EUROPEAN UROLOGY SUPPLEMENTS 15 (2016) 95–101

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Management of Uncomplicated Recurrent Urinary Tract Infections

Winfried Vahlensieck[a], *Tamara Perepanova*[b], *Truls E. Bjerklund Johansen*[c], *Peter Tenke*[d], *Kurt G. Naber*[e,*], *Florian M.E. Wagenlehner*[f]

[a] *Department of Urology, Hospital for Rehabilitation Kurpark-Klinik, Bad Nauheim, Germany;* [b] *Department of UTI and Clinical Pharmacology, N. Lopatkin Scientific Research Institute of Urology and Interventional Radiology, branch of the National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation, Moscow, Russia;* [c] *Urology Department, Oslo University Hospital, Oslo, Norway;* [d] *Department of Urology, Jahn Ference Del-Pesti Korhaz, Budapest, Hungary;* [e] *Department of Urology, Technical University of Munich, Munich, Germany;* [f] *Clinic for Urology, Pediatric Urology and Andrology, Justus-Liebig University of Giessen, Giessen, Germany*

Article info

Keywords:
Recurrent urinary tract infections
Cystitis
Prophylaxis

Abstract

Mostly young but also postmenopausal women are often affected by recurrent urinary tract infections (rUTIs), defined as three or more symptomatic UTI episodes per year or two or more UTIs within 6 mo. Approximately 20–30% of women with a UTI have a recurrence. UTIs are associated with considerable morbidity. Treatable predisposing factors in uncomplicated rUTI are rare but have to be considered. According to the 2015 European Association of Urology guidelines, the recommendations for prophylaxis of rUTI are first, behavioral changes and second, nonantimicrobial measures. Antibiotic prophylaxis should only be considered if the former recommendations are not sufficiently effective, to avoid adverse events and the collateral damage of unnecessary long-term antibiotic use. General behavioral recommendations can lower the recurrence rate by about 30%. Of the nonantimicrobial measures, immunoprophylaxis and local estriol substitution are effective to lower the recurrence rate, especially in postmenopausal women. Cranberry products on the market are widely variable and seem to have too low a proanthocyanidin content to prevent rUTI effectively. Other promising modalities need to be tested in further controlled trials to prove their preventive benefit. For long-term antibiotic prophylaxis, oral fosfomycin, nitrofurantoin, trimethoprim, cotrimoxazole, and oral cephalosporins (especially during pregnancy) are recommended. Placebo-controlled studies show a high efficacy of long-term antibiotic prophylaxis, but this strategy does not appear to modify the natural history of rUTI, and most of the studies were performed at a time when antibiotic resistance was not an issue.

Patient summary: Women of all ages experience recurrent urinary tract infections (rUTIs) that cause considerable morbidity. Treatable predisposing factors in uncomplicated rUTI are rare but have to be considered. Guidelines for the prophylaxis of rUTI episodes recommend behavioral changes followed by nonantimicrobial measures and only then by antibiotic prophylaxis to avoid adverse events and the collateral damage of unnecessary long-term antibiotic use.

* Corresponding author. Karl-Bickleder-Str. 44c, 94315 Straubing, Germany. Tel. +49 9421 33369.
E-mail address: kurt@nabers.de (K.G. Naber).

http://dx.doi.org/10.1016/j.eursup.2016.04.007
1569-9056/

1. Introduction

Uncomplicated urinary tract infections (UTIs) are bacterial infections that mainly occur in otherwise healthy women and are not associated with underlying anatomic or functional abnormalities or chronic comorbidities. The typical symptoms of lower UTIs include frequent urination (pollakiuria), pain at micturition with only a small amount of urine passed (dysuria), urgency, and blood in the urine (hematuria). In the case of upper UTIs, patients may present with fever and pain in the flank region [1].

Uncomplicated UTIs in women are frequently recurrent [2]. In contrast, recurrent urinary tract infections (rUTIs) are rarely seen in healthy men. However, rUTIs are frequently found in female and male patients with complicating urologic factors (eg, urinary catheters, infection, and stones). In contrast, treatable predisposing factors in uncomplicated rUTIs are rare but have to be considered. Uncomplicated rUTIs are defined as at least two documented UTI episodes within 6 mo or three within 12 mo [1]. It has been estimated that up to 50% of women experience at least one UTI episode during their lifetime and that 20–30% of them experience rUTIs [2]. UTIs are associated with considerable morbidity, resulting in restricted activity, work absenteeism, and time spent confined to bed [3,4].

This article focuses on the prevention of symptomatic uncomplicated rUTI episodes in adult women. According to the European Association of Urology (EAU) guidelines for prophylaxis of rUTI, first, behavioral changes; second, nonantimicrobial measures; and only third, if the former are not sufficiently effective, antibiotic prophylaxis should be considered to avoid adverse events and collateral damage of unnecessary long-term antibiotic use [1].

2. Pathogenesis

The classical understanding of the pathogenesis of rUTI was that almost all rUTIs are ascending reinfections (inoculation of the usually sterile bladder urine) by a new and different organism from the rectal reservoir [5,6]. Patients with infections at close intervals, particularly when they were caused by the same strain, were suspected of having a focus of bacterial persistence within the urinary tract. Careful radiologic and urologic evaluation of these patients was mandatory because localization and removal or correction of the underlying abnormality could result in a cure [7]. Today, an alternative pathway is discussed as well. In murine cystitis, it was demonstrated that uropathogenic *Escherichia coli* (UPEC) bind to, invade, and replicate within the bladder urothelium to form intracellular bacterial communities (IBCs). These IBCs dissociate, and bacteria flux out of bladder facet cells, some with filamentous morphology, and ultimately establish quiescent intracellular reservoirs that can seed recurrent infections. The presence of exfoliated IBCs and filamentous bacteria in the urine of women with acute cystitis suggests that the IBC pathogenic pathway characterized in the murine model may also occur in humans. The findings support the occurrence of an intracellular bacterial niche in some women with cystitis that may have important implications for UTI recurrence and treatment [8].

3. Risk factors for recurrent urinary tract infection

Several behaviors are thought to increase the risk of an rUTI, but their association with rUTI has not been clearly demonstrated in clinical trials. Such risk factors include reduced fluid intake, habitually delaying urination, delaying postcoital urination, wiping from back to front after defecation, douching, and wearing occlusive underwear. In older women, risk factors also include urinary incontinence, history of UTI before menopause, blood group antigen nonsecretor status, and having a cystocele and increased postvoid residual urine [9]. In addition, a growing body of evidence indicates that UTIs in children and adults are associated with genetic mutations that affect the innate immune system [10]. Cai et al [11] developed a nomogram predicting the recurrence risk in women with symptomatic UTI. Table 1 lists the most important known and possible age-related risk factors for UTI in women.

4. General behavioral recommendations

4.1. Fluid intake

The recommended fluid intake to prevent rUTI is controversial in the literature. A sufficient but not too high fluid intake, which of course depends on physical activity and the environment, to produce a daily urine production of about 1.5 l seems to be reasonable to reach, on one hand, a sufficient washout effect, and, on the other hand, avoiding too much dilution of immunoactive substances, such as defensins and Tamm-Horsfall proteins [12]. In a Taiwanese study, the UTI recurrence rate among female clean room workers was reduced significantly from 9.8% to 1.6% by only increasing water intake and urine voiding frequency to three times or more during a shift [13].

4.2. Voiding frequency

Frequent voiding of the bladder associated with increased diuresis reduces the incubation period of pathogens,

Table 1 – Risk factors for urinary tract infection in women [1]

Young and premenopausal women	Postmenopausal and elderly women
Sexual intercourse	History of UTI before menopause
Use of spermicide	Urinary incontinence
A new sexual partner	Atrophic vaginitis due to estrogen deficiency
A mother with a history of UTI	Cystocele
History of UTI during childhood	Increased postvoid urine volume
	Blood group antigen secretory status
	Urine catheterization and functional status
	Deterioration in elderly institutionalized women

UTI = urinary tract infection.