Title: The Role of Urine Alkalinization Using Lit Control Ph-Up in the Treatment of Uric Acid Kidney Stones post failed endoscopic procedure. A clinical Case Report.

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Abstract:

Uric acid kidney stones are a common form of nephrolithiasis and are primarily associated with conditions such as hyperuricosuria, acidic urine pH, and obesity. The management of uric acid stones requires addressing the underlying causes, including urine alkalinization, which plays a crucial role in preventing stone formation and promoting the dissolution of existing stones. This case report explores the therapeutic benefits of urine alkalinization in the treatment of a patient with recurrent uric acid kidney stones with previously failed endoscopic procedure. We discuss the pathophysiology of uric acid stones, the mechanisms by which urine alkalinization contributes to stone management, and the clinical implications of this approach.

Keywords: Uric acid kidney stones, urine alkalinization, nephrolithiasis, hyperuricosuria,lit Control

Introduction:

Kidney stones are a prevalent condition affecting millions worldwide, with uric acid stones accounting for approximately 5-10% of all kidney stone cases, and recurrence rate up to 50% in five years(1). The risk of recurrence depends on the stone composition and is based on an underlying cause. Uric acid (UA) stones are considered to have a high risk of recurrence(2). Uric acid stones formation occurs when urine becomes supersaturated with uric acid, along with low urine pH (acidic urine). Unlike calcium-containing stones, uric acid stones can often be dissolved or prevented through medical management by alkalinization of urine due to the fact that acidic urine is the most important factor in formation of uric acid stone(3). Furthermore UA urolithiasis is found to be more common in people with diabetes mellitus type II (4), disorders seen in the metabolic syndrome, high BMI and chronic diarrhea with bicarbonate loss resulting from bowel surgery or inflammatory bowel disease (5).The prevention of stone recurrence focuses on the three main components of UA stone formation; increase urine volume, hyperuricosuria prevention and increase of urinary pH.The risk of UA crystal formation is highest at a urine pH ≤5.5 which makes uric acid less soluble in water especially if uric acid is supersaturated. Accordingly; raising the urine pH to ≥6.0 can prevent or dissolve UA stone formation(6).
This case report highlights the clinical application of urine alkalinization in treating a patient with recurrent Uric acid kidney stones and failed endoscopic procedure.

Case Presentation:

Patient Information: A 60 year-old diabetic female with a history of recurrent renal colic presented to the outpatient clinic with symptoms of left flank pain, dysuria, and hematuria. The patient had a previous history of multiple episodes of kidney stones, diagnosed as uric acid stones on imaging, and had undergone extracorporeal shock wave lithotripsy(ESWL) two years ago. She was also diagnosed with obesity and mild hyperuricosuria. Her dietary history revealed high purine intake, consisting of excessive consumption of red meat and seafood.

Initial Evaluation: On physical examination, the patient had mild left costovertebral angle tenderness. Laboratory tests showed a normal serum creatinine level (0.9 mg/dL), elevated serum uric acid (8.5 mg/dL), and a urine pH of 5.2. Urinalysis revealed microscopic hematuria, but no signs of infection. Non-contrast abdominal CT scan confirmed the presence of two uric acid stones in the left kidneys, 1.5 cm stone in the renal pelvis and 2.1cm stone in lower calyceal group as shown in image(1).

Image 1 shows 2 large stones

Management Plan: All treatment options were discussed with the patient including urine alkalaisation , ESWL, and flexible ureteroscopy. Due to insurance issues the patient choose flexible ureteroscopy. During flexible URS the 1.5 cm stone was fragmented completely but we couldn't reach the lower calyceal stone due to narrow calayx .post operative CT scan is shown in image (2) which shows lower calyceal stone and Double J stent.

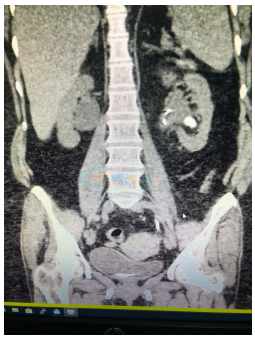

Image 2 shows lower calyces stone with double j stent in situ

The patient then was started on Lit control Ph-up as medical therapy for urine alkalization .the dose was 722 mg tablets given as 4 tablets on 2 divides doses for 3 months .CT scan after 3 months of treatment as shown on image(3) shows complete clearance of the lower calyceal stones . Then the double J was removed .

Image 3 shows complete stone clearance

Pathophysiology of Uric Acid Kidney Stones
Uric acid stones primarily form in conditions where urine pH is persistently low (below 5.5). Uric acid, a product of purine metabolism, is normally excreted in urine, but in acidic environments, it remains in its protonated form, uric acid (HA), which is poorly soluble. As a result, supersaturation of uric acid in the urine occurs, leading to crystal formation. Alkalinizing the urine promotes the ionization of uric acid to its more soluble form, urate (A-), thus reducing the risk of stone formation.

Uric Acid Stone Formation:

In acidic urine (pH < 5.5), uric acid (HA) is poorly soluble and may precipitate to form crystals.
In alkaline urine (pH > 6.0), uric acid dissociates to form the more soluble urate ions, which are less likely to precipitate and form stones.
Urine alkalinization effectively reduces supersaturation and increases urate solubility, thereby preventing new stone formation and dissolving pre-existing stones.
Therapeutic Role of Urine Alkalinization
Urine alkalinization is a cornerstone in the management of uric acid stones. By raising the urine pH above 6.0, urine alkalinization enhances the solubility of uric acid, thereby promoting the dissolution of existing stones and preventing further stone formation. The most commonly used agents for urine alkalinization include potassium citrate and sodium bicarbonate, with potassium citrate being preferred due to its potassium-sparing effects.

Mechanism of Action:

Potassium citrate which present in lit control ph-up dissociates in the urine to form potassium and citrate ions.
Citrate ions bind with calcium, preventing calcium oxalate crystal formation, and promote the excretion of citric acid, which alkalinizes the urine.
Elevated urinary pH increases the dissociation of uric acid to its ionized form, urate, which is more soluble in urine. Lit Control Ph-UP has also theobromine which inhibit crystallization of Uric acid stones.
Clinical Outcomes
Follow-up: At a follow-up visit 3 months later post Double J removal, during this period The patient was on prophylactic regimen of LIT Control Ph-UP as two tablets per day for 3 months, along with allopurinol 300 mg once daily.the patient reported significant improvement in symptoms, with no recurrence of colicky pain or hematuria. A repeat ultrasound demonstrated normal kidneys with no stone reccurence. The urine pH had increased to 6.5. His serum uric acid levels had decreased to 7.2 mg/dL, and his 24-hour urine uric acid excretion had decreased to within normal limits. The patient also reported improved compliance with dietary modifications.

Adherence and Monitoring: Throughout the treatment period, the patient was closely monitored for compliance with the urine alkalinization regimen and dietary changes. Regular urine pH monitoring and periodic imaging were conducted to assess the resolution of stones and to ensure that urine pH remained above 6.0.

Discussion
Uric acid kidney stones are a unique subset of nephrolithiasis that require tailored management strategies. The ability to dissolve uric acid stones with urine alkalinization represents a significant advantage over surgical interventions such as lithotripsy or percutaneous nephrolithotomy(7), which may carry risks of complications and recurrence. Alkalinization therapy, primarily through the use of potassium citrate, has been shown to effectively reduce stone size and prevent new stone formation by raising urinary pH above the critical threshold of 5.5.

This case report demonstrates the clinical efficacy of urine alkalinization in managing recurrent uric acid kidney stones. In addition to pharmacologic therapy, dietary interventions, such as reducing purine intake

and increasing fluid intake, are essential components of a comprehensive treatment plan. Monitoring urine pH and adjusting the alkalinizing agent dosage is crucial to ensure sustained alkalinity and optimal outcomes.

Limitations and Considerations: While urine alkalinization is effective in most patients with uric acid stones, it may not be suitable for individuals with significant renal insufficiency or hyperkalemia(8). Additionally, it is important to monitor for potential side effects of potassium citrate, such as gastrointestinal discomfort or electrolyte imbalances. Regular follow-up and adherence to therapy are critical for long-term success.

Conclusions and recommendations:

Urine alkalinization is a highly effective treatment strategy for uric acid kidney stones, offering a non-invasive better alternative to surgical interventions. This case report underscores the importance of raising urinary pH to dissolve existing stones and prevent recurrence. With appropriate monitoring, dietary modifications, and adherance to pharmacologic therapy, patients with recurrent uric acid stones can achieve long-term relief and prevent future complications.

References:

1-Kamphuis GM, Wouter van Hattum J, de Bie P, Somani BK. Method of alkalization and monitoring of urinary pH for prevention of recurrent uric acid urolithiasis: a systematic review. Transl Androl Urol. 2019 Sep; 8(Suppl 4):S448-S456. doi: 10.21037/tau.2019.05.01. PMID: 31656751; PMCID: PMC6790419.
2-Sorokin I, Mamoulakis C, Miyazawa K, et al. Epidemiology of stone disease across the world. World J Urol 2017;35:1301-20. 10.1007/s00345-017-2008-6 - DOI - PubMed.
3-Trinchieri A, Montanari E. Prevalence of renal uric acid stones in the adult. Urolithiasis 2017;45:553-62. 10.1007/s00240-017-0962-5 - DOI - PubMed.
4-Kenny JES, Goldfarb DS. Update on the pathophysiology and management of uric acid renal stones. Curr Rheumatol Rep 2010;12:125-9. 10.1007/s11926-010-0089-y - DOI - PubMed.
5-Gutman AB, Yu T. Uric acid nephrolithiasis. Am J Med 1968;45:756-79. 10.1016/0002-9343(68)90209-X - DOI - PubMed.
6-Sakhaee K, Nicar M, Hill K, et al. Contrasting effects of potassium citrate and sodium citrate therapies on urinary chemistries and crystallization of stone-forming salts. Kidney Int 1983;24:348-52. 10.1038/ki.1983.165 - DOI - PubMed.
7-Nevo A, Humphreys MR, Callegari M, Keddis M, Moore JP, Salih S, Stern KL. Is medical dissolution treatment for uric acid stones more cost-effective than surgical treatment? A novel, solo practice, retrospective cost-analysis of medical vs. surgical therapy. Can Urol Assoc J. 2023 Jan;17(1):E29-E34. doi: 10.5489/cuaj.7833. PMID: 36121885; PMCID: PMC9872829.
8-Wiederkehr MR, Moe OW. Uric Acid Nephrolithiasis: A Systemic Metabolic Disorder. Clin Rev Bone Miner Metab. 2011 Dec;9(3-4):207-217. doi: 10.1007/s12018-011-9106-6. PMID: 25045326; PMCID: PMC4100778.