Conservative management of urinary calculi

Reviewed by:

Prof. (Dr.) Deodatta Chafekar
MD (Med), DNB (Med), DM (Nephro), DNB (Nephro), MNAMS
FISN, FASN, FICP, FISCCM, FRCP (London), FGSI, FISOT
Director & Consultant Nephrologist, Supreme Kidney Care, Nashik.
Prof. of Medicine, Dr. V Pawar Medical College, Nashik, and MUHS, Nashik.

Introduction

Urolithiasis is an age-old disease and has a growing global incidence and prevalence.[1,2] In a 2017 study from northern India, the lifetime prevalence of urinary stones was noted to be 7.9%.[3] In the year 2019, more than a fifth of all incident cases of urolithiasis worldwide occurred in India.[4]

Stones develop in the kidney and usually do not cause any symptoms. As they travel down the ureter, they can cause pain termed renal or ureteric colic.[1] Stones can occur as a result of various causes (Figure 1).[5] Patients can present with unilateral colicky pain in the flank or abdomen, nausea, vomiting, fever, and hematuria.[6]

Figure 1. Causes of stones

Infections	Non-infectious causes
Magnesium ammonium phosphate Ammonium urate Highly carbonated apatite	Calcium oxalate Calcium phosphate Uric acid

Genetic factors	Drugs
Xanthine Cystine 2,8-Dihydroxyadenine	**Some compounds/drugs linked with drug stones** Allopurinol/oxypurinol, amoxicillin/ampicillin, magnesium trisilicate, quinolones, ceftriaxone, sulfonamides, calcium, laxatives, losartan, ascorbic acid, topiramate, vitamin D, etc.

Treatment of stones is tailored to each patient and depends on multiple factors. The size, location, and composition of stones are key factors guiding treatment decisions.[5]

Diagnosis of urolithiasis

A thorough medical history and examination are usual components while evaluating a patient for urolithiasis. The laboratory investigations include urine analysis and serum investigations. Urine analysis includes red and white cells, pH, nitrites, and microscopy and culture. Serum investigation includes cell counts, uric acid, creatinine, calcium, sodium, potassium, and C-reactive protein.[5] For recurrent stone formers, we do 24-hr urinary estimation of calcium, uric acid, and oxalates.

A coagulation test should be done if an intervention is required.[5] In all first-time stone formers, stone composition analysis should be done using procedures like infrared spectroscopy or X-ray diffraction. Repeat stone analysis is required in patients with recurrence while on pharmacological treatment, early recurrence following clearance, and late recurrence.[5]

Ultrasonography is the fundamental imaging modality for urolithiasis diagnosis with the potential to identify calculi in the pelvis, calyces, and pyeloureteric and vesico-ureteral junctions. It is also useful in those having upper urinary tract dilatation.[5] Contrast-enhanced computed tomography (CT) is also a helpful imaging modality for confirmation of diagnosis.

Magnetic resonance imaging can be used in pregnant women as a secondary option, while ultrasonography remains the choice of imaging modality. Low-dose CT is the last-line choice.[5] In children, ultrasonography is the imaging modality of choice, followed by kidney-ureter-bladder radiography if ultrasound is not helpful.[5]

Non-pharmacological management

Some measures can be adopted to prevent stone formation. These include fluid intake, dietary modifications, and lifestyle changes. A fluid intake of 2.5 to 3 liters a day is advised, particularly water. One should have a balanced diet which includes fruits and vegetables and fiber. Those having high oxalate excretion must restrict or avoid high-oxalate foods. The dietary calcium content should be 1 to 1.2 g/day and sodium intake should be up to 4-5 g/day. One should also limit the intake of animal protein. People having hyperuricosuric calcium oxalate and uric acid stones should limit purine-rich products. Patients with calcium

oxalate stones should watch their vitamin C intake.[5]

Patients should be advised to engage in physical activity and maintain a normal BMI. Alcohol, sodas, and high-calorie fluid intake should be limited.[5] Salt restriction is an important measure.

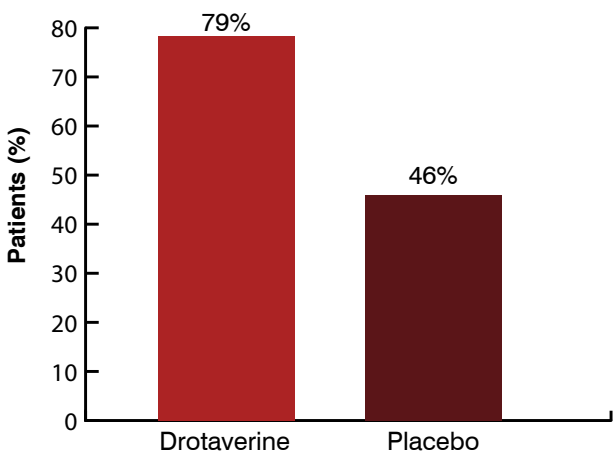
Pharmacological management

Pain management in urolithiasis

Pain control is a vital part of management. Non-steroidal anti-inflammatory drugs (NSAIDs) are the choice of therapy for pain relief. Paracetamol can also be effective. Opioids can be the next therapy option.[5]

Drotaverine has been shown to relieve pain in patients with colic due to stones. In an evaluation of the antispasmodic effect of drotaverine, the drug was found to be effective in 79% of patients (placebo in 46%; Figure 2), with no serious adverse effects.[7] A study compared the safety and efficacy of intramuscular drotaverine and diclofenac to manage acute renal colic in 100 patients.[8] At 30 minutes, there was a significant reduction in visual analog scale (VAS) in both groups (52.4% with drotaverine and 49% with diclofenac). At 60 minutes, the decrease was 61.3% with drotaverine vs. 60.4% with diclofenac. Drotaverine appears to be as effective and safe as diclofenac.

Figure 2. Proportion of patients in whom drotaverine and placebo were effective



NSAIDs are often combined with antispasmodics and administering these as injections can alleviate pain in acute renal colic and can also help decrease inflammation and swelling. Adding antispasmodics appears to enhance the effect of NSAIDs in managing spasmodic pain.[9]

Medical expulsive therapy

Medical expulsive therapy (MET) is a potential option in carefully selected patients. Targeted medical therapy was developed after identification of adrenergic receptors in the ureter and the understanding of smooth muscle physiology.[10]

α-adrenoceptor antagonists

α-blockers can be considered as an option for distal ureteral stones measuring >5 mm.[5] In a meta-analysis, patients treated with calcium channel blockers or α-blockers had 65% greater odds of stone expulsion compared to patients who did not receive these treatments.[11]

Tamsulosin, a selective α-1A and α-1B adrenoceptor blocker, has been noted to significantly increase passage of 10-15 mm lower ureteral stones. The adjusted spontaneous stone passage ratios were 10 and 0% for tamsulosin and control groups, respectively.[12] A multicenter trial noted that tamsulosin was associated with a higher stone expulsion rate for distal ureteral stones (86%) compared to placebo (79%). Additionally, the expulsion time was lesser and analgesic use was lower among patients given tamsulosin, compared to placebo. It also led to a significant relief in renal colic.[13] Not just in distal, but tamsulosin is beneficial for the management of proximal stones as well. A study evaluating the effectiveness of tamsulosin in the spontaneous passage of proximal ureteral calculi ≤10 mm noted that patients who received tamsulosin had higher spontaneous passage rate (71.4%) for stones <5 mm compared to those not receiving tamsulosin (50%). It also helped relocate 5-10 mm stones to a more distal ureteral part.[14]

Other agents in the class, including silodosin, do not seem to be better alternatives as the adverse effect profile of these agents and tamsulosin is comparable.[1]

Calcium channel blockers

These agents inhibit the calcium channels in the distal ureter. The contractions and spasms due to calculi are thus reduced.[15] While nifedipine has been reported to increase expulsion rate, its efficacy is inferior to tamsulosin, as per reports.[1] Tamsulosin was found to be better than nifedipine in terms of effectiveness, with greater expulsion rate, for patients with lower ureteral stones.[16]

Corticosteroids

Distal ureter stones can lead to inflammation and edema. Steroids have also been found to have a role in stone expulsion. They can decrease the inflammation as well as the damage caused by neutrophils. Combined with other medications, steroids can augment the passage of stones and also decrease the expulsion time.[15]

A study evaluating the role of corticosteroids and tamsulosin in MET for distal stones noted that steroids

could be effective only when used in combination with α-1 blockers (tamsulosin). The expulsion rates for different study groups are shown in Table 1. There was a significant difference between the group that received both tamsulosin and deflazacort and other groups (tamsulosin group, deflazacort group, only analgesic group).[17]

Table 1. Expulsion rates in study groups

Groups	Expulsion rate
Tamsulosin	60%
Deflazacort	37.5%
Tamsulosin and deflazacort	84.8%
Analgesics	33.3%

Phosphodiesterase inhibitors

In smooth muscles, phosphodiesterase (PDE) inhibitors inhibit the breakdown of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) by PDE, thus increasing their levels. This facilitates smooth muscle relaxation.[1] A study evaluating the effects of tamsulosin (Group A), tadalafil (Group B), and placebo (Group C) as MET in distal ureteral stones found a higher stone expulsion rate in Group A. Mean time to stone expulsion (days) was shorter in Group A (17.75±75), compared to Group B (21.13±1.17) and Group C (22.25±1.18). Additionally, analgesic requirement was significantly decreased in Group A. Tamsulosin was thus found to be superior in terms of effectiveness compared to tadalafil.[18]

β-adrenoceptor agonists

Mirabegron, a β_3-adrenergic receptor (β_3-AR) agonist, leads to bladder smooth muscle relaxation. It has been reported to have potential in MET for distal ureteral stones. It has been shown to augment stone expulsion rate and decrease pain episode frequency in comparison with control group.[19]

Alkalization of urine

Oral chemolysis with alkalization of urine can be a favorable approach in patients with suspected uric acid stones.[20] Administration of alkali for urinary alkalization has been suggested for stone dissolution.[21] A study explored the effectiveness of oral chemolysis (alkalization of urine) for the management of suspected uric acid stones. Oral chemolysis was associated with a complete response rate of 61% at 3 months and a partial response rate of 14%.[20] Urine alkalization using potassium citrate/bicarbonate has been found to be an effective and well-tolerated approach.[21]

A study evaluated the impact of potassium magnesium citrate and vitamin B_6 prophylaxis in calcium oxalate and phosphate stones. The study included patients having recurrent idiopathic hypocitraturia±hyperuricosuria. A statistically significant change was noted in the urinary pH, showing an increase from 5.62±0.2 to 6.87±0.01. There was a rise in urinary citrate from 221.79±13.39 to 604.04±5.00 mg (statistically significant). Additionally, the rate of stone formation was 3.23±1.04 per patient per year in control group 1 (patients with moderate to severe hypocitraturia±hyperuricosuria, recurrent stone formers, discontinued prophylaxis) compared to 0.35±0.48 per patient per year in group 3 (moderate to severe hypocitraturia±hyperuricosuria, recurrent stone formers, received prophylaxis). Therefore, this prophylaxis was found to decrease stone recurrence.[22]

Conclusion

Conservative management is a logical approach in select patients for the management of urolithiasis.

Pain relief is an important part of management and can be achieved with NSAIDs, paracetamol, and antispasmodics. Drotaverine has been shown to relieve pain in patients with colic due to stones. NSAIDs are often combined with antispasmodics to relieve pain.

MET is a promising approach in patients with urinary calculi. There are various agents that can be used as part of MET such a α-blockers, calcium channel blockers, steroids, PDE inhibitors, β-adrenoceptor agonists, and urinary alkalizers. Tamsulosin, an α-blocker, has been found to be effective for stone passage. It has been noted to be more effective than agents of other classes.

Stone dissolution can be achieved with alkali administration. Urine alkalization has been found to be effective.

References

1. Lim I, Sellers DJ, Chess-Williams R. Current and emerging pharmacological targets for medical expulsive therapy. *Basic Clin Pharmacol Toxicol.* 2022 Jan;130 Suppl 1:16-22.
2. Faridi MS, Singh KS. Preliminary study of prevalence of urolithiasis in North-Eastern city of India. *J Family Med Prim Care.* 2020 Dec 31;9(12):5939-43.

3. Lohiya A, Kant S, Kapil A, *et al.* Population-based estimate of urinary stones from Ballabgarh, northern India. *Natl Med J India.* 2017 Jul-Aug;30(4):198-200.
4. Lang J, Narendrula A, El-Zawahry A, *et al.* Global Trends in Incidence and Burden of Urolithiasis from 1990 to 2019: An Analysis of Global Burden of Disease Study Data. *Eur Urol Open Sci.* 2022 Jan 3;35:37-46.
5. Skolarikos A, Jung H, Neisius A, *et al*. EAU Guidelines on Urolithiasis. [Internet]. Available from: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Urolithiasis-2024.pdf. [cited Aug 24, 2024].
6. Thakore P, Liang TH. Urolithiasis. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559101/. [cited Aug 24, 2024].
7. Romics I, Molnár DL, Timberg G, *et al*. The effect of drotaverine hydrochloride in acute colicky pain caused by renal and ureteric stones. *BJU Int.* 2003 Jul;92(1):92-6.
8. Dash A, Maiti R, Akantappa Bandakkanavar TK, Arora P. Intramuscular drotaverine and diclofenac in acute renal colic: a comparative study of analgesic efficacy and safety. *Pain Med.* 2012 Mar;13(3):466-71.
9. Janczura M, Kobus-Moryson M, Sip S, *et al.* Fixed-Dose Combination of NSAIDs and Spasmolytic Agents in the Treatment of Different Types of Pain—A Practical Review. *J Clin Med.* 2021 Jul 15;10(14):3118.
10. Wood KD, Gorbachinsky I, Gutierrez J. Medical expulsive therapy. *Indian J Urol.* 2014 Jan;30(1):60-4.
11. Hollingsworth JM, Rogers MA, Kaufman SR, *et al.* Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet.* 2006 Sep 30;368(9542):1171-9.
12. Shalaby MM, Eldardery MA, Elderwy AA, *et al.* The use of tamsulosin in the treatment of 10–15 mm lower ureteral stones in adults: a double-blinded randomized controlled trial. *Afr J Urol*. 2022;28:54.
13. Ye Z, Zeng G, Yang H, *et al.* Efficacy and Safety of Tamsulosin in Medical Expulsive Therapy for Distal Ureteral Stones with Renal Colic: A Multicenter, Randomized, Double-blind, Placebo-controlled Trial. *Eur Urol.* 2018 Mar;73(3):385-91.
14. Yencilek F, Erturhan S, Canguven O, *et al.* Does tamsulosin change the management of proximally located ureteral stones? *Urol Res.* 2010 Jun;38(3):195-9.
15. Barnela SR, Soni SS, Saboo SS, Bhansali AS. Medical management of renal stone. *Indian J Endocrinol Metab.* 2012 Mar;16(2):236-9.
16. Cao D, Yang L, Liu L, *et al.* A comparison of nifedipine and tamsulosin as medical expulsive therapy for the management of lower ureteral stones without ESWL. *Sci Rep.* 2014 Jun 11;4:5254.
17. Porpiglia F, Vaccino D, Billia M, *et al.* Corticosteroids and tamsulosin in the medical expulsive therapy for symptomatic distal ureter stones: single drug or association? *Eur Urol.* 2006 Aug;50(2):339-44.
18. Falahatkar S, Akhavan A, Esmaeili S, *et al.* Efficacy of tamsulosin versus tadalafil as medical expulsive therapy on stone expulsion in patients with distal ureteral stones: A randomized double-blind clinical trial. *Int Braz J Urol.* 2021 Sep-Oct;47:982-8.
19. Song H, Liang L, Liu H, *et al.* Mirabegron for medical expulsive therapy of ureteral stones: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2024 Jan 5;10:1280487.
20. Tsaturyan A, Bokova E, Bosshard P, *et al.* Oral chemolysis is an effective, non-invasive therapy for urinary stones suspected of uric acid content. *Urolithiasis*. 2020 Dec;48(6):501-7.
21. Trinchieri A, Esposito N, Castelnuovo C. Dissolution of radiolucent renal stones by oral alkalinization with potassium citrate/potassium bicarbonate. *Arch Ital Urol Androl.* 2009 Sep;81(3):188-91.
22. Reddy SV, Shaik AB, Bokkisam S. Effect of potassium magnesium citrate and vitamin B-6 prophylaxis for recurrent and multiple calcium oxalate and phosphate urolithiasis. *Korean J Urol.* 2014 Jun;55(6):411-6.