The Clinical Guidelines for Acute Uncomplicated Cystitis and Acute Uncomplicated Pyelonephritis

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INTRODUCTION

1. Background and Purpose

Urinary tract infections (UTIs) are one of the most common infectious diseases. They are divided according to the site of infection, presence or absence of symptoms, anatomical or functional abnormalities, and the presence or absence of underlying diseases. The aim of this study was to develop a guideline for uncomplicated UTIs.

2. Methodology

The guideline presented here is based on the guidelines from the most recently published Asian Association of UTI & STI (2016), Asian European Association of Urology (2014), Infectious Diseases Society of America (2011), and AMMI Canada Guidelines Committee (2005). Major literature published in Korea was searched using MEDLINE (January 1976 to September 2014), Embase (January 1985 to September 2014), Cochrane Library (January 1987 to September 2014), and KoreaMed (January 1998 to September 2014). We used the following keywords to search these databases: “cystitis,” “pyelonephritis,” “urinary tract infections,” “necrotizing pyelonephritis,” “pyelonephritides,” “Korea.”
3. Level of Evidence and Grade of the Recommendation

The level of evidence (LE) and the grade (GR) of recommendation were accepted and used in accordance with the recent guidelines of the Oxford Center for Evidence-Based Medicine.

1) Level of evidence
   I: Evidence from at least one randomized controlled trial
   II: Evidence obtained from at least one well-designed controlled study without randomization
   III: Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies, and case reports
   IV: Evidence obtained from expert committee reports, opinions, or clinical experience of respected authorities

2) Grade of recommendation
   A: Good evidence to support the recommendation for or against use
   B: Moderate evidence to support the recommendation for or against use
   C: Poor evidence to support the recommendation

CLINICAL PRACTICE GUIDELINES BY DISEASE

1. Acute Uncomplicated Cystitis

Acute uncomplicated cystitis is the most common UTI occurring mainly in adult women, especially sexually active young women and postmenopausal women. It is the most frequently encountered disease in primary medical institutions, including urology, obstetrics, and gynecology. More than half of healthy adult women visit the hospital with acute uncomplicated cystitis at least once in their lifetime, *Escherichia coli* is the most common organism responsible for acute uncomplicated cystitis, followed by *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. trimethoprim-sulfamethoxazole (TMP-SMX) or fluoroquinolone was used as an empirical antibiotic. However, fluoroquinolone-resistant strains and extended spectrum beta-lactamase (ESBL)-bacteria have increased, requiring regional antibiotic resistance information and antibiotic guidelines.

1) Definition

Acute cystitis is a symptom characterized by lower urinary tract symptoms, such as discomfort in the pubic area, as well as storage symptoms, such as pain during urination without vaginal discharge, urinary frequency, urgency, and nocturia (LE: 2a, GR: B). There must be no risk factors that can cause complicated UTIs.

2) Diagnosis

Urine dipstick test and urinary microscopy are widely used basic diagnostic methods [1]. Although urinalysis is not mandatory, it is advised to perform a culture test, if acute pyelonephritis suspicion persists for 2-4 weeks or there is recurrent cystitis symptoms (LE: 4, GR: B). In Korea, UTIs have a high rate of resistance to antibiotics, Acute cystitis is diagnosed when the urine (microscopy, more than 10 leukocytes) is observed or the colony is more than 10,000 cfu/ml [2,3], Additional diagnostic studies should be considered when there is atypical symptoms, fever without costovertebral angle tenderness, or no response to treatment (LE: 4, GR: B) [4,5].

3) Treatment

Antibiotic treatment is recommended for patients with acute cystitis because antibiotics have a significant therapeutic benefit compared with placebos [6]. Since the resistance rate of *E. coli* to fluoroquinolone has already been reported to be greater than 20% in Korea, fluoroquinolone should be used carefully to empirically treat simple UTIs [7,8]. Therefore, in the selection of empirical antibiotics, it is important to consider the risk factors of antibiotic resistance in patients, as well as the tendency to susceptibility of the area. Moreover, antibiotics should be altered in accordance with clinical features, and the duration of treatment should be adjusted in accordance with clinical features and persistence of symptoms.

The criteria for determining empirical antibiotics are as follows:

- Clinical examination (no clinical symptoms of pyelonephritis such as high fever and flank pain, the history of complicated UTIs such as diabetes)
- Spectrum and susceptibility pattern of pathogenic bacteria
- Therapeutic patterns and antibiotic resistance rates in the community
Table 1. Empirical antibiotic therapy for acute uncomplicated cystitis

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Daily dose (oral)</th>
<th>Duration of therapy (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfomycin trometamol</td>
<td>3 g qd</td>
<td>1</td>
</tr>
<tr>
<td>Pivmecillinam[a]</td>
<td>400 mg tid</td>
<td>3</td>
</tr>
<tr>
<td>Nitrofurantoin macrocrystal[b]</td>
<td>100 mg bid</td>
<td>5-7</td>
</tr>
<tr>
<td>β-Lactams</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>250/125 mg tid</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>500/125 mg bid</td>
<td></td>
</tr>
<tr>
<td>Cefaclor</td>
<td>250 mg tid</td>
<td>7</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>100 mg tid</td>
<td>5-7</td>
</tr>
<tr>
<td>Cefcapene pivoxil</td>
<td>100 mg tid</td>
<td>5-7</td>
</tr>
<tr>
<td>Cefpodoxime proxetil</td>
<td>100 mg bid</td>
<td>5-7</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin[b]</td>
<td>500 mg bid</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>500 mg SR qd</td>
<td></td>
</tr>
<tr>
<td>Tosufloxacin[b]</td>
<td>150 mg bid</td>
<td>3</td>
</tr>
</tbody>
</table>

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

[a]April 2016, not available in Korea, [b]not available for pregnant women.

- Availability, tolerability, history of hypersensitivity to drugs, and side effects
- Cost
- Compliance to treatment

A 3-day fluoroquinolone therapy has been widely used and recommended as an empirical antibiotic treatment for acute cystitis (LE: 1, GR: A). Ciprofloxacin 500 mg oral bid (twice a day) for 3 days, ciprofloxacin SR 500 mg qd (once a day) for 3 days, and tosufloxacin 150 mg oral bid are recommended [9] (LE: 1b, GR: B). In Korea, fluoroquinolone is not approved to treat acute cystitis, which can lead to insurance-related problems. Due to increased resistance to fluoroquinolone, it is important to identify patients with suspected resistance through history taking. Risk factors for fluoroquinolone resistance are recent history of antibiotic treatment, recent hospitalization history, recent experience in nursing home care, and chronic respiratory disease. In any of these cases, it is desirable to select an antibiotic other than fluoroquinolone. Recently, antibiotic therapy that is recommended in many countries, mainly Europe, instead of fluoroquinolone, is fosfomycin trometamol 3 g oral single dose therapy, pivmecillinam 400 mg oral tid for 3 days, or nitrofurantoin macrocrystal 100 mg oral bid for 5-7 days [10,11] (LE: 1a, GR: A). However, pivmecillinam and nitrofurantoin are not produced and cannot be used in Korea.

As a beta-lactam antibiotic, amoxicillin-clavulanic acid 250 mg/125 mg oral three times a day or amoxicillin-clavulanate 500 mg/125 mg oral twice a day, cefaclor 250 mg oral three times a day, cefdinir 100 mg oral three times a day, cefcapene pivoxil 100 mg oral three times a day, and cefpodoxime proxetil 100 mg oral twice a day is recommended (LE: 1, GR: A).

In regions where the resistance rate of E. coli to TMP-SMX is less than 20%, it is possible to administer TMP-SMX 160/800 mg twice daily for 5 days [12-14] (LE: 1b, GR: B). However, according to a recent multicenter antibiotic resistance study for UTIs, 30% or more of E. coli identified in patients with acute uncomplicated cystitis is resistant to TMP/SMX, and thus, have limited role as an empirical antibiotic (Table 1) [7].

4) Follow-up

Urinalysis or urine culture in asymptomatic patients is not recommended [12] (LE: 2b, GR: B). Even if urine culture shows bacteriuria, asymptomatic bacteriuria is not recommended for treatment. Exceptionally, antibiotic treatment of asymptomatic bacteriuria is recommended only when planning an operation for the urologic urinary tract or only in pregnant women. In general, if there is recurrence within 2 weeks or if symptoms persist for 2 weeks, urine culture and antibiotic susceptibility are indispensable. Moreover, it is recommended to follow the results of the antibiotic susceptibility or retreat for more than 7 days with a different antibiotic (LE: 4, GR: C) (Fig. 1).

An increase in ESBL-producing bacteria has also been observed with increased resistance to fluoroquinolone in Korea. ESBL production is mainly seen in E. coli and Klebsiella strains, and most of them are resistant to antibiotics, except carbapenem antibiotics, making the treatment of acute cystitis difficult. Fosfomycin, an oral antibiotic, should be used when ESBL-producing bacteria are observed on the urine culture and when empirical antibiotic therapy fails. In such case, 3 g of fosfomycin trometamol is recommended to be administered three times at 48-hour intervals. Amoxicillin-clavulanate can be used in patients where the use of fosfomycin is difficult; additionally, ciprofloxacin or TMP-SMX may also be effective if it is susceptible to urine culture (Fig. 2).

2. Acute Uncomplicated Pyelonephritis

In Korea, amoxicillin, TMP-SMX, and cephalosporin have all been used as the primary treatment antibiotics for UTIs,
Fig. 1. Algorithm for clinical treatment of acute uncomplicated pyelonephritis. TMP-SMX: trimethoprim-sulfamethoxazole.

However, resistance to these antibiotics has been increasing as of late; therefore prescribing fluoroquinolone antibiotics, which have a relatively low resistance rate and can be used orally, has been on the rise [15-17]. However, resistance to fluoroquinolone antibiotics has also been increasing; thus, it is necessary to evaluate and prepare for this as well.

1) Epidemiology

The annual prevalence rate of acute pyelonephritis in Korea was reported to be 35.7 persons per 10,000 population between January 1, 1997 and August 30, 1999, according to the National Health Insurance data, with 59.0 in women and 12.6 in men. It was reported that 9.96 women and 1.18 men were hospitalized for every 10,000 people. Acute pyelonephritis in women has been associated with a sudden increase in prevalence among patients aged 15 to 25 years, while remaining stable in those aged 25 to 80 years; in men, this prevalence seems to increase with age [18].

According to a report in 2007, acute pyelonephritis was reported in 38.1% of males in their 60s or older and 38.6% of females in their 20s and 30s [19]. Despite limited data, recurrence of acute pyelonephritis is 7 per 10,000 population. The mean treatment duration was 8.4 days. And the mean treatment duration was 7.2 days in outpatients and 14.1 days in hospitalized patients, with an average hospital stay of 7.9 days. The mortality rate was 1.2 persons in 1,000 population; 2.0 males and 1.0 females [18]. In the case of acute uncomplicated pyelonephritis between 2010 and 2011, according to a multicenter study in Korea, the mean age was 43 years, with a male to female ratio...
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Fig. 2. Algorithm for clinical management of acute uncomplicated cystitis (AUC). UTI: urinary tract infection, ESBL: extended spectrum beta-lactamase, TMP-SMX: trimethoprim-sulfamethoxazole.

Table 2. Factors that suggest a potential acute complicated pyelonephritis

The presence of an indwelling catheter, stent or splint (urethral, ureteral, renal) or the use of intermittent bladder catheterisation, Post-void residual urine of >100 ml, An obstructive uropathy of any aetiology, e.g., bladder outlet obstruction (including neurogenic urinary bladder), stones and tumor, Vesicoureteric reflux or other functional abnormalities, Urinary tract modifications, such as an ileal loop or pouch, Chemical or radiation injuries of the uroepithelium, Peri- and postoperative urinary tract infection, Renal insufficiency and transplantation, diabetes mellitus and immunodeficiency.

of 1:14.4 [20].

2) Diagnosis

(1) Clinical diagnosis: Acute pyelonephritis is a UTI caused by acute bacterial infection of the renal pelvis and renal parenchyma, with clinical symptoms of flank pain, nausea, vomiting, fever of 38 degrees or more, and urinary symptoms, such as urinary frequency, dysuria, residual urine sense, and gross hematuria. However, physical examination may show costovertebral angle tenderness with fever without urinary symptoms [21]. For this reason, it is difficult to diagnose acute pyelonephritis only with high fever and flank pain, requiring further examinations [22]. All patients suspected of acute pyelonephritis should be evaluated for multiple factors associated with complicated acute pyelonephritis, and one of the most important methods is history taking. Making a distinction between uncomplicated and complicated acute pyelonephritis requires careful history taking at the initial diagnosis of pyelonephritis since the choice and duration of antibiotics as well as the need for other treatments are different. However, it is often difficult to distinguish between uncomplicated and complicated acute pyelonephritis with only the initial clinical symptoms. Factors that may cause complicated acute pyelonephritis are shown in Table 2 [23].

(2) Laboratory diagnosis: A urinalysis (dipstick method) is recommended as a basic test (LE: 4, GR: C). A colony count of >10³ cfu/ml of uropathogens is considered to be clinically significant, indicating bacteriuria (LE: 2b, GR: C).

The major causative organism of acute pyelonephritis is E. coli, and from 2000 to 2005, 79% of the 2,910 multicenter studies in Korea reported E. coli-induced pyelonephritis [24]. The most common causative organism for acute pyelonephritis was determined to be E. coli in other domestic studies, K. pneumoniae, Proteus mirabilis, Enterococcus strain, and S. saprophyticus have also been identified [7,17,24-26]. These causative organisms differ in
distribution, especially according to age. Urine cultures and susceptibility tests should be performed to promote the use of antibiotics in a cost effective manner because the use of inappropriate antibiotics can have serious consequences (Grade B). However, blood culture tests are not mandatory and should be performed according to the circumstances (Grade D). If two or more of the following conditions are present, blood culture should be performed more than two times: body temperature above 38°C, white blood cells below 4,000 or above 12,000, heart rate of less than 90/min, respiratory rate of more than 20/min, PaCO₂ below 32 mmHg, systolic blood pressure below 90 mmHg (Grade C).

The detection of bacteria in the urine culture under clinical diagnosis of acute pyelonephritis is 46.3-78.8% [24,26]. If causative organisms are not detected, it can be considered as one of two things: the infection cannot be cultured after inoculation on blood agar medium and MacConkey agar medium, or the antibiotics has been taken from primary medical institutions or pharmacies. Blood tests may result in increased neutrophil leukocytosis, elevated erythrocyte sedimentation rate, increased C-reactive protein (CRP), and elevated serum creatinine levels associated with renal failure and decreased creatinine clearance. Recently, procalcitonin levels in the blood have been reported to be a good predictor of mortality and sepsis in acute pyelonephritis compared with the traditional blood markers, such as CRP [27,28]. In women with acute pyelonephritis, blood culture is not recommended; however, it should be considered if the complicated acute pyelonephritis is suspected [29]. If there is persistent fever or flank pain even after 72 hours of treatment, aggravated acute pyelonephritis or complicated acute pyelonephritis should be considered. At this time, blood cultures may be positive.

(3) Imaging test: Ultrasonography must be performed to evaluate upper urinary tract disorders, such as obstruction of the urinary tract or renal stone (LE: 4, GR: C). If there is complaint of persistent fever even after 72 hours of treatment, unenhanced helical computed tomography, excretory urography, or dimercaptosuccinic acid renal scans should be considered as additional tests (LE: 4, GR: C). Recently, it has been reported that computed tomography may be more useful than ultrasonography. Especially, the classification according to the degree of parenchymal invasion of the contrast enhancement computed tomography image is associated with the severity and prognosis of pyelonephritis [30-33].

### 3) Treatment

Due to the lack of well-designed systematic studies, treatment for acute uncomplicated pyelonephritis can be empirical therapy based on the results of UTI pathogens and antibiotic susceptibility that lead to acute uncomplicated cystitis (LE: 4, GR: B) [34]. *S. saprophyticus*, a causative organism of acute uncomplicated pyelonephritis, is seen less frequently than acute cystitis (LE: 4, GR: B) (Table 3).

(1) Mild and moderate acute uncomplicated pyelonephritis: For patients with mild-to-moderate acute pyelonephritis, 10 to 14 days of oral antibiotic therapy is recommended (LE: 1b, GR: B) (Table 4). Ampicillin, TMP-SMX, first-generation cephalosporin, and etc., are recommended as first-line antibiotics for *E. coli*, which is a major cause of acute pyelonephritis with high resistance in Korea (Table 5). The resistance rates to *E. coli* are high with ampicillin (62.3%), TMP-SMX (36.7-37.2%), and first-generation cephalosporin (33.9-58.3%). It is not appropriate as a primary antibiotic for patients with acute uncomplicated pyelonephritis [24,26]. Fluoroquinolone can be used as a primary treatment in areas with its resistance rate of around 10% (LE: 1b, GR: A) [35]. In Korea, the resistance rate of fluoroquinolone (6.9-12.9%) and third-generation cephalosporin (ex, cefotaxim: 0.8-10.2%) antibiotics is reported to be around 10% [24,26]. If the dose of fluoroquinolone is increased, the treatment period may be

| Table 3. Initial therapy recommended for severe acute uncomplicated pyelonephritis |
|---------------------------------|---|---|
| Initial therapy | LE | GR |
| A parenteral fluoroquinolone, in communities with *Escherichia coli* fluoroquinolone-resistance rates <10% | 1b | B |
| A third-generation cephalosporin, in communities with ESBL-producing *E. coli* resistance rates <10% | 1b | B |
| An aminopenicillin plus a β-lactamase-inhibitor in cases of known susceptible Gram-positive pathogens | 4 | B |
| An aminoglycoside or carbapenem in communities with fluoroquinolone and/or ESBLs-producing *E. coli* resistance rates >10% | 1b | B |

Table 4. Initial empirical antimicrobial therapy in acute uncomplicated pyelonephritis in premenopausal women (oral therapy: mild and moderate acute uncomplicated pyelonephritis)

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Daily dose</th>
<th>Duration of therapy (d)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>500-750 mg bid</td>
<td>7-10</td>
<td>Talan et al. [35]</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>250-500 mg qd</td>
<td>7-10</td>
<td>Richard et al. [41]</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>750 mg qd</td>
<td>5</td>
<td>Klausner et al. [36]</td>
</tr>
<tr>
<td>Alternative (clinically equivalent to fluoroquinolone but not equivalent to bacteriological effect)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefpodoxime proxetil</td>
<td>200 mg bid</td>
<td>10</td>
<td>Cronberg et al. [38]</td>
</tr>
<tr>
<td>Ceftibuten</td>
<td>400 mg bid</td>
<td>10</td>
<td>Peterson et al. [37]</td>
</tr>
<tr>
<td>If an antibiotic susceptibility test is performed (not appropriate for primary treatment)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-sulphamethoxazole</td>
<td>160/800 mg bid</td>
<td>14</td>
<td>Rubin et al. [42]</td>
</tr>
<tr>
<td>Co-amoxiclavab,c)</td>
<td>0.5/1.25 g tid</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

BID: twice a day, qd: once a day, tid: three times a day, Co-amoxiclav: amoxicillin-clavulanic acid.

*Lower dose studied, but higher dose recommended by experts, b) not studied as monotherapy in acute uncomplicated pyelonephritis, c) mainly for Gram-positive pathogens.

Table 5. Antibiotic susceptibility (%)

<table>
<thead>
<tr>
<th>Antibiotic sensitivity of <em>Escherichia coli</em> and <em>Klebsiella pneumoniae</em></th>
<th>AP</th>
<th>SAM</th>
<th>AK</th>
<th>GM</th>
<th>TOB</th>
<th>CIP</th>
<th>LFX</th>
<th>SPT</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>27.2</td>
<td>77.1</td>
<td>92.1</td>
<td>75.5</td>
<td>83.7</td>
<td>79.0</td>
<td>67.4</td>
<td>44.7</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>43.2</td>
<td>63.5</td>
<td>98.1</td>
<td>97.2</td>
<td>97.3</td>
<td>88.3</td>
<td>66.7</td>
<td>85.6</td>
</tr>
</tbody>
</table>

Antibiotic sensitivity of Gram(-) organisms between 2000 and 2004

<table>
<thead>
<tr>
<th>Year</th>
<th>AP</th>
<th>SAM</th>
<th>AK</th>
<th>GM</th>
<th>TOB</th>
<th>CIP</th>
<th>LFX</th>
<th>SPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000 year</td>
<td>38.5</td>
<td>79.3</td>
<td>91.7</td>
<td>83.1</td>
<td>85.3</td>
<td>80.2</td>
<td>67.5</td>
<td>59.0</td>
</tr>
<tr>
<td>2004 year</td>
<td>18.9</td>
<td>74.4</td>
<td>95.4</td>
<td>72.1</td>
<td>79.1</td>
<td>76.7</td>
<td>65.5</td>
<td>38.1</td>
</tr>
</tbody>
</table>

Adapted from the article of Lee et al. J Korean Med Sci 2009;24:296-301 [19]. Comparison between *E. coli* and *K. pneumoniae* (p < 0.05). Comparison between 2000 and 2004 yr (p < 0.05).


shortened to 5 days (LE: 1b, GR: B) [36,37]. But, considering the global expression pattern of fluoroquinolone-resistant *E. coli*, the use of an initial high dose of fluoroquinolone should be limited.

Third generation cephalosporins, such as cefpodoxime proxetil, cefuroxime, and ceftibuten, can be used as an alternative drug (LE: 1b, GR: B) [36,38,39]. However, according to the reports to date, there have been clinically equivalent effects with ciprofloxacin, but bacteriological and efficacious aspects have not been proven. Considering that the community resistance rate for Cotrimoxazole is greater than 10% in most areas, it may not be appropriate as an empirical therapy; however, it may be considered if there is no resistance as shown on the antimicrobial susceptibility test (LE: 1b, GR: B) [40]. Amoxicillin-clavulanic acid is not recommended as a primary treatment agent (LE: 4, GR: B), but may be selected as a therapeutic agent if Gram-positive bacteria are cultured in an antimicrobial susceptibility test (LE: 4, GR: C). In regions where the resistance rate of fluoroquinolone is high and the resistance rate of ESBL exceeds 10%, aminoglycosides or carbapenems can be used as a primary treatment until antibiotic susceptibility test results are reported (LE: 4, GR: B).

(2) Severe acute uncomplicated pyelonephritis: In patients with severe acute pyelonephritis, without the possibility of oral administration due to systemic symptoms, such as nausea and vomiting, parenteral antibiotics should be considered as the initial treatment (Table 4) [35-38,41,42]. Hospital admission should be considered if complicating factors cannot be ruled out in diagnostic procedures or if patients have clinical signs and symptoms of sepsis (LE: 4, GR: B). After improvement, patients can be switched to oral therapy, and the treatment should continue for at least 1-2 weeks (LE: 1b, GR: B).

After improvement, the patient can be switched to an oral therapy (Table 4) and continue treatment for 1-2 weeks. Table 6 shows daily dose only [35,36,41,43-47].

4) Follow-up

Urinalysis or urine culture for follow-up in asymptomatic
patients is not recommended (LE: 4, GR: C). Acute uncomplicated pyelonephritis can be followed-up if risk factors for complicated UTI (Table 2) is suspected. If symptoms do not improve within 3 days after diagnosis, or if there is no symptom loss or recurrence within 2 week, urine culture and antibiotic susceptibility test, as well as kidney ultrasonography, computed tomography, and renal scintigraphy should be performed (LE: 4, GR: B). In patients without functional structural abnormalities of the urinary tract, and if an antibiotic-resistant bacterium is initially suspected, an alternative antibiotic should be administered based on urine cultures (LE: 4, GR: B). A recurrence of acute uncomplicated pyelonephritis by the same pathogen should be reevaluated for factors that may cause recurrent pyelonephritis (LE: 4, GR: C).

**CONCLUSIONS**

1. **Limitations**

The authors attempted to develop a guideline for UTIs considering domestic characteristics; however, domestic literature regarding this is severely lacking. It is necessary to provide guidelines that adheres to the domestic characteristics through continuous research. In addition, additional guidelines for UTIs, including recurrent UTIs and complicated UTIs, are needed.

**CONFLICT OF INTEREST**

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

**REFERENCES**


46. Naber KG, Savov O, Salmen HC. Piperacillin 2 g/tazobactam 0.5 g is as effective as imipenem 0.5 g/cilastatin 0.5 g for the treatment of acute uncomplicated pyelonephritis and complicated urinary tract infections. Int J Antimicrob Agents 2002;19:95-103.