Lit-Control devicare

V Edition of the Clinical Cases Contest on non-surgical clinical management of Kidney Stones

Official template

Title: Urinary alkalinization for the management of overactive bladder.

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1. Abstract (no longer than 150 words).

Overactive bladder has a global prevalence of 10.8–35.6% and a negative impact on patient's quality of life. There is limited evidence in the literature regarding the effects that a variation in urinary pH may have on symptoms associated with overactive bladder. The aim of our study was to evaluate the clinical changes related to bladder overactivity following a treatment for urinary alkalinization. We present the case of a 70-year-old male with detrusor overactivity and acidic urinary pH (pH 6), who underwent urinary alkalinization treatment with Lit-Control® pH Up, monitored by an electronic device. Upon completing the treatment, clinical improvement was observed, primarily in the patient's urinary frequency, significantly enhancing his quality of life.

2. Introduction

Overactive bladder is a prevalent condition in both men and women. The International Continence Society (ICS) defines overactive bladder as the presence of urinary urgency, with or without incontinence, usually accompanied by frequency and nocturia. The urodynamic finding identified in patients with overactive bladder is detrusor overactivity (1).

This entity has a global prevalence of 10.8%–35.6%, according to previous studies, and its incidence increases with age (2). There is some disagreement regarding the variability of its presentation by sex. While most studies indicate equivalent prevalence, some report a higher predisposition in women (3,4). The treatment for overactive bladder includes hygienic and dietary measures as a first step, aimed at improving patient's urinary quality. If this approach is not effective, detrusor muscle relaxant treatment is initiated. This treatment involves numerous drugs that, used either alone or in combination, can help control symptoms. However, finding the effective medication for each patient can be a challenging task, in addition to the side effects associated with this group of drugs. Patients with overactive bladder experience a negative impact on their quality of life, affecting daily activities, mental health, and sexual function (2).

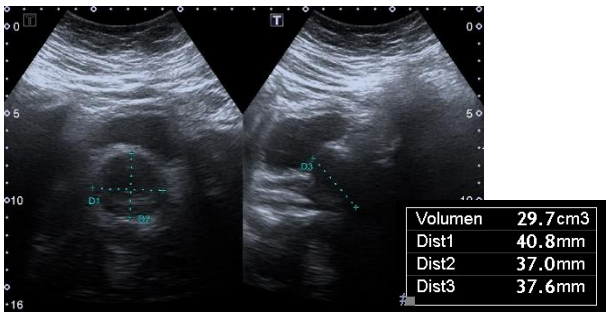
Several theories could explain the presence of urinary urgency, as detailed by *Martin C. Michael et al.* in their review published in European Urology in 2009. Although the pathogenic mechanisms of overactive bladder are not fully understood, both neurogenic and myogenic theories have been proposed (5).

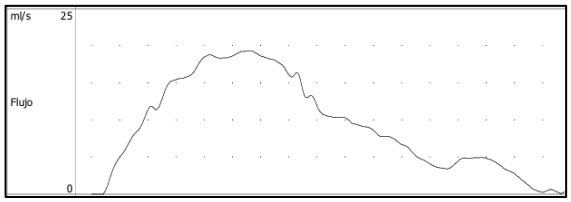
Lit-Control® pH Up is a dietary supplement that raises urinary pH through potassium citrate and magnesium citrate, and it inhibits uric acid crystallization in urine. To date, the available literature has slightly explored the relationship between urinary pH and overactive bladder in the population. For this reason, we propose this study to evaluate whether urinary alkalinization with Lit-Control® pH Up improves symptoms associated with overactive bladder.

3. Clinical Case description

a. Patient information / Medical records

We present the case of a 70-year-old male with a medical history of sleep apnea, asthma, thrombocytopenia, hyperglycemia, and hiatal hernia, with no relevant surgical history and an allergy to tramadol. The patient began follow-up at our center in 2022 for lower urinary tract symptoms, including increased frequency (daytime urinary frequency every thirty minutes, nocturnal frequency three to four times) and urgency. A complete prostate study was conducted, including a digital rectal exam, PSA test, renal-bladder ultrasound, and uroflowmetry. On rectal examination, the prostate was assessed as grade II. PSA level was 2.93 µg/L, and the renal-bladder ultrasound reported a prostate volume of 30 grams. Uroflowmetry ruled out infravesical obstruction (Qmax 19.3 mL/s, voided volume 313.1 mL, residual urine 33 mL).

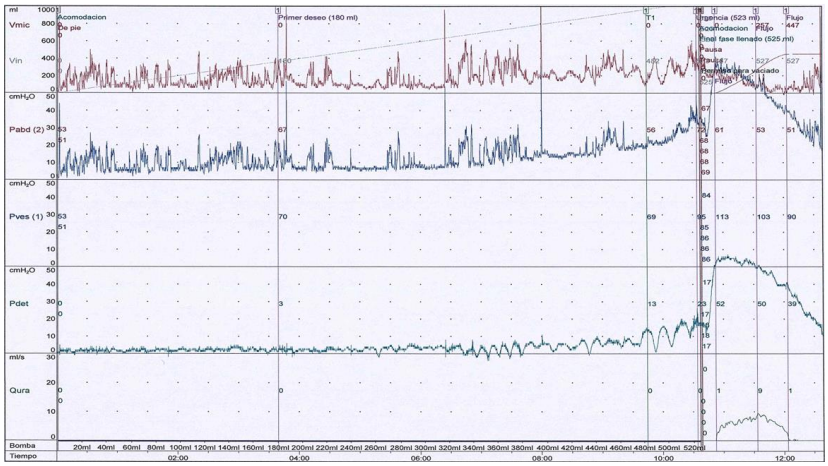




b. Diagnostic support studies and results

Urinalysis excluded urinary infection, and a 24-hour urinary pH study reported acidic urine (pH 6). Urodynamic studies identified uninhibited detrusor contractions during the filling phase at high bladder volumes without causing urinary incontinence. The voiding phase was normal, with proper detrusor contractility and no evidence of infravesical obstruction. The patient began treatment with a detrusor relaxant, fesoterodine, supplemented with a lipid-sterolic extract of *Serenoa repens* for symptomatic management. Subsequent follow-ups showed no significant clinical improvement (daytime frequency every hour, nocturnal frequency three to four times).

c. Diagnosis



d. Treatment

Given the diagnosis of overactive bladder and the exclusion of infravesical obstruction as a contributory factor, treatment with Lit-Control® pH Up was initiated at a dosage of one capsule every 12 hours for two months. The patient was instructed in the use of a pH meter for strict monitoring of urinary pH variations, with measurements taken twice weekly.

e. Evolution and progress

The patient tolerated the medication well, with no reported adverse effects, and found the pH meter easy to use without complications.

The use of Lit-Control® pH Up successfully alkalinized the patient's urinary pH. Sixteen measurements were taken (two per week), with the final pH reading at 6.4 and an average urinary pH of 6.5 (± 0.27 standard deviation).

f. Clinical results

Clinical symptoms were reassessed after two months of treatment, revealing marked improvement in urinary frequency, both daytime (every three to four hours) and nocturnal (none, one, or two times per night), significantly enhancing the patient's quality of life. There was less improvement in urgency, which persisted occasionally (less than four times per week), and urinary incontinence occurred only in exceptional cases. There were no changes in voiding symptoms, with the patient maintaining a normal urinary stream and complete bladder emptying sensation.

g. Discussion

Therapeutic options for patients with overactive bladder can involve lengthy processes to identify the appropriate medication in each case, which, as previously mentioned, becomes a challenging task. Following our approach, the use of oral citrates to maintain alkaline urinary pH levels could provide a quick and effective way to improve patients' clinical symptoms.

Overactive bladder has a multifactorial origin, as previously noted (5). Possible causes include spontaneous contractions or micromovements of the bladder smooth muscle, structural changes in the bladder wall (partial denervation, hypertrophy, fibrosis), disruption of urothelial mediators, impaired inhibitory mechanisms of bladder contraction, or failures in the central nervous system's signal processing to the bladder.

Beyond these considerations, various urinary metabolites have been studied in relation to lower urinary tract symptoms. However, the existing evidence is limited and inconsistent. *Satora Kira et al.* identified fourteen urinary metabolites with differential expression in patients with bladder overactivity compared to controls.

Two metabolites, 5-iso-prostaglandin F2α-VI and 5-methoxyindoleacetic acid, were directly associated with overactive bladder (6). These metabolites are part of the arachidonic acid and tryptophan metabolic pathways, suggesting that abnormalities in these pathways may contribute to bladder overactivity. Another metabolite associated with overactive bladder is dipentyl phosphate, part of the organophosphate ester family. This metabolite is an endocrine disruptor that may alter bladder functionality through endocrine pathways (7).

Animal models with bladder pathophysiology similar to humans have been used to evaluate medical treatments for overactive bladder. The literature describes a bladder overactivity model created with intravesical acetic acid infusion, demonstrating that higher concentrations of infusion resulted in increased urinary frequency and reduced voided volume in animals, thus confirming bladder overactivity (8). In this study, symptoms were predominantly nocturnal, suggesting that urinary acidification may exacerbate nocturnal symptoms in patients, further impairing quality of life. In our case, comparable clinical results were observed, with improved urinary frequency both during the day and at night following urinary alkalinization.

There is limited evidence regarding the relationship between urinary pH variations and bladder symptoms. *Brumfitt et al.* found no statistically significant differences in frequency, urgency, dysuria, nocturia, or hematuria based on urinary pH in their analyzed patients. However, their study only included patients with urinary tract infections, and their findings suggest that changes in urinary pH may not affect the presence of symptoms associated with overactive bladder (9).

A noteworthy study by *Arif Demirbas et al.* in 2014 linked urinary acidification with overactive bladder and evaluated symptom changes after urinary alkalinization (10). They defined acidic urinary pH as <6.2 and alkaline urinary pH as >7 in 24-hour urine samples. Their findings showed a significant association between acidic urinary pH and bladder overactivity, as well as statistically significant improvement in urgency and urinary frequency (defined as ≥8 voids per day) after a dietary program promoting urinary alkalinization. In our case, the patient did not exhibit a clear improvement in urgency but showed a clinically significant improvement in urinary frequency, leading to a notable enhancement in quality of life. Interestingly, in our study the patient reached median urinary pH of 6.5. There is a possibility that prolonged treatment with urine alkalizing agents could achieve more alkaline urinary pH values (> 7), thus causing a more obvious improvement of symptoms.

In our study, questionnaires were not used to assess the symptomatic improvement of the patient; instead, anamnesis was employed, which subjectively allows patients to express the symptomatic improvement they have experienced. While it is true that questionnaires standardize reported symptoms, the subjective assessment of patients holds greater importance.

h. Conclusions and recommendations

The available evidence shows some discrepancies regarding the clinical manifestations accompanying urinary pH changes. This case study suggests that urinary alkalinization can improve symptoms associated with overactive bladder, particularly those related to daytime and nocturnal urinary frequency.

4. Bibliographic references (* of special interest, ** of extraordinary interest)

1. Abrams P, Cardozo L, Fall M, et al. The standardization of terminology in lower urinary tract function: report from the standardization sub-committee of the International Continence Society. Urology 2003;61:37-49.

2. Renu S Eapen, Sidney B Radomski. Review of the epidemiology of overactive bladder. Research and Reports in Urology 2016:8 71-76.

3. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. Urology. 2011;77(5):1081–1087.

4. Milsom I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ. How widespread are the symptoms of an

overactive bladder and how are they managed? A population based prevalence study. BJU Int. 2001;87(9):760–766.

5. Martin C. Michel, Christopher R. Chapple. Basic Mechanisms of Urgency: Preclinical and Clinical Evidence. European Urology 56 (2009) 298-308.

6. * Satoru Kira, Tatsuya Miyamoto et al. Potential Targets for Overactive Bladder in Older Men Based on Urinary Analysis of Metabolomics. Urol Int 2022;106:672-678.

7. Veilong Lin, Haoxu Wang et al. Associations between exposure to organophosphate esters and overactive bladder in U.S. adults: a cross-sectional study. Front. Public Health 11:1186848.

8. ** Manabu Mitobe, Hirotaka Inoue et al. A new method for producing urinary bladder hyperactivity using a non-invasive transient intravesical infusion of acetic acid in conscious rats. Journal of Pharmacological and Toxicological Methods 57 (2008) 188-193.

9. W. Brumfitt, J.M.T Hamilton-Miller et al. Relationship of urinary pH to symptoms of cystitis. Postgrad Med J (1990) 66, 727-729.

10. ** Arif Demirbas, Hasmet Sarici et al. The Relationship between Acidic Urinary pH and Overactive Bladder; Alkalization of Urine Improves the Symptoms of Overactive Bladder. Urologia Internationalis. 2014.