International Urogynecology Journal (2020) 31:35–44
https://doi.org/10.1007/s00192-019-04079-5

REVIEW ARTICLE

Latin American consensus on uncomplicated recurrent urinary tract infection—2018

Jorge Milhem Haddad[1] · Enrique Ubertazzi[2] · Oscar Storme Cabrera[3] · Martha Medina[4] · Jorge Garcia[5] · Silvia Rodriguez-Colorado[6] · Efrain Toruno[7] · Priscila Katsumi Matsuoka[8] · Edgardo Castillo-Pino[9]

Received: 30 January 2019 / Accepted: 29 July 2019 / Published online: 7 September 2019

Abstract

An estimated 20–30% of adult women who experience an initial urinary tract infection (UTI) will have recurrent infection. In these patients, prophylaxis may be considered to improve their quality of life and control overuse of antibiotics. Despite this need, there is currently no Latin American consensus on the treatment and prophylaxis of recurrent UTIs. This consensus, signed by a panel of regional and international experts on UTI management, aims to address this need and is the first step toward a Latin American consensus on a number of urogynecological conditions. The panel agrees that antibiotics should be considered the primary treatment option for symptomatic UTI, taking into account local pathogen resistance patterns. Regarding prophylaxis, immunoactive therapy with the bacterial lysate OM-89 received a grade A recommendation and local estrogen in postmenopausal women grade B recommendation. Lower-grade recommendations include behavior modification and D-mannose; probiotics (*Lactobacilli*), cranberries, and hyaluronic acid (and derivatives) received limited recommendations; their use should be discussed with the patient. Though considered effective and receiving grade A recommendation, antimicrobial prophylaxis should be considered only following prophylaxis with effective non-antimicrobial measures that were not successful and chosen based on the frequency of sexual intercourse and local pathogen resistance patterns.

Keywords Cystitis · Recurrent uncomplicated UTI · Immunotherapy · Prophylaxis · Antimicrobial resistance · Non-antimicrobial prophylaxis

Introduction

Urinary tract infections (UTIs) are responsible for nearly 7 million visits to general practitioner's surgeries and approximately 1 million responses from the emergency services annually, resulting in > 100,000 hospitalizations each year. They have an annual estimated associated cost of $1.6 billion in the USA alone [1].

Recurrent urinary tract infections are more prevalent among women than men. *Escherichia coli* (*E. coli*), the most common bacterial pathogen in urinary tract infections, is responsible for > 75% of recurrent cases of uncomplicated UTI [2] and is associated with an impact on patient quality of life and activities of daily living, with costs to the health care system [1, 3].

Recurrent UTIs are associated with symptoms of anxiety and depression. The sudden, rapid, and painful onset of a UTI is often a source of anxiety in patients. Feelings of guilt related to a patient's inability to perform their usual activities, or the impact of recurrent infections on their social activities, may

✉ Jorge Milhem Haddad
Jorge_milhem@uol.com.br

[1] Faculdade de Medicina da Universidade de São Paulo, Rua Dr Renato Paes de Barros 901 ap 72, Itaim, São Paulo 04530000, Brazil

[2] Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

[3] Hospital Padre Hurtado, Universidad del Desarrollo, San Ramón, Chile

[4] Hospital Nacional Docente Madre-Niño San Bartolome, Lima, Peru

[5] Clínica del Country del Country, Bogota, Colombia

[6] National Institute of Perinatology, Mexico City, Mexico

[7] Faculdade de Medicina, UNAN León-Universidad Nacional Autónoma de Nicaragua, León, Nicaragua

[8] Department of Gynecology, Universidade de São Paulo, Sao Paulo, Brazil

[9] Hospital de Clínicas "Dr. Manuel Quintela", Facultad de Medicina, Universidad de la República, Montevideo, Uruguay

lead to clinical symptoms of depression. The social impact of recurrent UTIs may be particularly marked in premenopausal working women. Treatment of a UTI alone is often not enough to improve a patient's quality of life. However, the often-neglected impact of therapy on quality of life should be considered as part of treatment efficacy [4].

Composition of the consensus

Close to one-tenth of the world's population lives in Latin America. The unique ethnic makeup of patients, alongside local variation in the availability of medicines, antibiotic resistance, and health care practices, necessitates the creation of regional guidelines on the treatment of UTI. While guidelines published in the US, Europe, and Asia are available that outline recommended approaches to the management and prophylaxis of UTIs, and local guidelines from individual Latin American countries or regions exist, an overarching Latin American consensus/guideline is needed.

The consensus presented herein is part of a collective effort by a panel of regional and international experts to define Latin American guidelines for the management of a number of urogynecological conditions. The Latin American guidelines will cover all aspects of recurrent UTI, including diagnostic workup, risk factors, and behavioral changes, non-antimicrobial prophylaxis, and antimicrobial prophylaxis, and this is reflected in the consensus group opinion presented herein. This consensus proposes treatment recommendations based on evidence from studies described in the available literature. It was signed by a board of experts who met in São Paulo, Brazil, in 2017, including the Presidents (or their delegates) of all existing Latin American National Societies of Urogynecology (namely those for Argentina, Brazil, Chile, Colombia, Mexico, Nicaragua, Peru, and Uruguay), and aims to address a regional unmet medical need and to serve as the first step toward a broader Latin American consensus on a number of urogynecological conditions.

Level of evidence and grade of recommendation

The recommendations for clinical areas are classified in accordance with the Oxford Grades of Recommendation, 2011 version. References used in the text have been assessed according to their level of scientific evidence (1 to 4) and treatment/prophylaxis recommendations graded in accordance with the Oxford Centre for Evidence-Based Medicine Levels of Evidence system [5, 6]. The aim of grading these recommendations is to provide transparency between the underlying evidence and the recommendation given. When determining a grade, the quality of the underlying scientific evidence is balanced against the benefits and burdens, values and preferences, and cost of an intervention.

Our recommendations are in line with published evidence: 2019 EAU guidelines give a strong recommendation for OM-89 (level of evidence: 1a; grade of recommendation: strong), and OM-89 is currently recommended for prophylaxis by the EAU, German, Russian, Korean, and Brazilian guidelines, alongside those of Mexico City [7–12].

Grade A recommendation

Strong recommendation based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial. Clinicians should follow a grade A recommendation unless a clear and compelling rationale for an alternative approach is present.

Grade B recommendation

Recommendation based on well-conducted clinical studies, but without randomized clinical trials. Generally, clinicians should follow a recommendation but remain alert to new information and be sensitive to patient preferences.

Grade C recommendation

Recommendation made despite an absence of directly applicable clinical studies of good quality; patient preference may have a substantial influencing role in treatment with a grade C recommendation.

Grade D recommendation

Limited recommendation based on troublingly inconsistent or inconclusive studies of any level.

Recommendations made without a sufficient evidence base were the result of an expert-opinion consensus of the committee members; discrepancies were resolved by vote.

Epidemiology, classification, etiology, diagnosis, and treatment of urinary tract infections: a primer

Epidemiology

Although medical consultations attributed to UTIs only account for 1–6% of total consultations, they are the most prevalent type of bacterial infection, with particular presence in women. It is estimated that 40% of women will have at least one episode during their lifetime and that around 11% will have one every year. Furthermore, it is argued that sexual activity causes around 30% of all UTIs in sexually active women [1]. It is estimated that 20–30% of adult women who have experienced an initial UTI will have recurrent infections [13].

Classification

Classification of UTIs is important for clinical decisions, research, quality measurement, and teaching. Different classification systems exist for UTI. Most widely used are those developed by the Centers for Disease Control and Prevention (CDC) [14], Infectious Diseases Society of America (IDSA) [15], European Society of Clinical Microbiology and Infectious Diseases (ESCMID) [16], and the US Food and Drug Administration (FDA) [17, 18]. Current UTI guidelines frequently use the concept of uncomplicated and complicated UTI with a number of modifications.

Classification using ORENUC

In 2011, the EAU Section of Infections in Urology proposed the ORENUC classification system based on the clinical presentation of the UTI, anatomical level of the UTI, grade of severity of the infection, categorization of risk factors, and availability of appropriate antimicrobial therapy [19].

ORENUC

The mnemonic "ORENUC" [20] classifies the risk of UTI complication based on the following elements and presence/absence of risk factors:

- O: ("N**O**") no known risk factors
- R: **R**ecurrent risk of UTI, but no risk of worst outcome
- E: **E**xtra-urogenital risk factors
- N: relevant **n**ephropathies
- U: transient **u**rological risk factors
- C: permanent urinary **c**atheter and non-resolvable urological risk factors

Epidemiology

Uncomplicated UTIs [19]

Generally speaking, uncomplicated UTIs are characterized by dysuria, pollakiuria, lower abdomen pain, urgency, and nocturia. The urinalysis shows nitrite positivity, leukocituria with or without hematuria, and culture positive for bacteria [7].

Uncomplicated UTIs can be classified as:

Acute uncomplicated cystitis

An acute episode (sporadic or recurrent) of cystitis in non-pregnant women without functional or anatomical abnormalities of the urinary system and in the absence of comorbidities or relevant differential diagnoses that facilitate the occurrence of UTI or serious complications [19].

Recurrent cystitis

Where a patient experiences ≥ 3 episodes per year or ≥ 2 episodes every 6 months, cystitis is considered recurrent [19].

Acute pyelonephritis

Acute pyelonephritis can be considered either complicated/hospitalized or uncomplicated: complicated/hospitalized pyelonephritis is attributed to urological diseases or comorbidities; uncomplicated pyelonephritis consists of an episode of pyelonephritis in non-pregnant women without functional or anatomical abnormalities of the urinary system and in the absence of comorbidities [19].

Urosepsis

Urosepsis is defined as life-threatening organ dysfunction caused by a disregulated host response to infection originating from the urinary tract [19].

Herein we focus on uncomplicated UTIs in non-pregnant women.

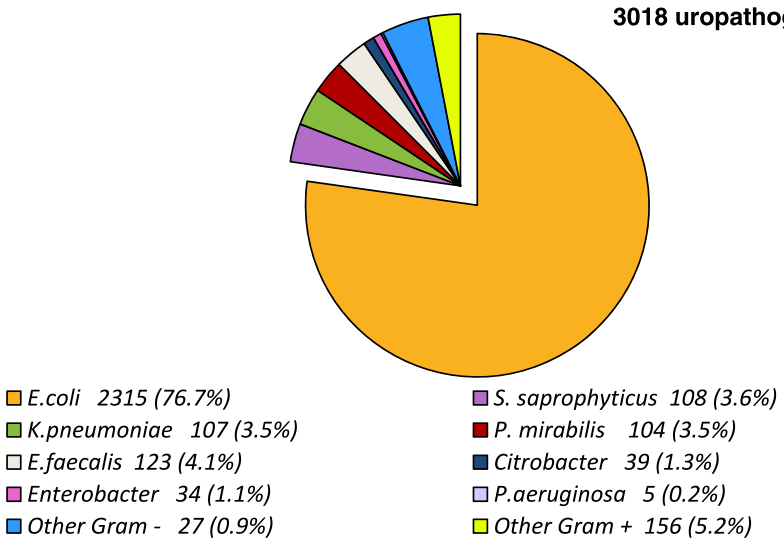
Etiology

The main etiological agent in uncomplicated UTIs is *E. coli* (which accounts for > 75% of cases) [2]. Between 5 and 10% of UTIs are caused by *S. saprophyticus, K. pneumoniae, P. mirabilis*, and *Enterococci* spp. In the Antimicrobial Resistance Epidemiology in Females with Cystitis (ARESC) study, the bacterial spectrum responsible for UTI collected from 2927 female patients' urine with bacteriuria is reported [2] (Fig. 1).

Etiology of UTIs in Latin America

Overall, regional data for Latin America are currently lacking. In a Colombian study, asymptomatic bacteriuria was found in 10.6% of participants; uropathogenic *E. coli* was the most common pathogen (25%) followed by *Enterococcus faecalis* (*E. faecalis*; 20.8%) [21]. Another Columbian study showed a prevalence of acute UTI for women and men, respectively, of 23.3% and 6.8%, and a prevalence of recurrent UTI of 54.2% and 15.7%, respectively [22]. In a third Colombian study (N = 1959), UTI prevalence was 31%, and the major causative agents were *E. coli* (69%), *Enterococcus spp*. (11%), and *Klebsiella spp.* (8%) [23]. A small Argentinian study (N = 87) examined hospital-acquired UTIs (48% of participants) and community-acquired UTIs (52% of participants). Uropathogenic *E. coli* was more common in the community-

Fig. 1 Etiology of UTI[2]



acquired UTI group (74%) than in the hospital-acquired UTI group (47%). *K. pneumoniae* and *E. faecalis* infection rates were 12% vs 20% and 5% vs 7% in the community vs health care settings, respectively [24].

Considering antibiotic resistance: the Latin American perspective

Though few resistance studies have been performed in the region, *E. coli*, *Klebsiella*, and *Pseudomonas* are recognized as being the dominant pathogenic species found in samples taken from patients with a multidrug-resistant infection in the Mexico region [24]. A 10-year study conducted in Mexican tertiary oncology hospitals found that > 50% of nosocomial isolates and > 20% of community-acquired infections had an extended-spectrum beta-lactamase (ESBL) profile. Resistance to ciprofloxacin in the region was 65%, and an increase was observed in ESBL-producing *E. coli* and *K. pneumoniae* in nosocomial infections between 2004 and 2013 [24]).

In a Colombian study ($N = 1959$), resistance levels in *E. coli* isolated from patients with UTIs were highest against ampicillin (61%), followed by nalidixic acid (48%), trimethoprim/sulfamethoxazole (48%), and ciprofloxacin (42%) [23]. As in the Mexican data above, a recent small study ($N = 87$) from Argentina showed substantial differences between resistance in community- and health care-acquired UTIs. Prevalence of multidrug-resistant pathogens was significantly higher in health care-acquired UTIs (49%) than in community-acquired UTIs (10%; $P < 0.01$) [25].

Prescription of antibiotics for recurrent UTI without consideration of preventative measures is common in many Latin American countries: in a survey of *E. coli* susceptibility in ten countries (nine countries in Europe and one in Latin America [Brazil]), the mean sensitivity to trimethoprim/sulfamethoxazole was 71.2%; in the sole representative Latin American country, Brazil, it was 54.4% [2].

It is therefore essential to observe the local epidemiology on both a regional and institutional level and to determine treatment plans accordingly.

Etiopathogenesis of recurrent UTIs and risk factors

Etiopathogenesis is linked to the balance of germ virulence factors and the patient's defenses (Table 1).

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 [26]. Understanding the risk factors associated with recurrent UTI can help physicians tailor prophylactic strategies to effectively reduce the potential for recurrence. Risk factors form a key part of the classification system of UTIs [27].

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

Table 1 Factors related to the pathogenesis of recurrent urinary tract infections

Virulence of the germ
Nephritogenic strains
Adhesion factors to the urothelium (fimbriae)
Patient defenses
pH and urinary osmolarity
Glycosaminoglycans (prevent bacterial adhesion)
T and B lymphocytes
Immunoglobulin A
Anti-reflux mechanisms
Regular urination
Vaginal lactobacilli

related to postmenopausal women. The level of evidence for individual proposed risk factors in both groups varies, and myths about risk and erroneous risk-avoidance behaviors persist among both patients and physicians alike. Treatment of asymptomatic bacteriuria (ABU) in patients with recurrent UTIs has been shown to increase the risk of subsequent symptomatic UTI episodes and is therefore not recommended for this patient group [7, 28].

Postmenopausal patients share sexual intercourse and blood group as risk factors for recurrent UTIs with premenopausal patients [29, 30]. As would be expected, a history of UTIs during premenopause increases postmenopausal risk of recurrence. Vulvovaginal atrophy is also a risk factor in this group due to the relationship between estrogen, glycogen production, and colonization by Lactobacilli, all of which are reduced following menopause. Lactobacilli colonization decreases pathogen colonization through the production of lactic acid via glucose metabolism, which decreases the vaginal pH [31, 32]. In addition, factors such as urinary incontinence, anterior vaginal wall prolapse, increased postvoid residual urine volume, and intermittent or permanent urinary catheterization predispose to complicated UTIs [33].

Women have also been shown to express two extended-chain glycosphingolipids, which in turn bind to pathogens, increasing risk of infection. The effect on uropathogen binding is estrogen-dependent, hence the relationship with hormonal status [34–38]. In addition, mouse and human data suggest that genetic polymorphisms which regulate the efficiency of the innate immune system are central to familial history of UTI [39].

The main risk factors related to UTI recurrence are summarized in Table 2 [7].

Diagnosis

The diagnosis of uncomplicated cystitis can be made with a high probability based on a focused history of lower urinary tract symptoms (dysuria, frequency, and urgency) and the absence of vaginal discharge or irritation [40, 41]. Urine culture is not required for empirical therapy of uncomplicated non-recurrent cystitis [19].

Table 2 Risk factors for uncomplicated recurrent urinary tract infections [7]

Premenopausal women	Postmenopausal/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 post-void urine volume
Blood group antigen secretory status	Blood group antigen secretory status
	Urine catheterization and functional status deterioration in elderly institutionalized women

European Association of Urology guidelines state that diagnosis of recurrent UTI should be confirmed by urine culture. An extensive routine workup including cystoscopy, imaging, etc., is not routinely recommended as the diagnostic yield is low [19]. However, it should be performed without delay in atypical cases, for example, if renal calculi, outflow obstruction, interstitial cystitis, or urothelial cancer is suspected, or when the patient presents with persistent hematuria, chronic pelvic pain, lumbar colic pain, and weight loss [19].

In patients presenting with symptoms of uncomplicated cystitis, a colony count of 10^3 colony-forming units (CFU)/ml uropathogens confirms the diagnosis microbiologically [19]. In the case of symptomatic UTI, microbiological diagnostic techniques that can detect a count of 10^3 CFU/ml in a midstream urine sample are reliable [19].

In this sense, asymptomatic bacteriuria is defined as a count $> 10^5$ CFU/ml with no symptoms [19]; treatment is indicated during pregnancy or before an interventional urological procedure, but not in other contexts, such as with diabetes, or with the detection of bacteriuria or candiduria in patients with bladder catheterization.

Imaging in uncomplicated cystitis

With the high prevalence of recurrent cystitis among women, most of the countries in Latin America may not be able to perform imaging examinations in all patients. Thus, we recommend it only for patients who do not evolve an expected course with the treatment or prophylaxis. Where imaging is necessary/feasible, we recommend following the EAU recommendations for diagnosis [19].

Differentiating between recurrent and persistent UTI

The only means to differentiate between recurrent UTI (occurrence of ≥ 2 symptomatic episodes within 6 months or ≥ 3 symptomatic episodes within 12 months) is by culture and urinalysis following treatment. In bacterial persistence, the same bacteria may be cultured in the urine 2 weeks after initiating sensitivity-adjusted therapy [42].

Treatment

The goals of uncomplicated UTI treatment include rapid symptom control, reduction of morbidity, and prophylaxis of re-infection. These objectives can be met through a short course of antibiotic treatment, but this is not exempt from an association with collateral events [43–45].

Latin American consensus panel recommendations for antibiotic-based treatment

The consensus panel proposed the following as antibiotic-based treatment options, according to availability and possibility of administration; this consensus is in agreement with treatment recommendations outlined in the EAU 2018 guidelines that consider antimicrobial susceptibility patterns in Europe [19].

- A single 3 g dose of fosfomycin
- 100 mg of nitrofurantoin twice daily (BID) for 5 days
- 400 mg of pivmecillinam 3 times daily for 3–5 days

Suggested alternatives are 160/800 mg of trimethoprim/sulfamethoxazole BID for 3 days (if local resistance is < 20%), 200 mg of trimethoprim BID for 5 days, or 500 mg of a cephalosporin (cefadroxil) for 5 days. Despite lower resistance rates in certain countries, fluoroquinolones should not be considered first choice because of adverse effects including negative ecological effects and selection for resistance [19].

The authors recommend the introduction of the chosen antibiotic after the antibiogram, which is available in all countries of Latin America (grade A recommendation; Fig. 2). The systematic incorporation of fosfomycin to the antimicrobials included in the antibiogram of urine cultures to define the level of susceptibility of uropathogens in Latin America is recommended.

Most of the countries of Latin America have these antibiotics available, and the authors strongly recommend following the antibiogram when deciding on the appropriate treatment course.

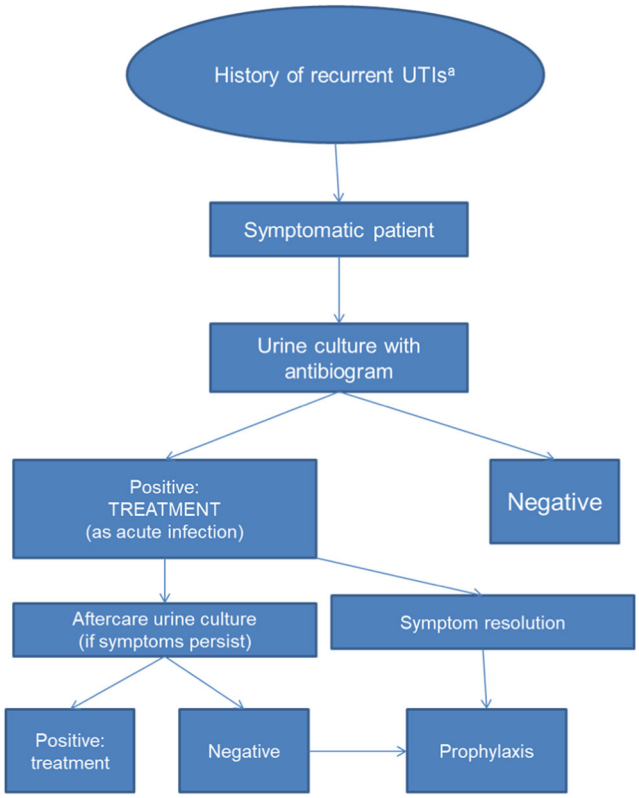


Fig. 2 Approach algorithm to symptomatic recurrent UTIs. [a]≥ 2 episodes in 6 months or ≥ 3 episodes in 1 year

Latin American group consensus on prophylaxis of urinary tract infections

Prevention of recurrent UTIs includes counseling on avoidance of risk factors, non-antimicrobial measures, and antimicrobial prophylaxis [19, 46]. A stepwise approach (Figs. 2 and 3) is recommended based on the evidence, but also on the need to mitigate the risks and collateral damage associated with frequent or prolonged use of antimicrobial agents.

Consensus group recommendations for prophylaxis of recurrent UTI

Grade A recommendations

Clinicians should follow a grade A recommendation unless a clear and compelling rationale for an alternative approach is present.

Immunotherapy (OM-89) OM-89 (*E. coli* lyophilized lysate) is defined as an active immunostimulant. It is administered orally, and its efficacy has been evaluated in a number of placebo-controlled trials and a few meta-analyses [47–52].

OM-89 is widely available in most Latin American countries.

The immunostimulatory properties of OM-89 lie in its ability to induce the terminal maturation of CD83+ human monocyte-derived dendritic cells in a dose-dependent manner that stimulates T cell and B cell proliferation and increases interferon gamma levels, which in turn increases immunoglobulin A and G levels [47–50, 53]. Studies suggest that OM-89 induces the production of specific types of serum and mucosal immunoglobulin A and G that recognize a broad spectrum of pathogen-associated molecular patterns (i.e., antigens on OM-89 and on *E. coli* strains and other bacteria). Furthermore, in a murine model of lipopolysaccharide-induced cystitis, OM-89 induced significant changes in vesical interleukin-6 and interferon-gamma levels, leading to a significant reduction in the scores of the bladder inflammatory index in OM-89 treated vs untreated mice, suggesting that, in this model of lipopolysaccharide induced cystitis, OM-89 could offer a long-term preventive effect. However, this murine model alone provides insufficient evidence for a graded recommendation [53].

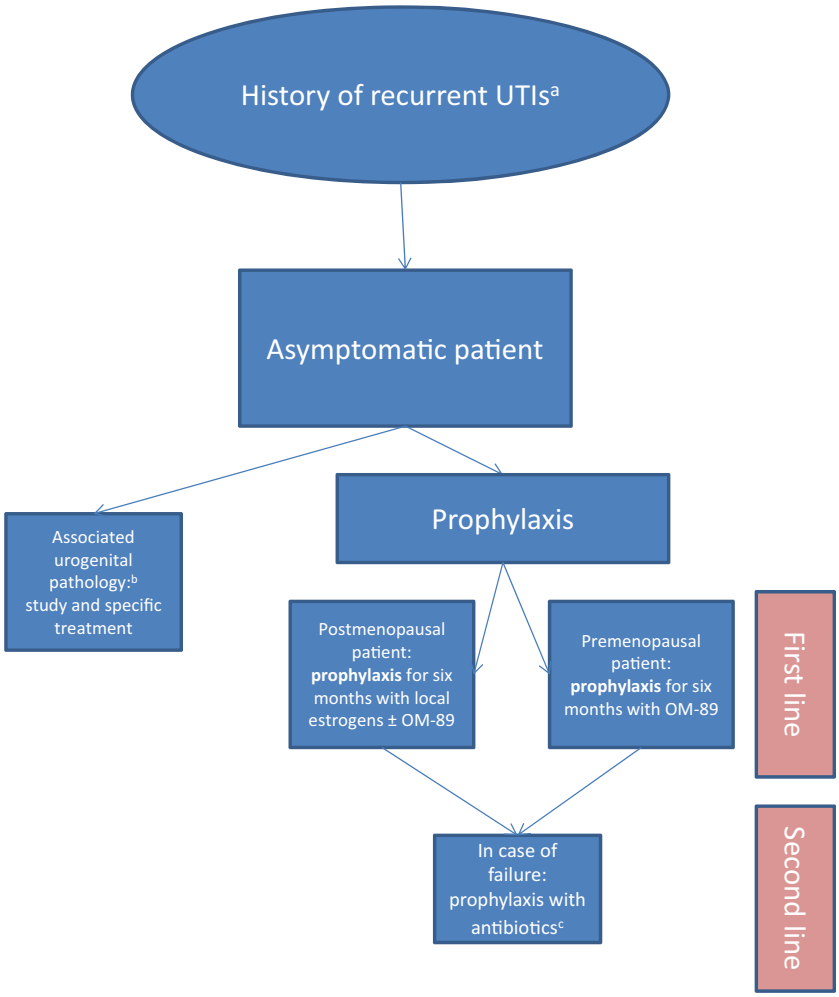


Fig. 3 Approach algorithm to asymptomatic recurrent UTIs. [a]≥ 2 episodes in 6 months or ≥ 3 episodes in 1 year. [b]Prolapse, urinary incontinence, vaginal discharge. [c]Continuous, postcoital, or self-treatment (prescribed by treating doctor). 'Asymptomatic' patients include those with asymptomatic bacteriuria

Antibiotics [19, 46, 54, 55] It should be noted that prophylactic antibiotics are not effective in the long term and may be associated with adverse reactions associated with prolonged use, including the onset of resistance. This recourse should be used only after prophylactic methods without antibiotics have been exhausted [4, 56, 57].

In line with EAU recommendations and on the basis of local studies such as ARESC in Brazil [2, 19], low doses of antibiotics are recommended after nocturnal bladder emptying (50 or 100 mg nitrofurantoin per day, 40/200 mg trimethoprim/sulfamethoxazole per day, or 3 g fosfomycin every 10 days; 250 mg cephalexin per day for pregnant women); medicinal products with a local resistance exceeding 20% should not be indicated.

As an alternative, antibiotics can be used after sexual activity when there is a strong association between intercourse and recurrent UTIs; 'self-treatment' with medical prescription is also a possible strategy [46, 54, 55].

Antimicrobials should be administered continuously and at low doses in the management of recurrent UTIs. Administration of the drug can be done daily for longer periods, generally between 3 to 6 months (recommendation A-I), or also as a single dose after vaginal intercourse (recommendation A-I) when there is a relationship between UTI and sexual intercourse [58].

Grade B recommendations

Clinicians should follow a recommendation but remain alert to new information and be sensitive to patient preferences.

Local estrogens Following an evaluation of the available meta-analyses, the authors identified seven systematic revisions that included four randomized studies (two on vaginal administration [59, 60] and two on oral estrogens [61, 62]) and concluded that, based on the quality of the studies, there is no robust evidence on the therapeutic benefit of oral estrogens, and it is not clear whether vaginal estrogens reduce the risk of symptomatic UTI—however, estrogens for vaginal application twice a week appear to be useful in postmenopausal women.

The use of estrogen stimulates the vaginal proliferation of lactobacilli, reduces vaginal pH, and prevents the colonization of enterobacteria, including *E. coli*. Therefore, it is a relevant measure in postmenopausal women to treat genitourinary atrophy with vaginal estrogen, to improve and prevent urinary tract infections. The use of vaginal estrogens should be considered in women during post-menopause (recommendation A-I) [59, 63].

Grade C recommendations [3, 4, 43, 44, 46]

Patient preference may have a substantial influencing role in treatment with a grade C recommendation.

General measures • Water intake of 1.5 to 2 l per day
- Periodic urination (every 3 to 4 h)
- Hygiene habits (neutral soap, avoid local deodorants)
- Urination before and after intercourse
- Avoid diaphragm, spermicides, and tampons

Cranberry derivatives In the last Cochrane revision, it was indicated that cranberry derivatives do not seem to significantly reduce the incidence of symptomatic UTIs on a global level [64]. Furthermore, there is no standard type of administration or dose to be used, and more randomized studies with standardized administration are required. However, they do not have relevant adverse reactions or bacterial resistance, and their use should be discussed with each patient [64–67].

A Cochrane meta-analysis shows that cranberry did not significantly reduce the occurrence of symptomatic UTI in adult women with recurrent infections. Therefore, cranberries are an individual option to be considered in the prevention of recurrent UTIs in postmenopausal women [64].

D-mannose According to data from an unblinded study recruiting a small number of patients, the prophylactic effect of D-mannose is similar to that of nitrofurantoin [68]; more studies are needed to validate the results [19], and its use should be discussed with individual patients.

Grade D recommendations

Limited recommendation.

Probiotics (*Lactobacilli crispatus* strains) Probiotics may be considered for the prevention of recurrent UTIs, but the supporting data are from studies in a limited number of participants, and the evidence is not clear; their use should be discussed with individual patients [4, 19, 43, 65].

Hyaluronic acid and its derivatives While data are available from a few studies in a limited number of patients that indicate some efficacy for hyaluronic acid and its derivatives, there is not enough evidence to support prophylactic use [44, 69, 70].

Methenamine salts (hippurate and mandelate) have been shown to be less effective in long-term prophylaxis than antibiotics, but more effective than placebo. The studies on the role in prophylaxis have, to date, included only a small number of patients and were of low quality, so these cannot be recommended based on the available evidence [71].

Conclusions

Consensus on the management and prophylaxis of UTIs in the Latin American region is essential if we are to move toward a broader Latin American consensus on urogynecological conditions.

Among the non-antimicrobial prophylaxis options, the *E. coli* lyophilized lysate OM-89 has been shown to be more effective than placebo for immunoprophylaxis in female patients with recurrent UTIs in several randomized trials with a good safety profile and has been recommended with a grade A level of evidence for inclusion in the treatment/prophylaxis algorithm. While both continuous low-dose antimicrobial prophylaxis and postcoital antimicrobial prophylaxis received a similar level of recommendation for recurrent UTI, their use should be considered as a last step of a stepwise preventative approach to mitigate the risks of antibiotic resistance and other collateral events.

The local estrogen for postmenopausal women was classified as grade B.

All other non-antimicrobial therapies, including behavioral modification, deserve a lower grade of recommendation—this applies in particular to cranberry, lactobacillus strains, and hyaluronic acid and derivatives, the use of which should be considered on a case-by-case basis and following discussion with the patient because of limited evidence supporting their recommendation.

Acknowledgments The meeting was supported by OM Pharma, a company of Vifor Pharma Group. English language writing and editorial assistance was provided by Daniel Guns of Intelligens Life Ltd.

Funding The meeting was supported by Vifor Pharma Group. Writing assistance was funded by OM Pharma.

Compliance with ethical standards

Conflicts of interest JHM has received speaker fees from OM Pharma.
EU has no relevant conflicts of interest to disclose.
OSC has received speaker fees from OM Pharma.
MM has no relevant conflicts of interest to disclose.
JG has no relevant conflicts of interest to disclose.
SRC has no relevant conflicts of interest to disclose.
ET has no relevant conflicts of interest to disclose.
PKM has no relevant conflicts of interest to disclose.
ECP has received speaker fees from OM Pharma.

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