


Effectiveness of D-mannose, *Hibiscus sabdariffa* and *Lactobacillus plantarum* therapy in prevention of infectious events following urodynamic study

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Abstract

Introduction and aim: The urodynamic study is an invasive examination that allows a thorough evaluation of the functional activity of the lower urinary tract (bladder, urethra). The execution of urodynamic study exposes the patient to the risk of contracting infections of the lower urinary tract. Prevention of urinary tract infections consists in the avoidance of risk factors and prophylaxis with antimicrobial and non-antimicrobial measures. In this article, we aimed to evaluate the effectiveness of a phytotherapeutic product composed of D-mannose, *Hibiscus sabdariffa*, and *Lactobacillus plantarum* in the prevention of infectious events following invasive urodynamic examination.

Materials and methods: We selected 100 female consecutive patients (age 19–87 years) that underwent urodynamic invasive procedure. We prescribed 14-day therapy with D-mannose, *H. sabdariffa*, and *L. plantarum* to these 100 patients after urodynamic invasive test. After that, we have examined urine cultures and urinary symptoms through telephone interviews and hospital outpatient visits to evaluate the possible presence of urinary tract infections.

Results: Urinary tract infections were observed through urine culture in 13% of the selected patients; of the 13 urinary tract infections, 9 were observed in patients with urinary tract recurrent infections in the last year and the other 4 cases were associated with patients with no urinary infection in the last year. Three women reported some urinary symptoms and underwent antibiotic therapy. The other 10 cases were classified as asymptomatic bacteriuria. Three cases were related to patients presenting with pelvic organ prolapse. Eight cases were instead related to significant post-voiding residue (>100). Six patients with urinary tract infection reported constipation in the last year. All patients completed the prescribed therapy due to the affordable price of the product and no side effects have been reported.

Conclusion: Our study about the administration of D-mannose, *H. sabdariffa*, and *L. plantarum* after invasive urodynamic examination underlined how this phytotherapeutic product can reduce the risk of bacteriuria and urinary tract infection in women.

Keywords

Urodynamic study, urinary tract recurrent infections, D-mannose, Ellirose™, *L. plantarum*

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Introduction

The urodynamic study (UDS) is an invasive examination that allows a thorough evaluation of the functional activity of the lower urinary tract (bladder, urethra). UDS evaluates the behavior of the urinary system during the voiding

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act. More precisely, it analyzes the urinary stream during voiding and the pressure in the bladder and abdomen.

UDS is performed as a second-level diagnostic study in patients suffering from functional diseases such as urinary urgency, urinary incontinence (urge, stress, or mixed), neurological diseases, or in the outcome of bone marrow injuries. UDS consists of four distinct phases:

- Uroflowmetry;
- Pressure-flow study (voiding phase);
- Cystometry (filling phase);
- Urethral profilometry.

In specialized centers, it is also possible to undergo two other phases of the examination: the electromyography of the pelvic floor muscles and the video UDS.

To perform UDS, the patient is placed in a supine position and subjected to the introduction of a bladder catheter and a rectal probe, equipped with appropriate sensors at the extremities. With the subsequent introduction of physiological solution, sensitivity, capacity, stability, and compliance of the bladder musculature are assessed by recording intravesical pressures. It is also possible to evaluate how the patient feels the urinary stimulus, providing useful information on the functioning of the bladder.

The execution of UDS exposes the patient to the risk of contracting infections of the lower urinary tract. For this reason, the patient must necessarily bring into view a negative urine culture performed in the previous 15 days or must already be taking targeted antibiotic therapy.

Urinary tract infections (UTIs) consist in the presence of microbial pathogens in the urinary tract and represent one of the most common bacterial infections.¹ Asymptomatic urinary bacteriuria (ABU) consists in the urinary growth of bacteria in an asymptomatic individual. ABU requires no treatment unless the patient is subjected to urological surgery or is pregnant.²

European Association of Urology (EAU) classification of UTIs includes uncomplicated UTIs, complicated UTIs, urinary tract recurrent infections (rUTIs), catheter-associated UTIs, and urosepsis.² rUTIs consist in recurrences of uncomplicated and/or complicated UTIs with a frequency of at least three UTIs/year or two UTIs in the last 6 months. About 20%–30% of women with a first UTI will have a recurrence and 5% will have chronic recurring infections.³ Clinically, UTIs can manifest as urethritis, cystitis, or pyelonephritis. Almost half of all women will experience at least one episode of cystitis during their life.¹

For young women (premenopausal), the risk factors are sexual intercourses, use of spermicide, a new sexual partner, a mother with a history of UTIs during her childhood, and blood antigen secretory status. For elderly women (postmenopausal), the following can be considered as risk factors: history of UTIs before menopause, urinary incontinence, atrophic vaginitis, cystocele, increased post-void

urine volume, blood group, antigen secretory status, urine catheterization, functional status, and deterioration in elderly institutionalized women.⁴

The spectrum of etiological agents includes *Escherichia coli* in 70%–95% of cases, *Staphylococcus saprophyticus* in 5%–10% of cases, and occasionally other enterobacteriaceae such as *Proteus mirabilis* and *Klebsiella*. Bacteria can be considered normal inhabitants of the gastrointestinal tract (the most important reservoir of uropathogenic *E. coli*) where they play an important role in the maintenance of health and development of diseases.⁵

Urogenital colonization by *E. coli* is feasible to a series of predisposing factors, hygiene habits, and sexual practices. In most cases, female urethra gets infected by fecal material containing uropathogenic bacteria according with the short distance between the female urethra and the anus that facilitates contamination.⁶

Diagnosis should be confirmed by urine culture: a colony count of 10,000 cfu/mL of uropathogens is microbiologically diagnostic in women who present lower urinary tract symptoms as dysuria, frequency, urgency, and suprapubic pain with the absence of vaginal discharges or irritation.

Prevention of rUTIs consists in the avoidance of risk factors and prophylaxis with antimicrobial and non-antimicrobial measures, unfortunately associated with the onset of resistance to the antibiotic. Non-antimicrobial prophylaxis includes the administration of probiotics, Cranberry, and D-mannose.

In particular, *Lactobacillus* probiotics and D-mannose are included in the phytotherapeutic drug preparation associated to *Hibiscus sabdariffa*. The clinical use of the phytotherapeutic drug is based on the molecular effects of its components and on their synergistic effects. D-mannose has an important role in the prevention of rUTIs. It is a sugar with a relevant role in human metabolism, especially in glycosylation of certain proteins. The supposed mechanism of action is inhibiting bacterial adherence to uroepithelial cells.⁷

Materials and methods

The phytotherapeutic drug is composed of D-mannose (1000 mg), *H. sabdariffa* (200 mg), and *Lactobacillus plantarum* Lp-115 (1 mld UFC). It can be used in non-antibiotic prophylaxis of rUTIs and its posology is two sachets daily (one in the morning and one in the evening) in the presence of urinary symptoms or after an invasive outpatient examination or one sachet daily in other clinical situations. It can be administrated for prolonged time for its generally minimal side effects.

In this study, we aimed to evaluate the effectiveness of D-mannose, *H. sabdariffa*, and *L. plantarum* in the prevention of infectious events following invasive urodynamic examination. We selected 100 female consecutive patients (age 19–87 years) that underwent urodynamic invasive procedure. Patients were chosen based of the absence of

important chronic disease, malformations of the urinary tract, and UTIs at the moment of the procedure.

Of the total, 23 had various episodes of rUTIs associated to urinary tract symptoms; 35 patients complained constipation; 32 had anatomical alteration of the pelvic organs, like colpocele, cystocele, and rectocele; 5 patients were affected by neurological diseases like multiple sclerosis (3), Parkinson's syndrome (1), and cauda equina syndrome (1). We discovered also a significant post-micturition residue (>80 mL) in 25 women (Table 1).

We prescribed 14-day therapy with D-mannose, *H. sabdariffa*, and *L. plantarum* to these 100 patients after urodynamic invasive test. After that, we have examined urine cultures and urinary symptoms through telephone interview and hospital outpatient visits to evaluate the possible presence of rUTIs.

Results

UTIs were observed through urine culture in 13% of the selected patients. More specifically, 9 of the 13 UTIs were observed in patients with rUTIs in the last year and the other 4 cases were associated with patients with no urinary infection in the last year.

Only three women reported some urinary symptoms (dysuria, frequency, urgency, or pain) and they underwent antibiotic therapy. The other 10 cases were classified as asymptomatic bacteriuria (no further urinary symptoms despite the positive urine culture).

Three cases of UTIs were related to patients presenting with pelvic organ prolapse and eight cases were instead related to significant post-voiding residue (>100). Six patients with UTIs reported constipation in the last year (Table 2).

All patients completed the prescribed therapy due to the affordable price of the product and no side effects have been reported.

Discussion

This phytotherapeutic drug is a dietary supplement (combination of *Lactobacillus* probiotics, D-mannose, and *H. sabdariffa*) widely used by the urologists in our region. The absence of side effects makes it easily and safely administrable for a long period, especially for non-antimicrobial prophylaxis in rUTIs, without risk of the development of any antibiotic resistance.

Kranjčec et al.⁸ investigated the role of D-mannose in the prevention of UTIs in women with history of rUTIs initially treated with antibiotic therapy. *H. sabdariffa* is a common herbal drink consumed both hot and cold by people around the world and used in traditional medicine for the treatment of hypertension and UTIs.

I Alshami et al. showed that *H. sabdariffa* extract significantly inhibits uropathogenic growth and prevents the "in vitro" biofilm-forming capacity of bacteria like *E. coli*

Table 1. Population considered in the study.

Population of 100 women	Rate (%)
rUTI	23
Constipation	35
Pelvic organ prolapse	32
Neurological disease	5
Significant post-voiding residue	25

rUTI: urinary tract recurrent infection.

Table 2. Results of the study.

Infectious events and risk factors	Rate (%)
Positive urine culture	13
- UTI	3
- Bacteriuria	10
- rUTIs in the last year	9
- No UTIs in the last year	4
Risk factors (in positive urine culture patients)	
- Pelvic organ prolapse	3
- Significant post-voiding residue (>100)	8
- Constipation	6

and *Klebsiella pneumoniae*. The antimicrobial activities of the extract observed provided basic evidence for the potential antimicrobial effects of this plant for preventing rUTIs.⁹

UDS is an invasive procedure that exposes patients to risk of UTI. Nóbrega et al.¹⁰ underlined that the incidence of bacteriuria, transient bacteriuria, and UTI in 232 women after UDS was 11.6%, 7.3%, and 4.3%, respectively.

D-mannose, *H. sabdariffa*, and *L. plantarum* can be used in prophylaxis to reduce the risk of UTI after invasive procedure like urodynamic studies. Nadeem et al.¹¹ reported that 14% of the patients who underwent urodynamic test had a positive urine culture and 12% required treatment with antibiotics. In our study, we observed that the combination of D-mannose, *H. sabdariffa*, and *L. plantarum* reduces the risk of symptomatic UTI.

Moreover, as is already known from the literature^{10,11} we ascertained how some conditions like post-voiding trace and pelvic anatomical alterations can predispose to asymptomatic bacteriuria or UTIs in women. Of course, this study presents several limitations mainly because this is a single-center, single-arm, uncontrolled observational study.

Conclusion

Our study about the administration of D-mannose, *H. sabdariffa*, and *L. plantarum* after invasive urodynamic examination underlined how this phytotherapeutic product can reduce the risk of bacteriuria and UTI in women. Certainly, further randomized controlled studies are needed in order to establish the efficacy with a sufficient level of evidence.

Declaration of conflicting interests

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