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Strategies in the Battle Against Recurrent UTIs: A Brief Overview

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Abstract

Recurrent urinary tract infections (UTIs) present a serious medical issue, and such conditions can disappoint those affected. They are uncomfortable, but a difficulty arises because treating such conditions with antibiotics comes with the risk of antibiotic overuse. This summary will evaluate the measures incorporated in treating frequent UTIs in the contemporary world. These measures include taking antibiotics regularly to prevent infections and alternatives to antibiotics, such as probiotics, cranberry extract, and D-mannose. Changes in lifestyle and behavior, such as drinking more fluids and practicing better hygiene etiquette, also help decrease the chances of repeated UTIs. There is also promising progress on the UTI vaccines and possibilities of individual-based medicine in treatment approaches improvement in the future. With these and other methods, it should be possible to curb the chances of reinfection while minimizing the use of antibiotics in the treatment, which is a beneficial strategy considering the issue of global antibiotic resistance.

Keywords: D-mannose, behavioral interventions, UTI vaccines, precision medicine, antibiotic resistance

INTRODUCTION

Urinary tract infections (UTIs) rank among the most prevalent bacterial infections in humans, especially in women. Multiple species of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus*, and *Enterobacter* are implicated in the incidence of urinary tract infections (Figure 1) [1–3]. Around 150 million individuals are annually impacted by urinary tract infections (UTIs).

The length of the urethra is another factor contributing to urinary tract infections (UTIs). The susceptibility to getting UTIs is higher in women comparatively due to their shorter urethras, which are prone to bacterial entry quickly into the bladder/ kidneys. There are variations in the risk factors among premenopausal and postmenopausal women [4, 5]. There are more chances of increased risk of UTIs if the patients have diabetes, urolithiasis, enlargement of the prostate in men, pregnancy, catheter usage, injured spinal cord/ nerve damage, urinary obstructions, holding urine for extended periods, low fluid intake, weak immunity level and with poor genital hygiene. Recurrent UTIs (UTIs) are more challenging when compared with individuals experiencing a single episode of UTI, which gets resolved with antibiotic treatment in a short period.

Experiencing two or more infections within six months or three within a year is classified as recurrent urinary tract infection (UTI). Recurrent UTIs are the consequence of overuse of antibiotics. Several treatments comprise a general

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way of counselling the patients for intake of fluids, prescribing antimicrobial/ antibiotics, post-coital therapy, novel immunological techniques, adjuvant measures, and acupuncture.

The review deeply discusses the most effective strategies to battle recurrent UTIs.

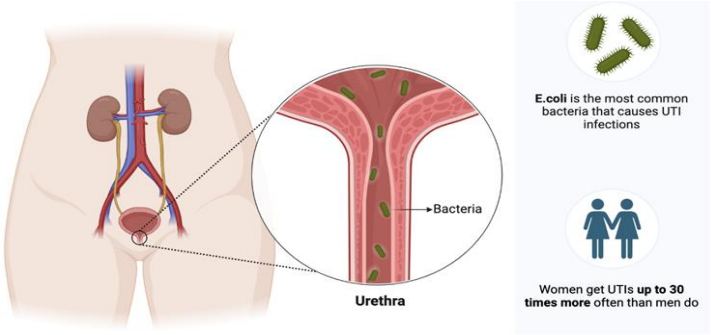

Figure 1. Urinary tract infections.

ANTIBIOTIC THERAPY: THE CONVENTIONAL APPROACH

Trimethoprim/Sulfamethoxazole (Bactrim, Septra)

- First-line treatment for uncomplicated UTIs.
- This single-dose medication combination is effective against a broad spectrum of microorganisms.
- Ineffective in areas with high antibiotic resistance.
- They are broadly used for women with acute, uncomplicated urinary tract infections.

Nitrofurantoin (Macrobid, Macrodantin)

- It works by killing the bacteria, mainly against *E. coli.*
- They are prescribed explicitly for lower UTIs.
- It has well-established prophylaxis.
- In low concentrations (5–10 pg/mL), it acts as bacteriostatic; in higher concentrations, it acts as bactericidal.
- Easily excreted by the kidneys.

Ciprofloxacin (Cipro)

- Fluoroquinolone antibiotic used for complicated/ resistant UTIs.
- Used in upper urinary tract infections.
- They are administered exclusively for chronic illnesses because of their possible adverse effects.

Amoxicillin/Clavulanate (Augmentin)

- Effective for urinary tract infections caused by gram-negative bacteria resistant to penicillin.

Ceftriaxone (Rocephin)

- Employed to treat urinary tract infections induced by multi-drug resistant *Enterobacteriaceae*.
- Broad spectrum third generation antibiotic with long $t_{1/2.}$

Cephalexin (Keflex)

- An oral cephalosporin antibiotic gets peak plasma concentration within 1 hour.
- First-generation cephalosporin with high safety and efficacy.

Fosfomycin (Monurol)

- Used for acute cystitis/lower UTIs.
- Single-dose regime for uncomplicated UTIs.

Antibiotic prophylaxis is a commonly employed intervention to prevent recurrent urinary tract infections. The choice of antibiotics is contingent upon the bacterial kind, the severity of urinary tract infections, and the patient's health status (Table 1).

Apart from antibiotic prophylaxis, the other two leading types of prevention include:
- Continuous Low-Dose Antibiotic Prophylaxis
- Post-Coital Antibiotic Prophylaxis

Table 1. Classification of various preventative methods.

Feature	**Continuous Low-Dose Antibiotic prophylaxis**	**Post-Coital Antibiotic Prophylaxis**
Administration	low dose of antibiotics	single dose antibiotic immediately after intercourse (women) [5]
Treatment period	Six months or longer	6–12 months
Associated risks/ adverse effects	Antibiotic-resistant strains/ GI disturbances	Antibiotic resistance/ very few side effects

NON-ANTIBIOTIC INTERVENTIONS

Focusing on Bacterial Adherence

Clinically, various approaches are available beyond antibiotic therapies, owing to the concern of antibiotic resistance in the prevention of UTIs. Henceforth, there is an emerging need to know about non-antibiotic therapies, which target uropathogens, particularly *E. coli*, which adhere to the bladder's mucosal lining, a critical step in developing infection.

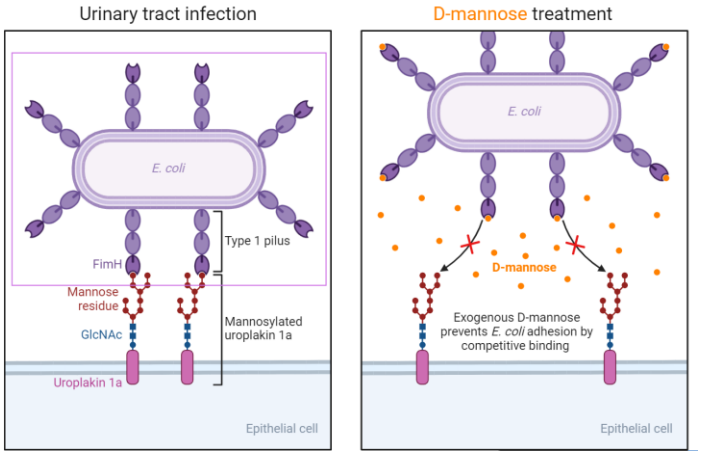

Figure 2. D-mannose in reducing UTI.

D-Mannose

D-mannose is a naturally occurring sugar that interferes with *E. coli*'s ability to adhere to the bladder epithelium. The uropathogen attaches to the bladder cells via its type 1 pili, which bind to mannose residues on the surface of urothelial cells. By supplying D-mannose orally, the sugar competitively inhibits bacterial binding, causing the bacteria to be flushed out with urine instead of colonizing the bladder (Figure 2).

D-mannose effectively lowers UTI recurrence rates, with outcomes comparable to antibiotic prophylaxis, according to several randomized controlled trials. According to one trial, D-mannose had

effectiveness rates comparable to nitrofurantoin and dramatically reduced recurrent UTIs in women compared to those receiving a placebo.

CRANBERRY SUPPLEMENTS

Cranberry products (juice/ capsules) have gained importance in preventing UTIs for decades. Bioactive substances, such as quinic acid, malic acid, and proanthocyanidins in cranberries prevent *E. coli* or other bacteria from adhering to the bladder wall containing the uroepithelial cells. As per the literature, quinic acid produces large amounts of hippuric acid excreted in the urine, further protecting against bacterial infections. Cranberry products were found to be beneficial in lowering the incidence of recurrent UTIs in some populations, especially women with a history of frequent UTIs, according to a 2012 meta-analysis of randomized controlled studies [6].

METHENAMINE HIPPURATE

It is generally advised that people with standard urinary tract architecture use methenamine hippurate. Methenamine and hippuric acid are excreted in the kidneys due to the gastrointestinal tract's absorption of methenamine hippurate. In acidic urine, methenamine hydrolyses to produce formaldehyde and ammonia. The hippuric acid maintains urine's acidity [7, 8].

IMMUNOPROPHYLAXIS

Harnessing the Body's Immune System

Immunoprophylaxis stimulates the immune system to fight against uropathogens (such as *E. coli*) to reduce the recurrence of UTIs. The body can identify and combat the germs that cause UTIs and support the immune system. Monoclonal antibodies and vaccines are also covered.

Uro-Vaxom

Uro-Vaxom is an oral immunostimulant containing lyophilized bacterial extracts from 18 *Escherichia coli* strains. It works by activating the immune system to recognize and mount a response against *E. coli*, thereby reducing the risk of infection. Studies have shown that Uro-vaxom can significantly reduce the incidence of recurrent UTIs, with reductions in recurrence rates of up to 50% compared to placebo [8]. Patients treated with Uro-vaxom demonstrate increased levels of immune markers, such as IF-6 and IgA, which are thought to enhance the body's ability to clear uropathogens.

PROBIOTICS

Restoring A Healthy Microbiome

Probiotics have been clinically demonstrated to prevent urinary tract infections. People may be more susceptible to UTIs if the balance of beneficial bacteria, especially Lactobacillus species, is upset. By repopulating beneficial bacteria, probiotics seek to restore this equilibrium and potentially stop the proliferation of dangerous bacteria like *E. coli*. There won't be any adverse effects or antibiotic resistance from this treatment.

Probiotics Derived from Lactobacillus

Multiple strains of Lactobacillus, such as *Lactobacillus rhamnosus* and *Lactobacillus reuteri*, have been investigated for their capacity to prevent urinary tract infections (UTIs). These bacteria sustain an acidic vaginal milieu and generate antimicrobial agents that impede the proliferation of uropathogens. Randomized controlled trials have shown that intravaginal or oral Lactobacillus supplementation can reduce UTI recurrence in some women [9].

Though probiotics represent a promising adjunct to UTI prevention, more large-scale studies are needed to establish optimal dosing, strain selection, and treatment duration.

BEHAVIOURAL AND LIFESTYLE MODIFICATIONS

Simple, Effective Strategies

Moderate behavioral and dietary changes significantly reduce the risk of recurrent UTIs. Some of the recommended strategies include:

Enhanced Hydration

- *Increased fluid intake elevates urine production, facilitating the expulsion of germs from the urinary system.* A study involving premenopausal women with recurrent UTIs found that increasing daily water intake significantly reduced UTI recurrence [10].
- *Post-coital urination:* Urinating following sexual intercourse can assist in eliminating any bacteria that may have infiltrated the urethra during the act, hence diminishing the chance of infection.
- *Appropriate hygiene protocols:* Wiping from anterior to posterior following urination or defecation might decrease the risk of bacterial entry into the urethra.

Avoiding spermicides is advisable, as they and diaphragms may disturb the vaginal flora, hence elevating the risk of urinary tract infections (UTIs). Switching to non-spermicidal forms of contraception may help reduce the risk of recurrent infections [11].

SURGICAL INTERVENTIONS

Correcting Anatomical Abnormalities

Occasionally, recurrent UTIs result from anatomical abnormalities predisposing patients to infections. Conditions like vesicoureteral reflux (VUR), characterized by the retrograde flow of urine from the bladder to the kidneys, can result in recurrent infections. Surgical intervention may be required in such instances. Especially surgical interventions are necessary for males, followed by 6 months of treatment with antibiotics.

Vesicoureteral Reflux Surgery

In patients with high-grade VUR, surgical interventions, such as ureteral reimplantation or endoscopic injection of bulking agents can correct the reflux and reduce the incidence of UTI [12]. Surgery is generally designated for individuals unresponsive to conservative therapies or those with significant anatomical abnormalities.

CONCLUSIONS

Recurrent UTIs are widely occurring bacterial infections clinically and remain a significant clinical challenge, but advances in treatment strategies are providing new hope for patients. While antibiotics are still a cornerstone of UTI management, alternative therapies, such as D-mannose, probiotics, immunoprophylaxis, behavioral modifications, and lifestyle modifications offer practical ways to prevent recurrence while minimizing the risks associated with long-term antibiotic use. However, care should be taken for the patients to avoid antibiotic resistance, which may occur due to overuse or misuse of antibiotics. Selecting an antibiotic suitable for the duration of the infection is a critical factor in treating UTIs.

Alternative strategies like probiotics, cranberry products, immunoprophylaxis, and methenamine salts could be the alternate mode of therapy to antibiotics. Personalized treatment plans that combine these strategies based on patient risk factors, lifestyle, and preferences are essential in accomplishing optimal outcomes. Future research will likely focus on refining these strategies and developing new, innovative approaches to prevent and manage recurrent UTIs.

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