



2017 Guidelines of The Korean Association of Urogenital Tract Infection and Inflammation: Acute Uncomplicated Cystitis

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Acute uncomplicated cystitis is the most common urinary tract infection that mainly occurs in adult females, particularly sexually active young women and postmenopausal women. It is commonly observed in primary health care settings, including urology as well as obstetrics and gynecology; more than half of healthy adult women visit clinics and hospitals at least once in their lifetime due to acute uncomplicated cystitis. The most common bacterium causing this condition is *Escherichia coli*, followed by *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and etc. Trimethoprim-sulfamethoxazole or fluoroquinolones have been used as an empirical antibiotic treatment. However, as fluoroquinolone-resistant organisms or extended spectrum beta-lactamase-producing organisms are becoming more prevalent worldwide, information on regional antibiotic resistance and guidelines on antibiotic use are becoming increasingly more desperate.

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DEFINITION

Acute cystitis is characterized by dysuria without vaginal discharge or irritative symptoms, such as frequency, urgency, nocturia, and etc., as well as supra-pubic discomfort. Risk factors of complicated urinary tract infection (UTI) should not be present.

DIAGNOSIS

For basic tests, the dipstick method and urinalysis (high-resolution microscopic examination) are advisable [1].

Urine culture is not essential, but preferable if there is suspicion of symptoms of acute pyelonephritis that persist for 2-4 weeks or if patients present symptoms of cystitis recur. Because antibiotic resistance of UTI-causing bacteria is high in Korea, it is better to perform a urine culture test prior to treatment. Acute cystitis is diagnosed if symptoms of lower UTI are present and additionally, pyuria (10 or more leukocytes found in high-power field microscopic examination) or bacterial colonies over 10,000 cfu/ml are observed [2,3]. Additional testing should be considered, if the patient shows atypical symptoms, has a fever without costovertebral angle tenderness, or does

not respond to therapy [4,5].

TREATMENT

Antibiotic therapy is recommended as it has been shown to have significant treatment effect compared with the placebo in patients with acute uncomplicated cystitis [6]. Since fluoroquinolone resistance of *Escherichia coli* has been reported to be over 20% in Korea, fluoroquinolone, as an empirical treatment of uncomplicated UTI, should be used carefully [7,8]. Accordingly, in choosing an empirical antibiotic therapy, it is important to consider all the risk factors of patients for antibiotic resistance and the regional trend of sensitivity. Switching to another antibiotic can be considered depending on the clinical features of the given patient. Treatment duration should also be adjusted depending on the clinical features and whether or not symptoms persist.

Criteria based on which to determine an empirical antibiotic therapy is described in Table 1.

A 3-day fluoroquinolone regimen has generally been recommended as the empirical antibiotic therapy for acute uncomplicated cystitis. Specifically, a 3-day course of ciprofloxacin 500 mg oral bid (twice a day), ciprofloxacin 500 mg SR (sustained-release) oral tid (three times a day), or tosufloxacin 150 mg oral bid is recommended [9]. Levofloxacin has not been approved to treat uncomplicated cystitis in Korea; and as such, there may be insurance-related problems if used. Due to the increase in fluoroquinolone-resistant organisms, if it is used as a first-line empirical antibiotic therapy, it is important to eliminate patients suspected of resistance by examining the disease history. Risk factors of fluoroquinolone resistance include recent histories of antibiotic therapy, hospital admission,

Table 1. Criteria based on which to determine an empirical antibiotic therapy

Clinical consideration (confirmation of the absence of clinical symptoms of pyelonephritis such as high fever and flank pain, examination of disease history regarding complicated urinary tract infection such as diabetes)
Bacterial spectrum and sensitivity pattern
Treatment pattern and antibiotic resistance within the community
Availability, tolerability, history of sensitive response to drugs, and adverse effects
Cost
Compliance of the patient in the past

admission to a nursing facility, and chronic respiratory disease. If any patient has these risk factors, it is advisable to avoid using fluoroquinolones.

Recently, instead of fluoroquinolones, a single dose of fosfomycin trometamol 3 g oral, a 3-day course of pivmecillinam 400 mg oral tid, and a 5-to-7 day course of nitrofurantoin macrocrystal 100 mg oral bid have been recommended in Europe and in many other countries [10,11]. However, pivmecillinam and nitrofurantoin are currently unavailable in Korea as they are not produced domestically.

Regarding the therapy with β -lactam antibiotics, amoxicillin-clavulanate 250 mg/125 mg oral tid, amoxicillin-clavulanate 500 mg/125 mg oral bid, cefaclor 250 mg oral tid, cefdinir 100 mg oral tid, cefcapene pivoxil 100 mg oral tid, and cefpodoxime proxetil 100 mg oral bid have been recommended.

In an area where *E. coli* resistance to trimethoprim-sulfamethoxazole (TMP-SMX) is under 20%, TMP-SMX 160/800 mg oral bid can be administered for 5 days [12,13]. However, according to a multi-institutional survey conducted in Korea on antibiotic resistance of UTI-causing bacteria, more than 30% of *E. coli* identified in women with uncomplicated cystitis showed a resistance to TMP-SMX; therefore, it has a limitation as empirical antibiotic treatment [7]. A summary of Empirical antibiotic treatment of acute uncomplicated cystitis is described in Table 2.

Table 2. Empirical antibiotic treatment of acute uncomplicated cystitis

Antibiotics	Dosage (oral)	Duration (d)
Fosfomycin trometamol	3 g qd	1
Pivmecillinam ^{a)}	400 mg tid	3
Nitrofurantoin macrocrystal ^{a)}	100 mg bid	5-7
β -Lactams		
Amoxicillin-clavulanate	250/125 mg tid 500/125 mg bid	7
Cefaclor	250 mg tid	7
Cefdinir	100 mg tid	5-7
Cefcapene pivoxil	100 mg tid	5-7
Cefpodoxime proxetil	100 mg bid	5-7
Fluoroquinolones		
Ciprofloxacin ^{b)}	500 mg bid 500 mg SR qd	3
Tosufloxacin ^{b)}	150 mg bid	3

qd: once a day, tid: three times a day, bid: twice a day, SR: sustained-release.

^{a)}Unavailable in Korea as of April 2017, ^{b)}contraindicated in pregnant women.

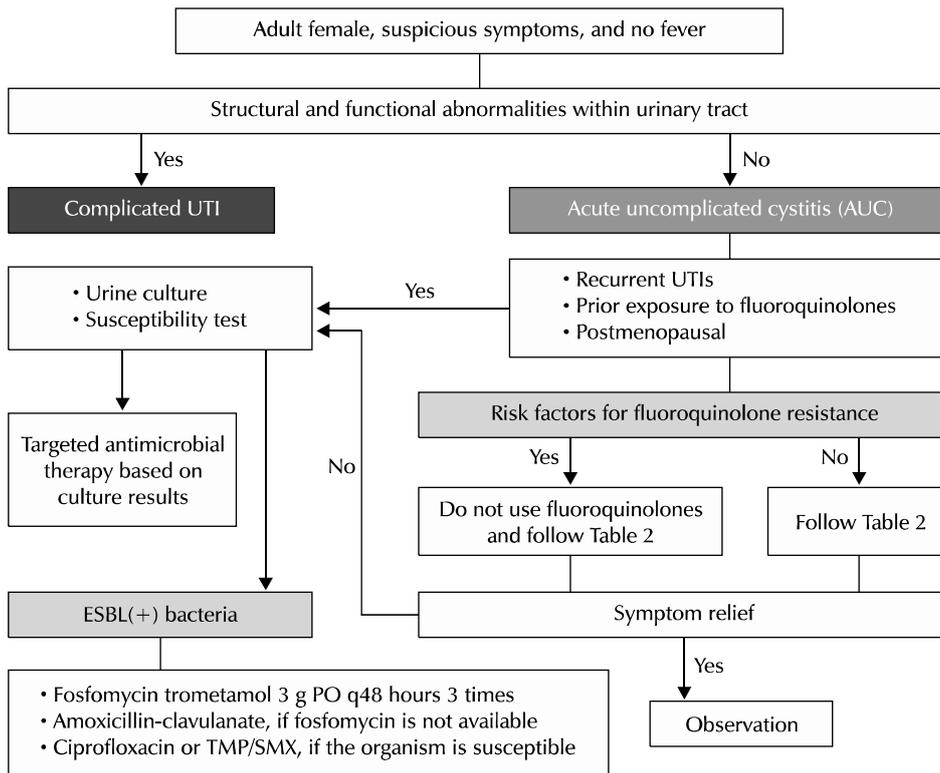


Fig. 1. Algorithm for clinical management of acute uncomplicated cystitis (adapted from Asian Association of UTI & STI). UTI: urinary tract infection, ESBL: extended spectrum beta-lactamase, TMP-SMX: trimethoprim-sulfamethoxazole.

FOLLOW-UP

It is not recommended to perform a urinalysis or a urine culture test in asymptomatic patients [12]. Even if bacteriuria is found on a urine culture test, treatment is not recommended for asymptomatic bacteriuria, with exceptions to pregnant women and patients for whom urinary tract surgery is planned; in such case, antibiotic treatment is recommended.

Generally, urine culture test and antibiotic sensitivity test should always be performed if there is recurrence of symptoms within 2 weeks or if there is persistence of symptoms for at least two weeks. Treatment is determined depending on the antibiotic sensitivity test results, or it is recommended to administer a second treatment course for at least 7 days using a different antibiotic.

In addition to fluoroquinolone resistance, extended spectrum beta-lactamase (ESBL) production is increasing in Korean communities, as well. ESBL production is mainly shown in *E. coli* and *Klebsiella* strains, and difficulty can arise in the treatment of acute uncomplicated cystitis due to many strains having resistance to most antibiotics, with the exception to carbapenems. Oral fosfomycin is recommended when an empirical antibiotic therapy fails and ESBL producers are found on a urine culture test. The

recommended regimen is fosfomycin trometamol 3 g, administered 3 times, with an interval of 48 hours. Amoxicillin-clavulanate can be tried if it is difficult to use fosfomycin, and ciprofloxacin or TMP-SMX can be effective if sensitivity is observed on a urine culture test (Fig. 1).

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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