Urinary Tract Infections & Treatment

An Overview to the Treatment of Bacterial Infections of Urinary Tract

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1. Introduction

Bacterial infection of the urinary tract is defined as the presence of bacteria in the urinary tract and the symptoms should be attributable to this organism. Urinary Tract Infections (UTI) are more common in women due to the anatomical disadvantage. Many UTI cases in males are complicated and are associated with abnormalities in the urinary tract. As age progresses, the incidence of UTI also increases.

UTI is generally divided into 3 types as cystitis, pyelonephritis and prostatitis [1]. More recently, a classification was made that takes into account clinical factors and mortality and morbidity: uncomplicated cystitis in young women, recurrent cystitis in young women, acute uncomplicated pyelonephritis in young women, complicated UTI, UTI associated with long-term catheters, UTI in men and asymptomatic bacteriuria [2].

Here we summarize the treatment of UTI in the main titles of asymptomatic bacteriuria, uncomplicated UTI and complicated UTI.

2. Asymptomatic Bacteriuria

Bacteriuria (the presence of > 105 organisms / mL in urine samples) is defined as asymptomatic bacteriuria. In adult patients, including elderly patients, asymptomatic bacteriuria does not require treatment; furthermore antibiotics can often complicate the situation, often with drug-related side effects [3]. Patients with asymptomatic bacteriuria who require screening and treatment include: pregnants and patients who have undergone urological intervention (transurethral resection, etc.).

3. Complicated uti

Uncomplicated cystitis

Uncomplicated cystitis is limited by several pathogens, and in nearly 80% the causative microorganism is E. coli. Other commonly encountered pathogens are *Enterobacter*, *Klebsiella*, *Pseudomonas, Proteus, Streptococcus faecalis, Staphylococcus saprophyticus, Enterococcus* and *Chlamydia* [4]. Acute cystitis occurs in about 20% of women. There are two forms: relapse (if all infections occur with the same microorganism) and re-infection (if the episodes are with different microorganisms). Relapses are considered as complicated UTI and require longer duration of antibiotics [5].

Antibiotics (oral route for 3-7 days) which may be used in the treatment of cystitis in healthy subjects may include nitrofurantoin, trimethoprim-sulfamethaxazole, phosphomycin, pivmecilliam, ciprofloxacin, levofloxacin [6]. If symptoms persist for more than 7 days, if a recent history of urinary infection is present, if the patient is older than 65 years, if diabetic or diaphragm use is indicated, 7 days of use of trimethoprim-sulfamethaxazole or fluoroquinolone is recommended [6]. Regional resistance rates must be taken into consideration.

Resistance rates to quinolones vary according to the countries. Quinolone resistance is reported to be 71-91% for E. coli and 65-94% for *Klebsiella spp* [7,8].

Amoxicillin, cephalexin, nitrofurantoin, trimethoprim-sulfamethaxazole can be used orally for 3-7 days in uncomplicated UTI in pregnancy [6,9]. The administration of sulfonamides in the last months of pregnancy should be avoided; otherwise the newborn may develop hyperbilirubinemia. In addition, the use of tetracycline should also be avoided [4].

While UTI is dominant in women, it is seen at very early ages (<1 year) and in UTIs in men is more common in elderly patients [10]. If the patient is male, trimethoprim-sulfamethaxazole, ciprofloxacin, levofloxacin are given for 7 days (1158.6).

Acute uncomplicated pyelonephritis

Classical findings of acute pyelonephritis are abrupt fever, flank pain and costovertebral angle sensitivity. There are no signs or symptoms that are pathognomonic. In some studies, acute pyelonephritis was detected in 30-50% of patients presenting with acute cystitis symptoms [11].

Prospective randomized controlled trials that will show whether the patient's treatments should be done in hospital are still not sufficient. Suitable parenteral agents for the treatment of patients with acute pyelonephritis in hospitalized patients include an aminoglycoside (Gentamycin), a third cephalosporin (ceftriaxone), or a fluoroquinolone (ciprofloxacin,

levofloxacin). If a normal gram-positive organism is considered or there is a gram-positive result in gram staining ampicillin-sulbactam or ampicillin treatment may be added [12].

Initially used empirical treatment regimens should include broad spectrum antibiotics (penicillins or beta-lactams, cephalosporins, fluoroquinolones and carbophenems).

Recurrent UTI in women

Recurrent uncomplicated cystitis can be defined as uncomplicated cystitis 2 times in the last 6 months or 3 times in the last 1 year. Following the first cystitis episode, there is a risk of recurrent uncomplicated cystitis in 20-30% of women [13].

Recurrent UTIs are also common in women who do not have any other disease. It can be in the form of relapses (same microorganisms) or re-infection (different microorganisms) (0008.13). Recurrent UTIs occur more frequently with the same microorganism [14].

Some host factors provide predisposition for recurrent infection in healthy women. These include pelvic anatomic differences such as local pH, changes in cervicovaginal antibody in the vagina, and short urethral anus [15].

The most important risk factor for recurrent UTI in young women is the frequency of sexual intercourse. The first UTI age is ≥15, the maternal recurrence UTI history, the new sexual partner in the last 1 year, the use of spermicide within the last 1 year can be considered as other risk factors [15].

Postcoital prophylaxis may be appropriate since sexual intercourse is the most important factor for recurrent UTI. Nitrofurantoin (once a day), fosfomycin (every ten days) and cephalexin or cefaclor are suitable options for this purpose. In general, other prophylactic agents that may be used are trimethoprim-sulfamethaxazole single dose, ceftibuten single dose, nitrofurantoin single dose, or cefixime single dose, in addition to these agents [12].

Women who frequently have recurrent UTI may be advised to treat themselves. At this point patient compliance would be very essential. When the symtoms develop, 200 mg of oflaxocin twice a day or 250 mg levofloxacin once a day will be appropriate without consulting a physician [16].

Continuous antimicrobial prophylaxis may be recommended in patients who cannot be successful in postcoital prophylaxis. In these cases, trimethoprim-sulfametaxazole, Nitrofurontaine, ciprofloxacin or norfloxacin may be given 3 times a week or before bedtime [17,18].

A recent meta-analysis concluded that nitrofurantoin has similar efficacy to other agents in the recurrent UTI prophylaxis, but the risk of side effects, especially gastrointestinal side

effects, headache and peripheral neuropathy, is higher [19].

The role of non-antibiotic behavioral measures in the treatment of women with recurrent UTIs should also not be underestimated. Although the scientific basis is not established, post-coitus voiding may be proposed [20].

Topical estrogen preparations may be recommended for postmenopausal women [21].

In a study. Recurrence of UTI was less common in women who were drinking cranberry-lingonberry concentrate for 6 months [22].

In another publication, recurrent UTI was less common in women who drink more than 1500 ml of water a day [23].

Complicated Uti

The most common cause of complicated UTI (cUTI) is E. coli, which produces pathogenic ESBL. Initially used empirical treatment regimens should include broad spectrum antibiotics (penicillins or beta lactams, cephalosporins, fluoroquinolones and carbophenems). Broad spectrum antibiotics should be narrowed according to culture results [24].

Although quinolones are a treatment option in cuTI treatment, ciprofloxacin resistance can reach up to 58% in some areas. However, levofloxacin is successfully used in the treatment of cUTI. There is not yet a consensus in cUTI treatment [25].

The combination of Ceftolozane-tazobactam is a β-lactam / β-lactamase inhibitor recently approved for cUTI therapy and it is beneficial not to avoid carbamazepine. It was found to be effective against resistant *Pseudomonas aeruginosa* [26]. However, there are phase-3 studies demonstrating that this combination is also effective against ESBL producing *Enterobacteria* [27]. The use of ertapenem should not be considered in the treatment of UTI in which *Pseudomonas aeruginosa* is suspected to be the causative agent. Ertapenem has a poor efficacy on *Pseudomonas aeruginosa* [28].

Fluid resuscitation should be performed to the patient with septic shock and vasopressor support should be provided if necessary [24].

Catheter-related UTI

Long-term urinary catheterization provides the basis for bacterial biofilm formation [29]. E. coli is not a first-line pathogen in catheter-related UTI epidemiology. *Enterococci* are more accused [30]. In the case of catheter-related UTI, the best approach seems to be to avoid unnecessary long-term catheterization. In general, removal of the catheter and initiation of antibiotic therapy is considered appropriate treatment [31]. Intermittent catheterization may be

preferred if required. This method is associated with fewer bacteriuria and UTI development [32]. Antimicrobial treatment should be done according to culture results. In some conditions empirical treatment is necessary. Gram staining can also help. Particular attention should be paid to the inclusion of gram-negative organisms when empirical therapy is needed.

If there is not a suspicion of multidrug resistant bacteria, a third generation cephalosporin or a fluoroquinolon may be treatment option. If multidrug-resistant bacteria are suspected, broad-spectrum antibiotics should be considered. For example, if Pseudomonas aurigunoza is suspected, ciprofloxacin, ceftazidime or cefepime may be used. Or, if suspicious of a microorganism producing an extended spectrum of beta-lactamase (ESBL), the options are usually carbapenems [33].

The following measures are often useful to protect against catheter-related UTI: [34]

- A closed catheter system should be used.

- Catheterisation duration should be minimal.

- Catheters should be inserted under antiseptic conditions.

- If a sterile or clean technique or an antiseptic gel is used, there is limited evidence that the risk of bacteriuria is equally high.

- The drainage bag should be positioned below the bladder level of and the connecting tube

- Catheterisation should always be introduced by trained personnel.

- Adequate lubricant and the smallest possible catheter calibre should be used to minimise the urethral trauma.

4. Neurogenic Bladder

Patients with neurogenic bladder should be treated only in the case of UTI. Treatment of asymptomatic bacteriuria is not beneficial [35]. According to the current knowledge, the benefit of routine antibiotic prophylaxis is not shown [36]. In the case of UTI, all catheters that are longer than 2 weeks should be removed, and urine samples should be obtained from the new catheter and then antibiotic therapy should be started [37].

Patients should be treated with as narrow spectrum antibiotics as possible and antibiotic use should be as short as possible. IDSA (Infectious Diseases society of America) recommends 7-day treatment for patients who receive rapid response to treatment. In patients with severe infection and delayed response, treatment should be extended to 14 days [38]. If methicillin-

resistant *S. aureus* is suspected, severe infections in the hospitalized patient should be treated with vancomycin. In outpatients trimetoprim-sulfamethoxazole can be considered orally [37].

Nitrofurantoin can be used in mild cases with systemic involvement, if *Pseudomonas* is not suspected in the epidemiology. There is no information on the use of phosphomycin in severe infections. However, it is safe to use in uncomplicated UTI. The effect on biofilms is good [39].

5. References

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