoxazole. The results showed a significant decrease in the number of symptomatic UTI recurrences in comparison to trimethoprim-sulfamethoxazole administration. [7] However, probiotics are studied mainly in the prevention and as a supportive treatment to antibiotics when it comes to symptomatic UTI.

### **Recurrent UTIs**

Recurrent UTIs (rUTIs) is a very significant problem considering antibiotic resistance and the bladder microbiome. Recurrent UTI is defined as at least three episodes of UTI within 12 months, or at least two episodes occurring within 6 months. [8] The diagnosis of rUTI should begin with a confirmation of prior UTI diagnosis, previous positive urine culture result must be documented. Patients with rUTI are prescribed with antibiotics at least a couple times a year or they are treated with antimicrobial drugs continuously. This raises a serious threat of the fast development of antibiotic resistance to common uropathogens.

### **Conclusions**

The article shows the ongoing need for updates in local resistance patterns. Recommendations for the empirical treatment should be constantly verified with reference to the local antimicrobial resistance status. Non-antibiotic preparations may be useful only in the prevention of UTI. However, when the infection is already in progress antibiotics should be incorporated into the treatment as soon as possible to avoid complications such as acute pyelonephritis.

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