

An Update On The Management Of Urinary Tract Infection

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Summary

Urinary tract infection (UTI) is commonly encountered in general medical practice. The majority of patients have uncomplicated infections affecting the lower urinary tract, which respond readily to a short course of oral antibiotics. Life-threatening complications or long-term morbidity can occur, especially in patients with underlying medical predispositions or urological abnormalities. Further investigations are warranted in patients with severe or recurrent UTI, or when UTI occurs in 'low risk' individuals. Special investigations to look for vesicoureteric reflux and renal cortical scars should be considered in children with UTI. Screening of pregnant women for asymptomatic UTI is important in view of its propensity to involve the upper urinary tract. A 3-day course of appropriate oral antibiotics is often sufficient for the treatment of uncomplicated lower UTI in young females. A longer treatment duration of up to 7 days may be indicated in elderly subjects. The optimal duration of antibiotic therapy for upper UTI remains controversial. In addition to antibiotic prophylaxis, simple advice on prophylactic measures during activities of daily living is often beneficial to patients with recurrent UTI. (HK Pract 1997; 19: 137-141)

摘要

泌尿道感染是日常診治中的常見病，大多數屬於無合併症的下泌尿道炎症，對短期口服抗生素治療反應理想，然而在有潛在疾病或尿道畸形患者，可能造成慢性併發症或致命病變。

復發性的、嚴重性的，或低危患者的泌尿道炎症，都須做詳細檢查。兒童患者應留意是否存在膀胱尿道返流和腎皮質疤痕。孕婦無徵狀尿道炎的診治尤為重要，因其容易引起上泌尿道炎症。短期三天口服抗生素對年青女性病人一般有效，年老患者則需延長至七天，但理想的治療療程仍存在爭議。

除預防用藥外，日常生活中簡單的預防措施對復發性泌尿道炎症亦有幫助。

Introduction

Infection of the urinary tract is a common problem. While most episodes of urinary tract infection (UTI) resolve after a short course of antibiotic therapy, severe cases of upper UTI can result in significant morbidity or even

mortality, especially in patients with underlying medical diseases (e.g. diabetes mellitus), as well as long-term sequelae (e.g. renal scarring). In addition, UTI may be the presenting feature of an underlying structural or functional abnormality of the urinary tract, such as obstructive uropathy or vesicoureteric reflux.

Epidemiology and causative factors

Among adults, UTI most commonly affects women of the reproductive age group, with a yearly incidence of 0.5–0.7 per person-year among young women, and a female to male ratio

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UPDATE ARTICLE

exceeding 8:1. About 40% of women have a history of UTI at some point in their lives. Established host risk factors include:

1. Recent sexual intercourse, which facilitates ascending migration of microorganisms.
2. Delayed post-coital micturition, which facilitates microorganism attachment to the uroepithelium.
3. Use of a diaphragm with spermicide, the former may impede efficient bladder emptying, while the latter alters the vaginal flora and reduces *Lactobacillus*, thus enhancing the growth of *Enterobacteriaceae*.
4. Structural abnormalities in the urinary tract.
5. A history of recurrent UTI.
6. ABO blood group non-secretor phenotype.

It is worth noting that the prevalence of 'asymptomatic' UTI increases by about 1% with each decade of life. It is therefore important to look for UTI in elderly subjects presenting with fever and/or deterioration in well-being, who may not have symptoms referable to the urinary tract.

The epidemiology of UTI among children is different from that in adults. While boys are more commonly affected in the first 3 months of life, there is a female predominance after 6 months. Approximately 1% of boys and 3% of girls before the age of 11 years are affected by UTI, but the incidence

is difficult to define in view of the often non-specific symptoms in this age group. Covert bacteriuria can be a prominent feature in children with UTI, and UTI is a recognized cause of febrile convulsion.

The commonest causative organisms of UTI are the gram-negative bacteria, e.g. *E. coli*. Factors that affect the spectrum of the causative agents include:

1. Associated pathology, e.g. *Proteus* species lower the urine pH and predispose to stone formation.
2. Urological abnormality, e.g. *Pseudomonas* species are associated with obstructive uropathy.
3. Underlying medical condition, e.g. Cytomegalovirus may be cultured from the urine of organ transplant recipients.
4. Geographical considerations, e.g. *Schistosoma haematobium* UTI occurs in endemic areas.
5. Urinary catheterization.

Patients with genitourinary tuberculosis can present with cystitis not responsive to conventional therapy, haematuria, flank pain, epididymitis, constitutional symptoms, chronic renal insufficiency, or abnormal radiological features such as calyceal irregularities, calyceal amputation, ureteric strictures, or dystrophic calcification. Non-bacterial microorganisms can also cause UTI, e.g. cystitis due to *Candida* and *Trichomonas* species, or urethritis due to *Herpes simplex*.

Clinical features, diagnosis, and management

Clinical presentation

Patients may present with predominantly lower urinary tract symptoms such as frequency, dysuria, haematuria, or with upper urinary tract symptoms such as loin pain. Fever is more common in patients with infection involving the upper urinary tract. However, distinguishing between upper and lower UTI based on clinical features may be difficult sometimes due to considerable overlap in symptomatology. Categorization is nevertheless useful, since patients with uncomplicated lower UTI usually require a short course of antibiotic therapy, whereas patients with complicated infection, recurrent UTI, or UTI occurring in 'low-risk' individuals, warrant further investigations to look for predisposing causes, and often more prolonged therapy.

Investigations

Urinalysis and urine culture constitute the first-line investigations in patients with UTI. Pyuria with >10 WBC/mm³ of unspun urine or >5 WBC/high-power field indicates significant inflammation in the urinary tract. Upper UTI is suggested by the detection of white cell casts in urine. The urine leukocyte esterase dipstick test is an alternative to microscopy. Gram smear of uncentrifuged urine showing ≥ 1 bacterium per oil immersion field is a useful screening test, but does not exclude low level bacteriuria. Urine culture yielding $>10^5$ colony-forming units (CFU)/ml, or $\geq 10^2$ CFU/

UPDATE ARTICLE

Table 1: Circumstances under which investigations are indicated to look for predisposing factors or complications of urinary tract infection (UTI)

1. Severe or repeated acute pyelonephritis in female patients
2. UTI not responsive to appropriate antibiotic therapy.
3. UTI occurring in male patients
4. Structural abnormalities in the urinary tract
5. Medical predispositions, e.g. diabetes mellitus, immunosuppression
6. Recurrent UTI, with ≥ 3 episodes within 1 year
7. UTI in children

ml of recognized uropathogen in a symptomatic patient, indicates significant bacteriuria.

Further investigations aim to look for predisposing medical conditions (e.g. diabetes mellitus), structural or functional abnormalities (e.g. obstructive uropathy due to calculi, prostatic hypertrophy, or ureteric stricture; neurogenic bladder; vesicoureteric reflux), as well as complications (e.g. renal cortical abscess, perinephric abscess, infected renal cyst, papillary necrosis, scarring, reflux nephropathy). Vigilance for predisposing factors or complications is especially relevant in patients with severe clinical features, in 'low-risk' groups, and in patients with repeated infections (Table 1).

The abdominal x-ray and ultrasonogram are useful in detecting stones and obstruction. Intravenous urogram to look for obstructive uropathy

is usually deferred after resolution of acute pyelonephritis, since the quality is often sub-optimal due to poor filling of the pelvicalyceal system during active infection. CT examination can reveal severe focal bacterial nephritis (acute lobar nephronia) as localized reduction in contrast opacification.

Screening of pregnant women for asymptomatic bacteriuria is important, since 30% of women with asymptomatic bacteriuria in early pregnancy will subsequently develop acute pyelonephritis.

Special considerations in children

Acute pyelonephritis in childhood may lead to parenchymal scarring. In severe cases, this may result in chronic renal failure in adulthood. New scars are uncommon beyond the age of 5, while children less than 1 year old are most susceptible. Since scarring can be minimized by early diagnosis and prompt

therapy, it is important to identify patients at risk of subsequent renal morbidity for urological investigations for consideration of prophylactic antimicrobial therapy and careful follow-up. Ultrasonogram can diagnose obstructive uropathy or renal calculi, but may not be sensitive enough to detect variable degrees of scarring (Figure 1).

Although renal parenchymal infection plays a more important role than vesicoureteric reflux (VUR) in causing renal scarring, the risk of scarring has been demonstrated to correlate with the severity of reflux. In children less than 1 year old, a micturating cystogram (Figure 2) and a dimercaptosuccinic acid (DMSA) scan should be performed, the former to look for VUR and posterior urethral valve and the latter to look for renal scarring. A DMSA scan should be arranged for a child between 1 and 7 years old who has UTI. To assess VUR, one can choose between a micturating cystogram and indirect radionuclide cystogram. For the over 7-year old child with normal ultrasonogram and abdominal x-ray, further investigations can be withheld at the first episode of UTI, unless the clinical features are severe. There is an increasing tendency to screen for reflux in siblings of patients with VUR, because of the possibility of autosomal dominant inheritance. In view of the high sensitivity of DMSA scan in detecting renal scarring, the intravenous urogram is usually reserved for anatomical delineation before surgical interventions. Diethylene triamine penta-acetic acid (DTPA) or mercaptoacetyl triglycine (MAG 3) scans are useful in the functional assessment of obstructive uropathy.

UPDATE ARTICLE

Figure 1: Intravenous urogram demonstrating renal cortical scarring at the upper pole



Figure 2: Micturating cystogram in a child demonstrating unilateral vesicoureteric reflux and hydronephrosis



Treatment

The choice of appropriate antibiotic therapy depends on the sensitivity pattern of common urinary pathogens. Trimethoprim-sulfamethoxazole, quinolones, and oral cephalosporins are useful and convenient first-line therapeutic agents for uncomplicated lower UTI, often caused by gram-negative enterobacteriaceae. Amoxicillin per se is not recommended in view of the high prevalence of drug resistance encountered among the gram-negative species. There has been controversy on the duration of antibiotic therapy for lower UTI. Current data suggest that

3-day treatment regimens are sufficient for young subjects. Whether the same holds true for the more elderly population remains to be established, thus a 7-day treatment duration has been recommended for women over the age of 65. Microscopy and culture of midstream urine 7-10 days after treatment is advisable.

Patients with upper UTI and/or severe symptoms may require hospital admission, especially those with medical complications or suspected obstructive uropathy. Cephalosporins with or without aminoglycoside are appropriate first-line antibiotics. Patients should have a high fluid intake. Predisposing

factors (e.g. obstruction, calculi) and complications (e.g. papillary necrosis, pyonephrosis) should be looked for and managed accordingly. Again there has been controversy with regard to the duration of antibiotic therapy for upper UTI. While it has been common practice to prescribe antibiotics for 2 weeks, more prolonged therapy of up to 6 weeks has been recommended for patients with severe upper UTI, especially in patients with urinary calculi, diabetes mellitus, or recurrent infections. There is evidence that even in adults, severe upper UTI can lead to cortical scarring, although its long-term functional significance remains to be established.

UPDATE ARTICLE

Table 2: Prophylactic measures to prevent recurrent urinary tract infection

1. Liberal fluid intake
2. Voiding every 2-3 hours, with double micturition if reflux present
3. Voiding at bedtime and after sexual intercourse
4. Avoid bubble baths and chemical additives in bath water
5. Avoid constipation which may impair bladder emptying

Key messages

1. Life-threatening complications or long-term morbidity can occur, especially in patients with underlying medical predispositions or urological abnormalities.
2. Gram-negative enterobacteriaceae represent the commonest urinary pathogens, non-bacterial causes must not be overlooked.
3. Special investigations to look for vesicoureteric reflux and renal cortical scars, such as micturating cystogram and dimercaptosuccinic acid (DMSA) scan, should be considered in children with UTI.
4. A 3-day course of appropriate oral antibiotics is often sufficient for the treatment of uncomplicated lower UTI in young females.
5. The optimal duration of antibiotic therapy for upper UTI remains controversial, and can vary from 2 to 6 weeks.
6. In addition to antibiotic prophylaxis, simple advice on prophylactic measures during activities of daily living is often beneficial to patients with recurrent UTI.

In children with VUR, antibiotic prophylaxis is recommended until the age of 5. Parental education and vigilance are important in the surveillance for breakthrough infections. In 70% of children the reflux will resolve spontaneously. Surgery may be considered in children less than 5 years old who have severe VUR associated with recurrent infections despite antibiotic prophylaxis, and in patients with obstructive uropathy, but may not be always effective in preventing breakthrough infections.

Recurrent UTI in adult women is often attributable to vaginal colonization by Enterobacteriaceae. Prophylactic measures with regard to activities of daily living can be considered in patients

with recurrent UTI (Table 2). In addition, the use of topical estrogen should be considered in post-menopausal women. For infections related to coitus, single dose antibiotic prophylaxis administered after sexual intercourse is usually sufficient. After exclusion of correctable predisposing factors, regular nocturnal antibiotic administration is often effective in the management of other patients with recurrent UTI.

Conclusion

The management of UTI necessitates consideration of both host and microbial factors. In addition to treatment of the acute episode, it is

imperative to look for underlying predispositions, diagnose complications or long-term sequelae of the acute infection, and prevent recurrence. ■

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