Urinary tract infection – 2003

Duława J

Department of Internal Medicine and Metabolic Diseases, Silesian University of Medicine, Katowice, Poland

Abstract

Urinary tract infections (UTI) are one of the most common and most intensively studied infections encountered in clinical practice. It is, however, an area where significant confusion has existed in agreeing the criteria for diagnosis, the natural history of disease, and the treatment.

In the present paper etiology and risk factors for uncomplicated UTI, treatment of UTI, estrogen in UTI treatment in postmenopausal women and UTI in patients with diabetes and renal insufficiency were discussed.

Key words: urinary tract infection, risk factors, etiopathogenesis, diabetes, asymptomatic bacteriuria.

Uncomplicated, community-acquired urinary tract infections (UTI) in women

Discussion of uncomplicated urinary infection primarily relates to a condition affecting women. It has been estimated that most women will experience at least one urinary tract infection during their lifetime. Uncomplicated UTI may involve the bladder or the kidneys and may be symptomatic or asymptomatic.

Most acute lower UTI (also termed acute bacterial cystitis) are uncomplicated – that is, they are not associated with structural abnormalities of the urinary tract, diabetes, immunosuppression, pregnancy, previous pyelonephritis, or symptoms lasting more than 14 days.

ADDRESS FOR CORRESPONDENCE:
Department of Internal Medicine and Metabolic Diseases
GCM, Katowice–Ochojec
ul. Ziołowa 45/47
40-635 Katowice
Tel/Fax: +48 32 2523593
e-mail: jdulawa@slam.katowice.pl

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After an initial infection, most women have sporadic recurrences, and a quarter to half have another infection within one year [1].

Etiology

Escherichia coli causes 75 to 90 percent of episodes of acute uncomplicated cystitis, and Staphylococcus saprophyticus accounts for 5-15%, mainly in younger women. Enterococci and aerobic gram-negative rods other than E. coli, such as Klebsiella sp. and Proteus mirabilis, are isolated in the remainder of the cases [2]. E. coli that encode the type 1 pilus, an organelle containing the adhesin FimH, which recognizes a wide range of cell types, are commonly associated with cystitis as well as sepsis and meningitis [3].

Considerable evidence supports the concept that the initial event leading to community-acquired UTI is intestinal colonization with a uropathogenic strain of E. coli. Once colonization has occured, the strain may remain part of the colonic flora for months, whether or not it causes a UTI. Its persistence in the colonic flora is facilitated by the same bacterial adhesins that promote attachment to the uroepithelium [4].

Risk factors

Women who experience acute UTI are characterized by both a genetic predisposition and behavioral factors. The most exposed are non-secretors of blood group substance and first degree female relatives with recurrent urinary infections. The most important behavioral risk factors are: recent sexual activity, use of spermicidal agents and diaphragm. Other behavioral factors include: frequency of urination, aspects of personal hygiene or use of the birth control pill. Despite the frequency of acute uncomplicated UTI, there is little long-term morbidity and no evidence for mortality attributable to this problem [5]. These women are not at increased risk of developing hypertension or renal failure. Short-term morbidity due to acute symptoms may however be substancial, especially for women with frequent UTI.

Table 1. **Antimicrobial regimens for prevention and treatment of recurrent urinary tract infections [8].**

Antimicrobial agent	Dosage for treatment	Daily dosage for prevention
Cefalexin	500 mg three times daily for three days	125 mg
Ciprofloxacin	100 mg twice daily for three days	125 mg
Amoxiclav	375 mg thrice daily for three days	No data available
Co-trimoxazole	960 mg twice daily for three days	240 mg (or three times a week)
Nitrofurantoin	50 mg four times daily for seven days	50-100 mg
Nitrofurantoin macrocrystals and monohydrate	100 mg twice daily for seven days	100 mg
Norfloxacin	200 mg twice daily for three days	200 mg
Trimethoprim	200 mg twice daily for three days	100 mg (or three times a week)

Treatment

In some locales, such as the southeastern and western United States and in Poland, resistance to trimethophrim-sulfametoxazole has become widespread and is detected in up to 20-25% of the pathogens cultured from the urine of women with acute cystitis, most commonly those who have received this agent within the preceding six month [5,6]. The prevalence of such resistance varies not only from country to country, but even from hospital to hospital [7].

The alarming reports of community-acquired UTI caused by fluoroquinolone-resistant E. coli strains in some parts of the world suggest that we will see an evolution of resistance to these agents just as we have with sulfonamides, ampicillin, oral cephalosporins, and now trimethoprim - sulfamethoxazole unless we take a much more aggressive approach to the control of antimicrobial resistance [4].

Nevertheless most of authors maintain that the first choice of treatment is trimethoprim, except in women from communities with a high rate of resistance, when one should follow the local guidance. The main alternatives are: norfloxacin, amoxiclav and nitrofurantoin. Antimicrobial regimens for treatment and prevention of recurrent UTI are enlisted in *Tab. 1*. A three day course of antibiotic treatment should suffice for most women with lower UTI. If, despite treatment, symptoms persist or worsen, urine culture should be performed and antibiotics according to the results of the culture and sensitivity tests should be prescribed. Upper UTI in otherwise healthy women can be treated with oral antibiotics for 7-10 days. Women who are systemically unwell should be admitted to hospital [8].

Women who have frequent recurrences (arbitrarily defined as three or more infections a year) should be advised to avoid exposure to vaginal spermicides and should be offered prophylaxis or methods of self-treatment. Imaging studies should be reserved for women with complicated infections [5].

Interestingly, there is some evidence that cranberry juice treats UTI and prevents its recurrence [9].

Exogenous estrogen in preventing recurrent UTI in postmenopausal women

It has been hypothesized that exogenous estrogen can prevent recurrent cystitis by reversing genitourinary mucosal atrophy and restoring a more normal milieu in the vagina. In a randomized, open-label study, the use of an estrogen–impregnated ring, or topical estriol cream were associated with a significant reduction in recurrent infections [10], but further studies with larger sample sizes are needed.

Although small studies have suggested a benefit associated with oral estrogen replacement therapy, recent randomized trials have failed to show a favorable effect in preventing cystitis, and there is currently no rationale for prescribing oral estrogens to prevent recurrent cystitis [11].

Urinary tract infections in patients with diabetes mellitus and renal insufficiency

Diabetic patients with renal disease are at increased risk of developing urinary tract infections due to functional complications of the urinary tract, impaired host defence mechanisms, and poor urinary flow. Interestingly, the frequency of UTI has been shown to be increased only in diabetic women compared with non-diabetic women, but not in diabetic men compared with non-diabetic men. This difference may be secondary to the increased incidence of vaginitis among women with diabetes mellitus. UTI in these patients may be further complicated by pyelonephritis, intrarenal or perinephric abscesses, papillary necrosis, and sepsis. In addition, the wide spread use of broad-spectrum antibiotics in recent years has selectively causes an increased incidence of fungal infections in the urinary tract [12].

Pathogenesis

Microorganisms may infect urinary tract by ascending through the urethra into the bladder or by haematogenous or lymphatic spread. The first mechanism is by far most common and can explain the association of the increased incidence of urinary tract infection in patients with frequent vaginitis and lower urinary tract abnormalities. Reported antibacterial host factors include the urea, organic acids, and salt content of the urine, and a high osmolality in the presence of the low pH. Other factors protecting the host include urinary inhibitors to bacterial adherence such as Tamm-Horsfall protein (THP), bladder mucopolysaccharide, low-molecular-weight oligosaccharides, secretory IgA and lactofferin.

In addition, proper urine flow, micturition and emptying of the bladder are crucial in inhibiting bacterial proliferation and extension to the upper urinary tract.

Role of Tamm-Horsfall protein in pathogenesis of UTI

There are some interesting informations concering the role of THP in the kidney defence against UTI, particularly those caused by E. coli.

Pak et al. [13] recently showed, that THP binds type 1 fimbriated E. coli in vitro and efficiently competes with uroplakin Ia and Ib in binding to these pathogens. These results support the notion that in vivo, urinary THP represents a protective agent against UTI, because type 1 E. coli strains represent the predominant phenotypic variants of isolates from patients with UTI, and uroplakin Ia and Ib behave as efficient cell receptors for type 1 fimbriated E. coli [14].

On the other hand it is known, that glication of THP in patients with diabetes, or in renal diseases can changes its ability to inhibition of bacterial adherence to human uroepithelial cells.

Asymptomatic bacteriuria in diabetics

The incidence of asymptomatic bacteriuria in diabetic patients is estimated from several studies to range between 7 and 32%. Despite its high incidence in diabetic patients, asymptomatic bacteriuria is not affected by hyperglycaemic control or the degree of renal failure [15]. Empirical treatment of asymptomatic bacteriuria still remains a clinical challenge. Undertreatment may theoretically predispose to pyleonephritis, renal papillary necrosis, and renal insufficiency, whereas overtreatment may give rise to multiple complications including poor tolerance to the side effects of antimicrobial agents, development of antibiotic-resistant organisms, fungal superinfections, and antimicrobial-induced renal failure. The latter complication may be irreversible in patients with underlying renal insufficiency. In diabetic patients, the presence of asymptomatic bacteriuria may be more problematic, especially in those with associated diabetic neurogenic bladder and urinary retention.

Treatment of asymptomatic bacteriuria requires careful clinical judgment. In general, the prognosis for asymptomatic bacteriuria is excellent. 14-year follow-up study of untreated asymptomatic bacteriuria in diabetic patients revealed similar frequencies of acute pyelonephritis, deterioration of kidney function, and systemic hypertension compared with control subjects [16].

Currently, treatment of asymptomatic bacteriuria is recommended for patients with frequent episodes of symptomatic UTI, pregnancy, after renal transplantation, and prior to urological interventions, but there are no substantial benefits from treating diabetics with asymptomatic bacteriuria [17].

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