South African Family Practice 2016; 58(1):6-10

S Afr Fam Pract
ISSN 2078-6190 EISSN 2078-6204

REVIEW

Urinary tract infections in women

Jacky van Schoor

Amayeza Info Centre
Correspondence to: Jacky van Schoor, e-mail: jacky@jvschoor.co.za

Abstract

Symptoms suggestive of acute urinary tract infections (UTIs) are common reasons why women consult a health professional. Antimicrobial agents are usually prescribed for the treatment of symptomatic UTIs seen in clinical practice. However, the extensive use of antimicrobial agents for community-acquired UTIs has resulted in the emergence of antimicrobial resistance. Increasing concern about the association between the use of antimicrobial agents and acquired antimicrobial resistance has highlighted the need for rational pharmacotherapy when treating UTIs. This article discusses currently recommended antimicrobial therapy for uncomplicated UTIs in women, UTIs during pregnancy and recurrent UTIs.

Keywords: urinary tract infection, cystitis, pyelonephritis, antimicrobial agents, resistance

Introduction

Urinary tract infections (UTIs) are common bacterial infections in women, with half of all women experiencing at least one in their lifetime.[1] Of the women affected, 25-30% develop recurrent infections unrelated to any functional or anatomical abnormality of the urinary tract.[2] Most UTIs in women are episodes of acute uncomplicated cystitis which occur in women of childbearing age.[1] Although acute uncomplicated cystitis may not be thought of as a serious condition, it affects the patient's quality of life by causing an estimated six days of discomfort.[1]

Acute cystitis refers to symptomatic infection of the bladder in the lower urinary tract.[3] It can occur alone or in conjunction with pyelonephritis, i.e. infection of the kidney in the upper urinary tract.[3] Most episodes of cystitis and pyelonephritis are considered to be uncomplicated infections when occurring in otherwise healthy non-pregnant women.[3] A complicated UTI can occur in either the upper or lower urinary tract, but is accompanied by an underlying condition which increases the risk of therapy failing, such as obstruction, an anatomical abnormality, urological dysfunction, pregnancy or resistant pathogen.[3-5]

The characteristics of patients with uncomplicated and complicated UTIs are detailed in Table I.[1]

Table I: The characteristics of patients with uncomplicated and complicated urinary tract infections[1]

Uncomplicated urinary tract infections	Complicated urinary tract infections
• Immunocompetent (otherwise healthy) • An absence of co-morbidities • No known urological abnormalities • Non-pregnant • Premenopausal	• Immunocompromised • Underlying metabolic disorders, e.g. diabetes mellitus • Urological abnormalities, e.g. stones and neurogenic bladder • Preadolescent or postmenopausal* • A history of childhood urinary tract infections

* However, some experts consider urinary tract infections to be uncomplicated in otherwise healthy postmenopausal women[5]

Pathogenesis

The urinary tract is normally sterile and resistant to bacterial colonisation, despite frequent contamination of the vaginal introitus by uropathogens from the faecal flora.[3,5] Completely emptying the bladder during urination is the major defense against UTIs.[5] Other mechanisms which maintain the sterility of the urinary tract include urine acidity, the vesicoureteral valve and various immunological and mucosal barriers.[5]

Approximately 95% of UTIs occur when bacteria ascends the urethra to the bladder, and in the case of pyelonephritis, ascends the ureter to the kidney.[5] On rare occasions, haematogenous UTI can occur when the pathogen is delivered to the urinary tract via the bloodstream from a distant source of infection, such as the lungs in a patient with pneumonia.[4]

Risk factors

Several risk factors for UTIs have been described in the literature, and include frequent sexual intercourse, lack of urination after sexual intercourse, a new sexual partner in the last year, the use of a diaphragm or spermicide, a history of recurrent UTIs and the occurrence of a UTI in a first-degree female relative.[5]

Microbiology

The microbial spectrum of uncomplicated UTIs in women consists mainly of *Escherichia coli* (75-95%). Occasional other species of *Enterobacteriaceae,* such as *Proteus mirabilis* and *Klebsiella pneumoniae,* and other bacteria, such as *Staphylococcus saprophyticus,* also cause infection.[3] Other bacterial species are rarely isolated in uncomplicated UTIs.[3] Therefore, the local antimicrobial susceptibility patterns of *E. coli,* in particular, should be considered in empirical antimicrobial selection when treating uncomplicated UTIs.[3]

The isolation of organisms from a urine sample in otherwise healthy non-pregnant women, such as lactobacilli, enterococci, group B streptococci, and coagulase-negative staphylococci (other than *S. saprophyticus),* is often representative of contamination of the sample, rather than infection in the urinary tract.[3]

Clinical presentation

UTIs are typically diagnosed by clinical presentation and a limited number of findings on physical examination.[4] Otherwise healthy patients with cystitis usually report a sudden onset of dysuria, with urinary frequency and urgency; the voiding of small volumes of urine; haematuria, but no fever; and constitutional symptoms.[4,5] The latter refer to a group of symptoms, including weight loss, fever, fatigue, chills, night sweats and a decreased appetite.

Although suprapubic pain and tenderness may occur, they are only found in approximately 20% of women with an uncomplicated UTI.[4] The urine is often turbid.[5]

The clinical manifestations of pyelonephritis consist of cystitis symptoms (which may or may not be present), together with fever, chills, flank pain, costovertebral angle tenderness (back pain) and nausea or vomiting.[3,4] Pyelonephritis is a more serious infection than cystitis.[3] Outpatient management of patients with mild to moderate illness, who can be stabilised with rehydration and oral antibiotics under close supervision, is acceptable.[3]

It is noteworthy that while vaginal infection and irritation can cause dysuria, most women who have dysuria without vaginal discharge have a UTI, not vaginitis.[4]

The clinical findings in women with dysuria[4] are detailed in Table II.[4]

Table II: Clinical findings in women with dysuria[4]

Clinical findings in addition to dysuria	Possible aetiology
• Suprapubic tenderness • Pelvic discomfort, specially before and immediately after passing urine • Urinary urgency and frequency • Small-volume voiding • Haematuria	• Cystitis • A lower urinary tract infection
• Flank pain • Fever • Costovertebral angle tenderness • Nausea and vomiting • Bacteraemia • Suprapubic tenderness • Urinary urgency and frequency (may be present or absent)	• Pyelonephritis

Diagnosis

A clinical diagnosis of uncomplicated cystitis or pyelonephritis is made in a patient who has the signs and symptoms of a UTI and laboratory evidence of pyuria, i.e. the presence of white blood cells in the urine; and/or bacteriuria, i.e. the presence of bacteria in the urine.[3] Laboratory diagnostic tools include urinalysis, either by microscopy or dipstick, and urine culture.[3]

A laboratory investigation is often not necessary to confirm a diagnosis of acute cystitis in otherwise healthy, premenopausal, non-pregnant women who present with a classic, uncomplicated UTI, and no vaginal discharge or irritation.[3,6] This is because the probability of a UTI in these women is 90%.[6] This means that the decision to treat can be made on the strength of the clinical presentation.[6] Further tests, such as dipstick urinalysis or urine culture, do not influence management of the patient.[6]

However, urinalysis is recommended to support the diagnosis if the clinical presentation is not typical of acute, uncomplicated cystitis.[3] The presence of nitrites on a dipstick urinalysis of a midstream urine sample is highly predictive of UTI, since nitrites are formed only as a metabolic product from bacteria.[6] Therefore, a positive nitrite test is highly indicative of bacteriuria.[6,7] Pyuria is present in almost all women with acute cystitis or pyelonephritis. Its absence suggests an alternative diagnosis.[3] The leukocyte esterase test on dipstick urinalysis detects the esterase enzyme which is released from the white blood cells in the urine.[7] If the dipstick urinalysis is positive for nitrites (reflecting bacteriuria) and leukocytes (reflecting pyuria), this increases the probability of a UTI (approximately 80%), while a dipstick test which is negative for both nitrites and leukocytes reduces the probability of a UTI to roughly 20%.[6]

Urine culture with susceptibility data is recommended if there is a reason to suspect antimicrobial resistance, i.e. reinfection, or persistent or recurrent symptoms, in patients with known or suspected pyelonephritis, and in patients with complicated UTIs.[3,5]

Antimicrobial resistance of common uropathogens implicated in urinary tract infections

The extensive use of antimicrobial agents for community-acquired UTIs has resulted in the emergence of antimicrobial resistance.[8] There is considerable geographical variability among *E. coli* in terms of antimicrobial susceptibility.[3] In general, resistance rates > 20% have been reported in many regions for ampicillin and trimethoprim, with or without sulphamethoxazole.[3,8] Fluoroquinolone resistance rates < 10%

have been reported in most parts of North America and Europe, as well as South Africa, but there appears to be a clear trend of increasing resistance over time.[3,8]

Resistance rates for first- and second-generation oral cephalosporins and amoxicillin and clavulanic acid are regionally variable, but are generally < 10%.[3] For instance, gram negative urinary tract pathogens have shown a 95% susceptibility to cefixime, a 93% susceptibility to cefuroxime and an 81% susceptibility to amoxicillin/clavulanate in Gauteng.[8] Nitrofurantoin and fosfomycin appear to offer good activity against most uropathogens implicated in uncomplicated UTIs, suggesting that these agents may also be appropriate antimicrobial agents for the empirical therapy of uncomplicated UTIs in most regions.[3]

It was shown in a recent study in which the antimicrobial susceptibility of uropathogens causing community-acquired UTIs in patients presenting to public and private healthcare facilities in Gauteng province was evaluated, that the susceptibility profiles for fosfomycin, fluoroquinolones (ciprofloxacin, levofloxacin and norfloxacin), nitrofurantoin, cefixime and cefuroxime were similar, i.e. over 90%.[8] However, the uropathogens were less susceptible to amoxicillin and clavulanic acid, when compared with fluoroquinolones and fosfomycin.[8]

Trimethoprim and sulphamethoxazole (cotrimoxazole) was the least effective agent against the uropathogens in this study (44.3% susceptible).[8]

International guidelines recommend that the resistance threshold at which trimethoprim and sulphamethoxazole should not be used for acute uncomplicated UTIs is 20%.[3] There are insufficient data to determine the resistance levels at which the likelihood of failure outweighs the potential benefits for other antimicrobial agents.[3]

Antimicrobial treatment of urinary tract infections

Considerations in selecting an agent to treat an uncomplicated UTI include efficacy, the risk of adverse effects, resistance rates, the propensity to cause ecological adverse effects, i.e. the selection of drug-resistant organisms, and cost and availability.[3]

The South African Stewardship Programme 2014 recommendations for the treatment of acute uncomplicated cystitis and pyelonephritis include ciprofloxacin 500mg 12 hourly for 3 and 7 days respectively.[9] These recommendations contrast with those of Ampath, whose local data show sufficiently high *E-coli* resistance rates not to recommend either fluoroquinolones or cotrimoxazole as first line empiric therapy for uncomplicated cystitis in women.(ref 10) Instead, they recommend beta-lactams, nitrofurantoin or fosfomycin, which are also included in some international guidelines.[3] (Table III)

It should be noted that if there is any uncertainty regarding whether the diagnosis is cystitis or early pyelonephritis, the use of nitrofurantoin and fosfomycin should be avoided because they do not achieve adequate renal tissue levels.[3]

Table III: Ampath's recommendations for the oral treatment of acute uncomplicated cystitis, based on current susceptibility patterns for *E-Coli*[10]

Amoxycillin-clavulanate 875/125 mg (1 g) twice daily for 5 days
Cefuroxime 250 mg twice daily for 5 days
Cefixime 200 mg twice daily for 5 days
Cefpodoxime 100 mg twice daily for 5 days
Nitrofurantoin 100 mg 8 hourly for 7 days
Fosfomycin 3 g orally as a single dose

Oral antimicrobials for women with acute uncomplicated pyelonephritis treated on an outpatient basis include the fluoroquinolones (ciprofloxacin or levofloxacin), amoxycillin-clavulanate, cefixime or cefpodoxime.[10] Intravenous therapy with a long-acting parenteral antimicrobial agent, e.g. ceftriaxone 1 g intravenously daily, or gentamicin 6 mg/kg/day intravenously, should be administered to patients with severe pyelonephritis, or those with risk factors for resistance until susceptibility data are available.[3,9]

The symptomatic treatment of urinary tract infections

Clinical manifestations of UTIs should respond to antimicrobial therapy within 48 hours.[3] In the interim, patients with acute cystitis may be managed with a urinary tract analgesic, such as phenazopyridine, three times daily for two days, to relieve discomfort due to severe dysuria.[3] A two-day course is usually sufficient to allow time for a symptomatic response to antimicrobial therapy to occur, and to minimise inflammation.[3]

Urinary tract infections and asymptomatic urinary tract infections in pregnancy

A UTI in a pregnant woman is a significant risk factor for low-birthweight infants and prematurity.[4] Asymptomatic bacteriuria, i.e. the presence of bacteria in the urine without UTI symptoms, occurs in 5-9% of women, and does not require treatment, except in pregnant women.[4,9] Therefore, pregnant women should be screened at 12-16 weeks' gestation for bacteriuria.[9,11] If left untreated during pregnancy, progression to a symptomatic UTI, including acute cystitis and pyelonephritis, occurs in 15-45% of pregnant women.[4] This is largely owing to a less robust immune response in pregnant women.[4]

Bacteriuria should be treated in pregnant women with a three-day course of an antimicrobial agent, e.g. cefixime 250 mg, once daily, for three days, which reduces the risk of a symptomatic UTI by 80-90%.[4]

Fluoroquinolones are contraindicated in pregnancy.[9] Therefore, the following empirical antimicrobial agents should be used for the treatment of acute cystitis, with de-escalation to a narrower-spectrum agent once the urine culture and susceptibility results have become available:[9]

- Amoxicillin and clavulanate 875 mg/125 mg orally, 12 hourly, before the third trimester

- Cefuroxime 250 mg orally, eight hourly, is preferred in the third trimester
- Cystitis should be treated for five days.

The management of acute pyelonephritis in pregnant women usually includes hospital admission so that a parenteral antimicrobial agent can be administered.[11] Antimicrobial therapy can be converted to an oral regimen tailored to the susceptibility profile of the isolated organism following clinical improvement.[11] Broad-spectrum parenteral beta-lactams, e.g. cefazolin, are preferred as initial empirical therapy for pyelonephritis.[11]

Fluoroquinolones and aminoglycosides, which are often used for pyelonephritis in non-pregnant women, should be avoided in pregnancy, if possible.[11] Once afebrile for 48 hours, pregnant patients can be switched to oral therapy, and discharged to complete 10-14 days of antimicrobial treatment.[11]

Recurrent urinary tract infections in women

Recurrent uncomplicated UTIs are common in young, healthy women, even though these women have anatomically and physiologically normal urinary tracts.[12] Recurrent UTIs are ≥ 2 infections in six months, or ≥ 3 infections in one year.[11] Most recurrences are thought to represent reinfection, rather than relapse.[12]

Antimicrobial prophylaxis has been shown to be highly effective in reducing the risk of recurrent UTIs in women.[12] Continuous prophylaxis and postcoital prophylaxis (taken within two hours of intercourse) are effective in the management of recurrent uncomplicated cystitis.[12] The choice of treatment depends on the frequency and pattern of recurrence, as well as patient preference.[12] The choice of an antimicrobial agent should be based on the susceptibility patterns of the strains which caused the patient's previous UTIs.[12] Before any prophylaxis regimen is initiated, eradication of a previous UTI must be assured by obtaining a negative urine culture 1-2 weeks after treatment.[12]

Options for continuous and post-coital antimicrobial prophylaxis in women with recurrent UTIs are outlined in Table IV.[12]

Table IV: Options for continuous and post-coital antimicrobial prophylaxis for women with recurrent urinary tract infections[12]

Continuous antimicrobial prophylaxis	Post-coital antimicrobial prophylaxis
• Cotrimoxazole 40/200 mg, once daily, or • Nitrofurantoin 50-100 mg, once daily	• Cotrimoxazole 40 mg/200 mg *stat,* or • Nitrofurantoin 50-100 mg, *stat*

stat: immediately

Conclusion

UTIs are common bacterial infections seen in women in general practice, and a frequent indication for the prescription of an antimicrobial agent.[13] Antimicrobial resistance in uropathogens, particularly *E. coli,* is directly associated with prescribing in primary care.[13] Increasing concern about an association between the use of antimicrobial agents and acquired antimicrobial resistance has highlighted the need for rational pharmacotherapy when treating UTIs.[13] Healthcare professionals should discuss the appropriate use of an antimicrobial agent with patients. The potential for antimicrobial resistance developing can also be reduced if patients complete the recommended treatment course, and do not stop treatment as soon as their symptoms improve. Such practices are also linked to an increased risk of antimicrobial resistance.

References

1. Colgan R, Williams M. Diagnosis and treatment of acute uncomplicated cystitis. Am Fam Phys. 2011;84(7):771-776.
2. Kucheria P, Dasgupta P, Sacks SH, et al. Urinary tract infections: new insights into a common problem. Postgrad Med J. 2005;81(952):83-86.
3. Hooton TM, Gupta K. Acute uncomplicated cystitis and pyelonephritis in women. UpToDate [homepage on the Internet]. 2014. c2015. Available from: http://www.uptodate.com/contents/acute-uncomplicated-cystitis-and-pyelonephritis-in-women
4. Fitzgerald MA. Urinary tract infection: providing the best care. Medscape [homepage on the Internet]. 2002. c2014. Available from http://medscape.org/viewarticle/436592
5. Bacterial urinary tract infections. Merck Manual [homepage on the Internet]. 2013. c2014. Available from: http://www.merckmanuals.com/professional/genitourinary_disorders
6. Best Practice New Zealand. Laboratory investigation of UTI [homepage on the Internet]. 2006. c2014. Available from: http://www.bpac.org.nz/Supplement/2006/July/uti.aspx
7. Van Biljon G. A practical approach to urine dipstick abnormalities in relation to kidney and urinary tract disorders in children. S Afr Fam Pract. 2012;54(5):392-396.
8. Lewis DA, Gumede LYE, van der Hoven LA, et al. Antimicrobial susceptibility of organisms causing community-acquired urinary tract infections in Gauteng Province, South Africa. S Afr Med J. 2013;103(6):371-381.
9. Wasserman S, Boyles T, Mendelson M. A pocket guide to antibiotic prescribing for adults in South Africa, 2014. Southern African HIV Clinicians Society [homepage on the Internet]. c2015. Available from: http://www.sahivsoc.org/upload/documents/Guide%20to%20Antibiotice%20prescribing%20for%20adults%20in%20SA_2014.pdf
10. Ampath ref
11. Hooton TM, Gupta K. Urinary tract infections and asymptomatic bacteriuria in pregnancy. UpToDate [homepage on the Internet]. 2015. c2015. Available from: http://www.uptodate.com/contents/urinary-tract-infections-and-asymptomatic-bacteriuria-in-pregnancy
12. Hooton TM, Gupta K. Recurrent urinary tract infection in women. UpToDate [homepage on the Internet]. 2015. c2015. Available from: http://www.uptodate.com/contents/recurrent-urinary-tract-infection-in-women
13. Vellinga A, Cormican M, Hanahoe B, et al. Antimicrobial management and appropriateness of treatment of urinary tract infection in general practice in Ireland. BMC Fam Pract. 2011;12(1):108.