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Dolna 17, Warsaw,
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+48 226 0 227 03
editorial_office@rsglobal.pl

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PREVENTIVE STRATEGIES FOR RECURRENT URINARY TRACT INFECTIONS: THE ROLE OF DIET AND NON-ANTIBIOTIC AGENTS

Martyna Różańska *(Corresponding Author, Email: martyna.ro899@gmail.com)*
University Hospital Wroclaw, Wroclaw, Poland
ORCID ID: 0000-0002-3351-7992

Bartłomiej Kusy
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0000-8355-2262

Agnieszka Bajkacz
University Hospital Wroclaw, Wroclaw, Poland
ORCID ID: 0000-0002-2027-8216

Karolina Niewola
4th Military Clinical Hospital, Wroclaw, Poland
ORCID ID: 0009-0003-8096-9742

Michał Robak
Independent Public Healthcare Center in Ostrów Wielkopolski, Ostrów Wielkopolski, Poland
ORCID ID: 0000-0001-6318-4095

Marcin Płonka
HCP Medical Centre, Poznań, Poland
ORCID ID: 0009-0003-8141-1409

Maciej Dudziński
Mazovian Provincial Hospital of St. John Paul II in Siedlce, Siedlce, Poland
ORCID ID: 0009-0001-5059-0403

Hanna Ćwirko
University Clinical Hospital of Jan Mikulicz-Radecki in Wroclaw, Wroclaw, Poland
ORCID ID: 0009-0005-4947-5343

ABSTRACT

Background: Recurrent urinary tract infections remain a significant clinical and public health concern due to their high prevalence, considerable recurrence rates, and the growing challenge of antimicrobial resistance. In light of the limitations associated with long-term antibiotic use, non-antibiotic prophylactic strategies have garnered increasing interest. This review synthesizes current evidence on the efficacy of various non-antibiotic interventions, including behavioral and dietary modifications, probiotics, cranberry products, D-mannose, methenamine hippurate, topical vaginal estrogen, and immunoprophylaxis.
Aim: This study aims to introduce non-antibiotic approaches to the prevention of recurrent urinary tract infections and to highlight how their integration into clinical practice may decrease reliance on antibiotics and improve long-term patient outcomes.
Methods: This narrative review synthesizes current research findings on the topic. The literature search was conducted using PubMed and Google Scholar database, focusing on recent studies relevant to non-antibiotic strategies for the prevention of recurrent urinary tract infections.

KEYWORDS

Recurrence, Urinary Tract Infection, Prevention, Prophylaxis

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Introduction

Urinary tract infections (UTIs) represent a major global health issue, affecting over 150 million people each year [1]. Typical symptoms include increased urinary frequency, urgency to urinate, dysuria, hematuria, suprapubic pain, and foul-smelling urine [2]. These infections are broadly categorized into uncomplicated and complicated UTIs. Uncomplicated UTIs are most commonly caused by Escherichia coli, followed in decreasing frequency by Staphylococcus saprophyticus, Proteus spp., Klebsiella spp., Enterococcus spp., and Pseudomonas aeruginosa [3]. In cases of complicated UTIs, Escherichia coli remains the most common etiological agent. Additionally, with lower frequency, pathogens such as Klebsiella spp., Enterococcus spp., and Pseudomonas spp. are also involved [4]. Complicated UTIs, in contrast to uncomplicated ones, often involve anatomical abnormalities of the urinary tract and may require prolonged antibiotic therapy or surgical interventions [5]. UTIs are more common in women due to the shorter length of the female urethra, which facilitates easier ascension of bacteria into the bladder. Besharati et al. reported that these infections occur more than twice as frequently in women compared to men [6]. The incidence of UTIs among women is approximately 33% by the age of 25 [7]. Moreover, nearly 50% of all women experience at least one infection during their lifetime [7]. Infections occurring more than twice within a six-month period or at least three times within one year are classified as recurrent urinary tract infections (rUTIs) [8]. In the prevention of rUTIs, prophylactic antibiotics are commonly administered either as long-term low-dose regimens or as postcoital prophylaxis. According to the latest guidelines of the European Association of Urology, recommended prophylactic agents include nitrofurantoin, trimethoprim, or fosfomycin trometamol [9]. Continuous antibiotic prophylaxis has demonstrated high efficacy. However, as with all pharmacotherapeutic interventions, its use may be accompanied by adverse drug reactions and is implicated in the emergence and propagation of antimicrobial resistance [10, 11]. For this reason, non-antibiotic prophylactic strategies should be considered as the first-line approach [9]. In this review, we present the current state of knowledge on non-antibiotic prevention strategies for patients with rUTIs, along with the role of dietary and behavioural interventions.

Behavioural modifications

The European Food Safety Authority recommends a daily water consumption of 2.0 liters for adult females and 2.5 liters for adult males [12]. The volume of fluid intake represents a significant determinant in the incidence of rUTIs. Elevated consumption promotes increased urinary frequency, thereby reducing bacterial colonization in the urinary tract via enhanced mechanical clearance [13]. Hooton et al. reported that increasing fluid consumption beyond habitual levels in premenopausal women reduced the frequency of rUTIs by up to 50% [14]. Such a simple measure represents a cost-effective strategy that has been shown to significantly reduce healthcare expenditures associated with the management of rUTIs [15]. Another critical behavioural determinant is the direction of perineal hygiene following defecation or urination. Wiping in a front-to-back direction is recommended, as wiping from back to front increases the risk of transferring enteric bacteria from the anal region to the periurethral area, thereby elevating the likelihood of UTI [16,17]. UTIs are also associated with sexual activity. Increased frequency of sexual intercourse is positively correlated with a higher incidence of infections [18, 19]. However, postcoital voiding significantly reduce the likelihood [20]. Another recognized risk factor is the use of tight-fitting synthetic underwear, which promotes the development of a warm and moist environment in the perineal region, thereby facilitating bacterial growth and increasing the risk of urinary tract colonization and subsequent infection [20, 21].

Diet

Dietary modification represents a promising, non-pharmacological strategy for UTI prevention, particularly in individuals experiencing frequent recurrences [22]. In a case–control study, Kontiokari et al. reported that higher intake of fresh fruits, berry juices, and fermented milk products was significantly associated with a lower incidence of UTIs [22]. These findings suggest that specific dietary components may exert a protective effect, potentially through antimicrobial, anti-adhesive, or microbiota-modulating mechanisms. Another study found that the consumption of oily fish and cheese is associated with a reduced incidence of UTIs, whereas high alcohol intake appears to exert the opposite effect [23]. The observed associations may be explained by the distinct effects of the investigated dietary components on immune system and gut microbiota composition [23]. Several studies indicated that a vegetarian diet may lower the risk of UTIs by approximately 16%, with the protective effect being especially notable in women [24]. Maintaining a healthy, well-balanced diet together with an appropriate body weight constitutes a key modifiable factor in reducing the risk of recurrent infections [25].

Cranberry products

Cranberries contain high amounts of bioactive polyphenols such as phenolic acids, anthocyanins, and flavonoids [26]. A particularly important role in the prevention of rUTIs is attributed to proanthocyanidins (PACs), which reduce the adherence activity of E. coli to bladder or vaginal epithelial cells [27]. PACs also exhibit anti-inflammatory properties related to the inhibition of interleukin-8, interleukin-6 and interleukin-1β release [28, 29, 30]. A Systematic Review and Network Meta-analysis demonstrated that cranberry juice is the most effective form of cranberry product, with its use reducing the need for antibiotic therapy in nearly half of the cases [31]. Conversely, a recent randomized, double-blind, placebo-controlled trial found that whole cranberry fruit powder was associated with a lower rate of culture-confirmed UTIs, and that its supplementation was considered safe [32]. Although there have been many findings, there is currently a lack of sufficiently well-designed scientific studies to conclusively consider cranberry-containing products as effective in the prevention of UTIs [33]. However, due to the low incidence of adverse effects and the favorable safety profile of cranberry-containing products, their use is recommended for prophylactic purposes and as an adjunct to standard treatment [34].

Probiotics

Lactobacilli can UTIs through many mechanisms, including competitive inhibition of uropathogen binding to vaginal epithelial cells, congregation around uropathogens, production of bacteriocins, hydrogen peroxide and lactic acid, acidic environment caused by lactic acid, inhibition of bacterial biofilm formation and downregulation of pro-inflammatory cytokines [35, 36, 37, 38]. Only selected strains of Lactobacillus demonstrate significant activity in the prevention of UTIs. The most effective outcomes have been observed with the administration of Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 [39]. A randomized, placebo-controlled trial demonstrated that the use of the Lactobacillus crispatus strain may also provide benefits in reducing recurrences [40]. Premenopausal women using the Lactobacillus crispatus probiotic

(Lactin-V) experienced nearly a 50% lower recurrence rate of UTIs compared to those receiving a placebo [40]. Another randomized, double-blind, placebo-controlled trial showed that both vaginal probiotics alone and the combination of vaginal and oral probiotics effectively prevent rUTIs, with the combination showing superior efficacy [41]. However, recent systematic reviews and meta-analyses reported no significant reduction in rUTIs among individuals using probiotics, attributing this to the limited number of well-designed studies, small sample sizes, and inconsistent probiotic dosing across trials [42, 43, 44].

D-mannose

D-mannose, the C-2-epimer of glucose, is a naturally occurring monosaccharide and a biologically significant constituent used in dietary, cosmetic, and pharmaceutical applications [45]. This substance has the ability to block the adhesion of Escherichia coli to uroepithelial cells [46]. A post hoc analysis conducted by Wagenlehner et al. showed that the use of D-mannose as monotherapy exhibits therapeutic effects comparable to antibiotics in cases of acute UTIs [47]. A randomized clinical trial by Kranjčec et al. investigated the effectiveness of D-mannose in the prevention of rUTIs [48]. The study showed that daily supplementation with 2 g of D-mannose over six months resulted in fewer UTI recurrences compared to nitrofurantoin treatment, and significantly fewer than placebo [48]. A randomized controlled trial comparing a new D-mannose-based dietary suplement DAPAX also demonstrated significant clinical benefits in cases of uncomplicated UTIs [49]. The DAPAX complex supplement, in addition to its main ingredient, contained citric acid, prebiotic fibers, astragalus, and dandelion [49]. Contrasting conclusions were drawn from a randomized controlled trial involving 598 women with a history of at least two UTIs in the previous six months or three infections within the past twelve months [50]. This study did not demonstrate significant benefits from the use of D-mannose [50]. A systematic review from 2022 evaluated the effectiveness of D-mannose for preventing and treating UTIs in adults and children [51]. Seven randomized controlled trials were included in the analysis, although they provided low-quality evidence, which prevented D-mannose from being recognized as an effective agent for the prevention of UTIs [51]. Further well-designed studies are needed before this substance can be recommended for prophylactic use.

Methenamine hippurate

Methenamine hippurate has been used for many years to prevent UTIs, and its antiseptic effect is attributed to the release of formaldehyde in an acidic environment [52]. A Cochrane review by Lee et al. that assessed 13 studies concluded that patients without a neuropathic bladder or structural abnormalities of the urinary tract may benefit from the use of methenamine hippurate [53]. In contrast, a 2021 meta-analysis including six studies with a total of 557 participants demonstrated a statistically non-significant trend favoring methenamine hippurate over other agents for the prevention of rUTIs [54]. The authors concluded that further research is needed to reliably assess the utility of this agent in prophylaxis [54]. A retrospective study from 2019 evaluated methenamine hippurate as a well-tolerated compound that rarely causes adverse effects [55]. A recent meta-analysis demonstrated methenamine hippurate as a cost-effective and well-tolerated alternative to antibiotics [56]. However, it also underscored the necessity for larger, rigorously designed randomized controlled trials to validate these findings and strengthen the evidence base [56].

Estrogens

Under physiological conditions, the distal urethra and periurethral area are covered with vaginal secretions rich in microorganisms, predominantly composed of bacteria from the genus Lactobacillus [57]. The vaginal microbiome in menopausal women undergoes significant restructuring, characterized by a decline in Lactobacillus species and their replacement by intestinal organisms including Escherichia coli [58, 59]. This change is linked to decreased estrogen levels, which lead to an increase in vaginal pH [59]. A Cochrane review by Perrotta et al. demonstrated that vaginal estrogen therapy reduces the incidence of UTIs, whereas oral estrogens shows no comparable effect [60]. Similar conclusions were reported by a 2021 meta-analysis of randomized controlled trials, which states that vaginal estrogen significantly reduces the recurrences of UTIs and represents a safe therapy for postmenopausal women [61]. Topical estrogen therapy constitutes a cost-effective approach that has been demonstrated to significantly decrease healthcare costs related to the management of rUTIs [62].

Vaccines

OM-89 (Uro-Vaxom) is an oral vaccine containing a lyophilized lysate derived from 18 uropathogenic strains of Escherichia coli [63]. A 2020 retrospective study showed that a 3-month regimen of 6 mg Uro-Vaxom, followed by three booster doses administered over 10 days within the same year, significantly reduced the frequency of recurrences in patients with a prior history of rUTIs [64]. A recent systematic review evaluated the efficacy of vaccines including Uro-Vaxom, Uromune, Solco-Urovac and ExPEC4V in the prevention of rUTIs [65]. The vaccines have demonstrated substantial preventive potential predominantly in short-term prophylaxis, with adverse events reported infrequently and generally characterized as mild [65]. Another study demonstrated the efficacy of the StroVac vaccine, showing fewer adverse effects compared to nitrofurantoin [66]. StroVac also provided superior long-term outcomes, with 79.3% of patients remaining recurrence-free in the second year versus 59.2% in the nitrofurantoin group [66].

Conclusions

Recurrent urinary tract infections continue to pose a therapeutic challenge due to their high incidence, recurrence, and the risks associated with long-term antibiotic use. Non-antibiotic preventive measures, including behavioral and dietary modifications, hold significant value in reducing infection frequency, especially when tailored to individual risk profiles. Among these, adequate hydration, postcoital voiding, and dietary improvements are simple yet effective strategies. Vaginal estrogen therapy is well-supported for postmenopausal women, while cranberry products and probiotics show moderate efficacy across populations. Methenamine hippurate may serve as a safe alternative, though more robust comparative data are needed. D-mannose and UTI vaccines offer promise but require further validation. Integrating non-antibiotic options into clinical practice can reduce antibiotic dependency and improve quality of life for patients with rUTIs.

Disclosures:

Author's contribution

Conceptualization, Martyna Różańska and Michał Robak; methodology, Martyna Różańska and Marcin Płonka; software, not applicable; check, Maciej Dudziński and Bartłomiej Kusy; formal analysis, Agnieszka Bajkacz and Martyna Różańska; investigation, Martyna Różańska, Michał Robak, Marcin Płonka and Agnieszka Bajkacz; resources, not applicable; data curation, Martyna Różańska and Maciej Dudziński; writing - rough preparation, Martyna Różańska, Hanna Ćwirko and Karolina Niewola; writing - review and editing, Martyna Różańska and Michał Robak; visualization, Agnieszka Bajkacz, Maciej Dudziński and Bartłomiej Kusy; supervision, Martyna Różańska and Hanna Ćwirko; project administration, Martyna Różańska; receiving funding, not applicable

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List of abbreviations

UTIs - Urinary tract infections
rUTIs - Recurrent urinary tract infections
PACs - Proanthocyanidins

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