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UTI in Primary Care: Are we Prescribing Too Much?

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Abstract **Review Article**

Objectives: The aim of this article were to review usefulness of early clinical detection of UTI without lab tests as diagnostic tool for UTI in primary care and to describe when to start antibiotic treatment for management of UTI according to international guidelines. The emphasis of this review is uncomplicated UTI. ***Methods:*** A search was conducted on PubMed and official webpages of major urological, infectious diseases and general practice organisations to identify peer reviewed original articles and reviews, using the search terms 'UTI'. I considered only papers written in English, with emphasis on more recent articles published up to July 2023. ***Results:*** There is a variation in recommendations between guidelines can be a source of confusion and controversy for clinicians in primary care. However, early detection and treatment, education of patients and removal of risk factors may reduce the number of symptomatic episodes, antibiotics usage and antimicrobial resistance in primary care. ***Conclusion:*** The diagnosis of acute uncomplicated cystitis in healthy women can be made with reasonable certainty by evaluation of symptoms and signs without a doctor's visit or urine tests. Individualised assessment of risk factors and previous clinical history is needed to choose the most suitable antimicrobial treatment. Immediate antimicrobial therapy with Trimethoprim-sulfamethoxazole (160/800 mg twice daily for 3 days), Nitrofurantoin (100 mg twice daily for 5-7 days), or Fosfomycin (3g in a single dose) is indicated for acute cystitis in adult women. However, local guidelines advice that immediate antibiotic treatment was not considered necessary for women with uncomplicated lower UTI. Antimicrobial resistance have complicated treatment of UTI worldwide.

Keywords: Urinary tract infection, cystitis, primary care, urinary symptoms, urine dipstick.

INTRODUCTION

UTI is a number of clinical conditions due to microbial pathogens in the urinary tract. UTI are amongst the most common infectious conditions seen in Primary and Emergency Care. It is defined by the presence of a pure bacterial growth ≥105 cfu/ml. It can happen in the upper tract (kidney and ureter), lower tract (bladder, prostate) or both. In the majority of patients (75%-95%) the infection is due to E. coli, 5%-15% Staphylococcus saprophyticus and 5%-10% enterococci. Klebsiella, Proteus [1].

UTI occur more frequently in women. However, lower urinary tract symptoms (LUTS) are common in men and increase in frequency and severity with age. Over one third of men aged 50 or more are living with moderate to severe symptoms, equating to 3.4 million men in the United Kingdom alone and 24 million in countries of the European Union [2]. About 60% of women will experience at least one UTI in their life and 30%–40% will experience recurrent UTIs [10].

UTI presents with different symptoms according to the site of the infection and patient factors. They are two kind of presentations: non-complicated and complicated UTI. The diagnoses of uncomplicated cystitis and pyelonephritis is usually made on the clinical presentation, whereas the complicated cases are often more complex. Acute uncomplicated cystitis in women is manifested by dysuria, urgency, and/or frequency without fever, often with supra pubic pain and haematuria. Pyelonephritis is usually manifested by fever and back pain/costovertebral angle tenderness. Symptoms and signs of complicated cystitis are similar but can be subtle in the very young and very old such as vague symptoms of malaise or changes in the mental status [9].

A Cystitis in healthy women is often associated with recent sexual intercourse, recent use of a spermicidal product, asymptomatic bacteriuria, or previous history of cystitis. Women with a previous history of physician-diagnosed UTI are able to accurately self-diagnose a subsequent UTI. The accuracy of diagnosis based on patients' symptoms supports the findings of several studies demonstrating that selected

women with cystitis symptoms can be successfully managed without further assessment. Acute uncomplicated cystitis in women can be diagnosed without an office visit or urine tests. The aim of this strategy by self-diagnosis and self-treatment with a short-course regimen of an antibiotic is not to prevent recurrent UTI but instead to give the woman more autonomy in managing her recurrences by providing instructions on diagnosis and prescriptions for her to obtain antibiotics without having to consult with her doctor.

Acute uncomplicated pyelonephritis in women is suggested by fever (temperature ≥38.5°C), chills, flank pain, nausea and vomiting, and costovertebral angle tenderness. Cystitis symptoms may or may not be pres ent. Patients with acute complicated pyelonephritis may also present with sepsis, multiple organ system dysfunc tion, shock, and/or acute renal failure. In some cases, complicated pyelonephritis may be associated with weeks to months of insidious, nonspecific signs and symptoms such as malaise, fatigue, nausea, or abdominal pain. In the setting of what appears to be pyelonephritis, a pelvic examination or imaging studies may be indicated, and pregnancy testing may be appropriate.

Men with cystitis or pyelonephritis manifest the same symptoms as women, but prostatic inflammation, if pres ent, may cause obstructive symptoms such as hesitancy, nocturia, slow stream, and dribbling in association with UTI symptoms. As with women, sexually transmitted diseases such as N. gonorrhoeae and C. trachomatis must be included in the differential diagnosis of men presenting with UTI symptoms

These findings and conclusions should not be generalized to patients with complicated or recurrent UTI [9].

A recurrent UTI refers to the occurrence of more than two symptomatic episodes within 6 months or more than three symptomatic episodes within 12 months [10].

INVESTIGATIONS

The most useful laboratory tests for UTI are dipsticks that test for leukocyte esterase (LE) and nitrites and urine cultures. Urine dipsticks are used extensively in primary care settings as aids to the diagnosis of UTI. Urine dipstick accuracy in predicting UTI has been widely reported [7]. Nitrite sensitivity alone is 81%, that of leucocytes (leucocyte esterase) alone is 77%. If both are present, sensitivity is 94%. Nitrites are only converted from nitrates in the presence of certain bacteria including E.coli. However, urine samples can be contaminated by the patient's skin flora, distal urethra, vagina, labia, periurethral skin, or vaginal secretions then repeating testing is necessary. It has been reported that up to 30% of urine samples from women with suspected urinary tract infection (UTI) are contaminated and repeat test is necessary [7]. In a quantitative study, it was proposed as a solution the use of urine collection devices (UCDs) to reduce the problem of contamination in urine samples collected from women with a suspected UTI. Many females participants were able to use the devices and found them acceptable, although UCDs maybe more appropriate for asymptomatic cases in other clinical population (pregnant women). Urine cultures are more useful in men and women with complicated UTI than in women with uncomplicated cystitis because UTIs in the former group are less likely to be associated with classic UTI symptoms and more likely to be associated with antimicrobial-resistant uropathogens.

Sexually transmitted diseases such as N. gonorrhoeae and C. trachomatis must be included in the differential diagnosis of women and men presenting with UTI symptoms. These conditions can usually be distinguished from acute cystitis with data from the history and physical examination and simple laboratory tests.

Urinalysis

General Considerations

Urinalysis cannot substitute for urine culture to document the presence of UTI but needs to be used in conjunction with culture. Because urine culture results are not available for at least 24 hours, there is considerable interest in tests that may predict the results of the urine culture and enable presumptive therapy to be initiated at the first encounter. Urinalysis can be performed on any specimen, including one collected from a bag applied to the perineum. However, the specimen must be fresh (<1 hour after voiding with maintenance at room temperature or <4 hours after voiding with refrigeration), to ensure sensitivity and specificity of the urinalysis. The tests that have received the most attention are biochemical analyses of leukocyte esterase and nitrite through a rapid dipstick method and urine microscopic examination for white blood cells (WBCs) and bacteria (**Table 1**).

Table 1: Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

Test	Sensitivity %	Specificity %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test positive	93 (90–100)	72 (58–91)
Microscopy, WBCs	73 (32–100)	81 (45–98)
Microscopy, bacteria	81 (16–99)	83 (11–100)
Leukocyte esterase test, nitrite test, or microscopy positive	99.8 (99–100)	70 (60–92)

RISK FACTORS

Risk factors for recurrent uncomplicated UTI in women can be broadly split into those related to premenopausal women, and those related to postmenopausal women.

Risk factors in premenopausal women include sexual intercourse, changes in bacterial flora, history of UTIs during childhood or family history of UTIs. History of UTIs during premenopause increases postmenopausal risk of recurrence. Vulvovaginal atrophy is also a risk factor in this group due to the reduction of Lactobacilli following the menopause. Reduction of lactobacilli decreases the vaginal pH. In addition, factors such as urinary incontinence, anterior vaginal wall prolapse, increased post void residual urine volume, and intermittent or permanent urinary catheterization predispose to UTI. Incomplete voiding represents the primary risk factor for UTIs associated with conditions such as urinary incontinence and prolapse. Correcting the presence of residual urine remains the most effective prophylaxis in these populations. Asymptomatic bacteriuria is generally benign; however, during pregnancy it is more common and is associated with an increased likelihood of symptomatic infection, which may harm the mother or fetus [5].

Lower urinary tract symptoms (LUTS) in men have many causes and are often multifactorial. A full assessment helps in making a diagnosis and avoids the assumption that LUTS in all men are due to benign prostatic hyperplasia (BPH) [2].

TREATMENT

Empiric antimicrobial choices are influenced by geographical location and individual predictors of resistance [6], (Table 1, 2, 3, 4).

Studies conducted in North America and Europe found >20% resistance rates to E. coli, the most common uropathogen causing uncomplicated UTI, for ampicillin in all areas, and for trimethoprim and TMP-SMX in most areas. The prevalence of E. coli resistance to nitrofurantoin is generally less than 5%, although nitrofurantoin is inactive against Proteus species and some Enterobacter and Klebsiella strains [9].

All guidelines recommended short (<7 days) courses of antibiotics for treatment of acute episodes in those with recurrent UTI rather than prolonged courses (Table 1). Also the guidelines recommend prophylactic antibiotics and post-coital regimens [9]. NICE guidelines recommend immediate antibiotics for pregnant women (Table 3), men or children. They do not recommend antibiotic prescription to women with lower UTI but advice on the evidence for back-up antibiotic prescriptions if symptoms do not start to improve within 48 hours or worsen [4].

Nitrofurantoin, on the market for more than half a century, has had a resurgence in use in recent years, given its continued activity against most uropathogenic E. coli [9]. NICE guidelines recommend Nitrofurantoin and Trimethroprim to men with lower UTI as first-choice, if acute prostatitis is suspected quinolones are the first-choice antibiotic (Table 4).

The NICE guidelines suggest referral or consultation with specialists for men aged ≥16 years, patients with upper tract rUTI, lower tract rUTI when the cause is unknown, pregnant women, children aged <16 years and, those with suspected cancer.

The majority of guidelines limited their recommendations to otherwise healthy non pregnant women with uncomplicated cystitis. Future guideline versions could consider widening their audience appeal and varying content appropriately to optimise assessment, management, and specialist referral for timely treatment.

Table 1: Empiric antimicrobials for acute uncomplicated cystitis

Antimicrobial category	Antimicrobial and dosing
First-line antimicrobials	Nitrofurantoin monohydrate/macrocrystals 100 mg twice daily for 5 days
	TMP-SMX 160/800 mg twice daily for 3 days
	Trimethoprim 100 mg twice daily for 3 days
	Fosfomycin trometamol (Monurol) 3-g sachet in a single dose
Second-line antimicrobials	Ciprofloxacin 250 mg twice daily for 3 days
	Levofloxacin 250–500 mg once daily for 3 days
	β-lactam (e.g.,amoxicillin-clavulanate, cefaclor for 3-7 days)

Table adapted from reference 9

Table 2: Empiric oral antimicrobials for outpatient management of acute uncomplicated pyelonephritis

Antimicrobial and dosing
Ciprofloxacin 500 mg twice daily or 1 g (extended release) once daily for 7 days
Levofloxacin 750 mg once daily for 5 days
TMP-SMX 160/800 mg twice daily for 14 days
Oral β-lactam (e.g., amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil) Duration 10–14 days

Table adapted from reference 9

Table 3: Empiric Antimicrobial for pregnant women

Antimicrobial category	Antimicrobial and dosing
First-choice oral antibiotic	Cefalexine 500 mg twice or three times a day (up to 1 g to 1.5g three or four times a day for severe infections) for 7 to 10 days

Table adapted from reference (4)

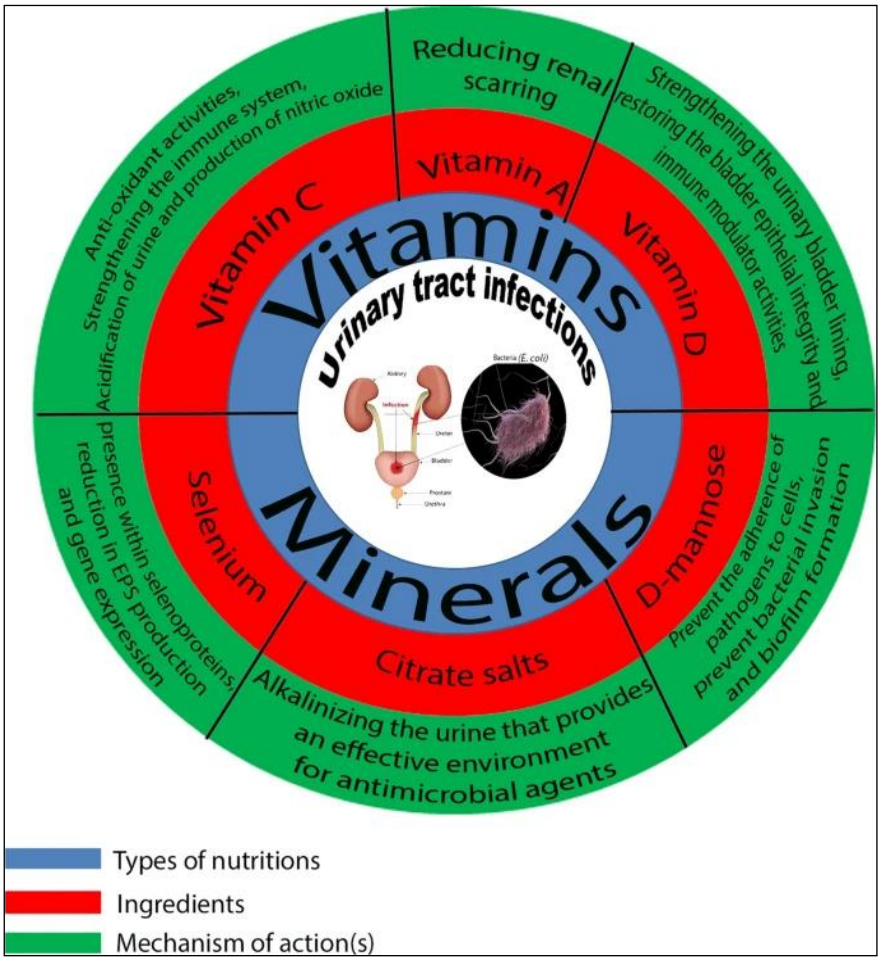
Table 4: Empiric Antimicrobial for men for acute prostatitis

Antimicrobial category	**Antimicrobial and dosing**
First-choice antibiotic	Ciprofloxacin 500 mg twice a day for 14 days
	Trimethoprim 200 mg a day for 14 days
Second -choice antibiotic	Levofloxacin 500 mg a day for 14 days

Table adapted for reference (4)

Nutrition Therapy

Using nutrients is an integral part of the management, prevention, and treatment of UTIs. In most cases, micronutrients have been used to this end and they are included vitamins and minerals in general. The role of each agent in the prevention or treatment of UTIs is illustrated in Fig 2.



Footnote: I conceived the idea, acquired, reviewed and edit this manuscript.

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ABREVIATIONS

UTI: Urinary Tract Infection
rUTI: recurrent Urinary Tract Infection
CFU: Colony Forming Units
MSU: Mid-Stream Urine
LUTS: Lower urinary tract symptoms