Management Strategies for Renal Colic and Calculi

Reviewed by:

Dr Manoj Singhal
MBBS, MD (Medicine), DM (Nephrology), DNB (Nephrology)
Director- Nephrology and Kidney Transplantation
Max Super Speciality Hospital, Vaishali

Overview

Nephrolithiasis, or kidney stones, is one of the most common conditions affecting the urinary system.[1] It is mostly caused by a crystal or crystalline concretion (renal calculi) migrating from the kidney along the urinary tract and becoming stuck creating an obstruction to urinary flow.[2] This obstruction causes proximal ureteral and renal pelvic dilation resulting in the immediate and intense pain known as renal colic. Renal colic is one of the most painful events in a person's life and is one of the most common presentations of acute pain in emergency.[2-4]

Epidemiology

Nephrolithiasis affects approximately 12% of the global population at some point in their lives.[1,5] Its prevalence varies worldwide, ranging from 1–5% in Asia, 5–9% in Europe, 10–15% in the USA, and 20–25% in the Middle East.[6,7] In Asia, it stands out as one of the most common urologic diseases. Prevalence of nephrolithiasis in India aligns with the global average at 12%, and the northern region experiences a higher prevalence (15%) compared to the southern region.[6,8] Men are twice more likely to be affected than women, which is likely attributed to rising obesity from poor dietary habits and sedentary lifestyles.[1,5]

Risk factors for calculi formation

Risk factors for the formation of renal calculi can be categorized as intrinsic factors like age, gender, and ethnicity, or extrinsic factors like climate, diet, occupation, and education. Climate and dietary habits, particularly high salt and animal-derived protein intake, low fluid consumption, and elevated oxalate levels in foods, contribute significantly. Personal and familial calculi history increases the risk, and lifestyle factors like obesity increase susceptibility to calcium oxalate stone formation. Additionally, medical conditions such as chronic kidney disease, hypertension, gout, diabetes, hyperlipidemia, and malignancies elevate the likelihood of renal calculi formation.[7-10]

Management of renal calculi and associated colic

The initial management of nephrolithiasis focuses on three key principles: firstly, identifying emergency and urgent conditions that warrant urologic referral; secondly, administering medications for efficient pain relief and control; and thirdly, recognizing the impact of stone size and location on the natural progression and proceeding with definitive urologic management.[11]

Immediate intervention with analgesia and antiemetics

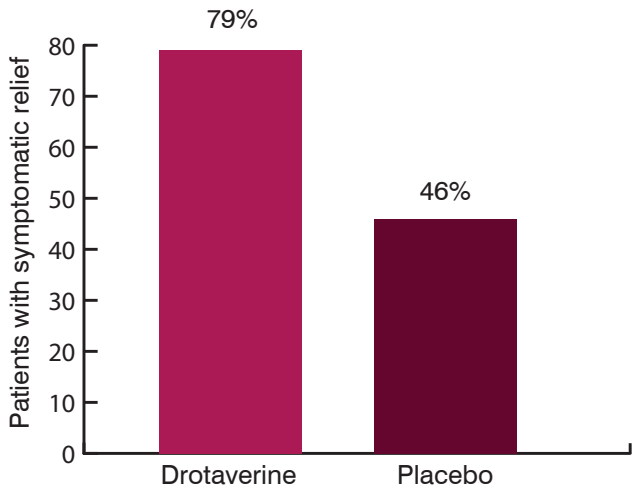
Managing acute pain in nephrolithiasis is a priority, with a focus on reducing pain severity. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as standard analgesics, while opioids serve as rescue medications for renal colic. Concurrent use of antiemetics may be considered to prevent or control nausea and vomiting. Phosphodiesterase (PDE) inhibitors like drotaverine have the potential to alleviate ureteral spasm and pain by inhibiting cAMP and cGMP breakdown, promoting smooth muscle relaxation.[4,12]

Drotaverine in acute renal colic

Drotaverine is a potent spasmolytic, which inhibits PDE type IV in smooth muscle cells, thus exerting a mild calcium-channel blocking effect without anticholinergic properties. Administered orally, intramuscularly, or intravenously, it serves as a well-established, directly acting antispasmodic, ensuring rapid and effective pain relief in emergencies and postoperative scenarios.[4,13]

Clinical studies have assessed efficacy and safety of drotaverine hydrochloride in the setting of acute renal colic. A placebo-controlled study[14] examined the efficacy

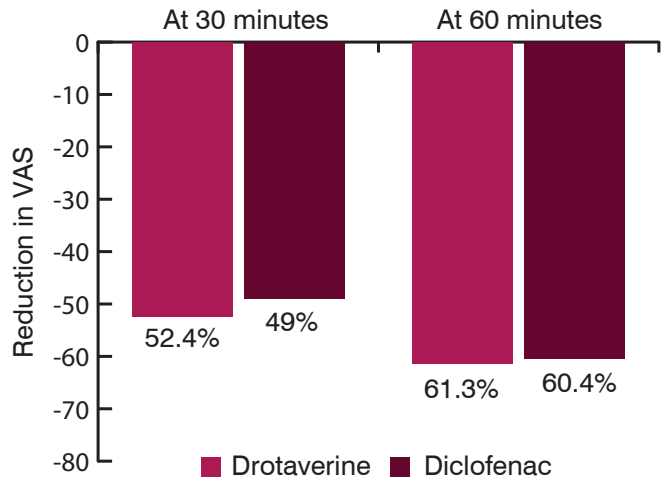
Figure 1: Patients with renal colic reporting symptomatic relief after treatment with drotaverine versus placebo[14]



and safety of drotaverine hydrochloride in managing acute colicky pain caused by renal and ureteric stones. The study included 102 patients with renal or ureteric stone-induced acute colicky pain, randomly assigned to drotaverine (n=48) or placebo (n=54). The primary endpoint was the antispasmodic effect of drotaverine over a 3-hour period, assessed by abolishment or decrease in pain intensity in renal colic. Symptomatic relief was reported by 79% in the drotaverine group, compared to 46% in the placebo group. Drotaverine demonstrated a significant pain-relieving effect, supporting its efficacy in acute renal colic management (Figure 1).

In another randomized, single-blind study[4] comparing intramuscular drotaverine hydrochloride and diclofenac sodium in 100 emergency department patients with renal colic, both drugs showed a significant decrease in pain intensity, measured by visual analogue scale (VAS). At 30 minutes, VAS reduction was 52.4% for drotaverine and 49% for diclofenac, while at 60 minutes, it was 61.3% for drotaverine and 60.4% for diclofenac (Figure 2). The effectiveness, defined as ≥50% decrease in pain intensity within an hour of administration and without exacerbation in the following 2 hours, was reported by 90% in the drotaverine group and 88% in the diclofenac group. Need for rescue medication was in five patients of the drotaverine group and six patients in the diclofenac group.

Figure 2: Reduction in pain intensity (measured by VAS) with drotaverine versus diclofenac in patients with renal colic[4]



Drotaverine along with NSAIDs

In routine clinical practice, drotaverine is often used in combination with analgesics to enhance its spasmolytic effect.[14] This fast-acting antispasmodic provides pain relief within 12 minutes and is often paired with aceclofenac for an effective and prolonged anti-inflammatory/analgesic effect. Studies, such as one by Pareek *et al,*[15] demonstrate the superiority of combining drotaverine with aceclofenac over aceclofenac monotherapy. Likewise, a prospective clinical trial by Vinod and Ashish demonstrated the enhanced efficacy of the drotaverine and aceclofenac combination over aceclofenac alone, showing statistically significant pain reduction at postoperative days 1, 3, and 5.[13]

Medical expulsive therapy for calculi

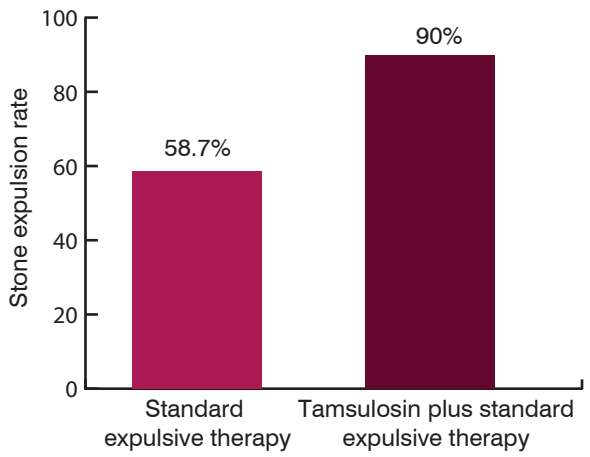
Medical expulsive therapy (MET) is an effective conservative watchful approach for managing renal calculi, which utilizes drug combinations to aid spontaneous passage of ureteric calculi.[16,17] Investigated therapies include alpha-blockers, calcium channel blockers, corticosteroids, and PDE5 inhibitors.[17,18] Both the American Urological Association and European Association of Urology (EAU) endorse MET to support spontaneous stone expulsion, providing a non-invasive option for patients suitable for conservative management, potentially averting the need for surgery.[19,20]

Alpha-blockers are currently the only recommended monotherapy, with current guidelines endorsing the use of alpha-blockers to facilitate passage of ureteral stones <10 mm in diameter in appropriately selected patients.[17,18] Alpha-blockers decrease smooth muscle tension, releasing spasms and enabling faster passage of ureteric calculi. They are considered superior to calcium-channel inhibitors in facilitating stone passage and additionally reduce colic episodes while promoting spontaneous expulsion.[20-22]

Tamsulosin – The preferred alpha-blocker for stone expulsion

Tamsulosin, a selective alpha-1 receptor antagonist, has been extensively studied for treating ureteral stones and enhancing spontaneous stone expulsion.[16] Acting upon alpha adrenergic receptors on ureteral smooth muscles,

Figure 3: Effect of add-on tamsulosin with standard expulsive therapy on stone expulsion rate[27]



tamsulosin dilates the lumen and inhibits spasms, particularly in the distal ureter.[19] With equal affinity for alpha-1a and alpha-1d receptors, tamsulosin is effective in expulsion therapy, increasing passage rates for stones up to 10 mm.[23-26]

De Sio and colleagues[27] demonstrated that addition of tamsulosin to standard expulsive therapy for distal-ureteral stones significantly increased expulsion rates (90% vs. 58.7%, respectively; Figure 3) and reduced stone passage time (4.4 days vs. 7.5 days, respectively). The tamsulosin group also showed lower analgesic use and fewer hospitalizations for recurrent colic. The study concluded that tamsulosin is effective in the conservative management of uncomplicated distal-ureteral stones.

Tamsulosin with ADS technology

Tamsulosin with advanced delivery system (ADS) technology offers significant advantages. It ensures sustained drug release throughout the gastrointestinal tract, even in limited water availability. This innovation addresses issues of conventional formulations dependent on water presence, potentially reducing adverse effects on physiological parameters. The ADS technology provides consistent 24-hour drug release, minimizing maximum concentration (Cmax) related side effects and improving the efficacy/tolerability ratio. It also allows flexible dosing times, reducing the risk of postural hypotension, especially in cardiovascular patients, thus decreasing overall risks of cardiovascular events, falls, and fractures, with an overall lower incidence of adverse events.[28,29]

Salient features of tamsulosin: Excerpt from EAU 2023 Guidelines on Urolithiasis

- Combination of alkalinization with tamsulosin can increase the frequency of spontaneous passage of distal ureteral uric acid stones for stones > 5 mm
- Consider the use of oral chemolysis with tamsulosin in case of (larger) ureteral stones, if active intervention is not indicated

Source: Guidelines on Urolithiasis. European Association of Urology 2023. Available at: https://uroweb.org/guidelines/urolithiasis. Accessed on 14/11/2023.

Potassium citrate therapy for preventing stone recurrence: 2019 NICE recommendation

- Consider potassium citrate for adults with a recurrence of stones that are predominantly (>50%) calcium oxalate
- Consider potassium citrate for children and young people with a recurrence of stones that are predominantly (> 50%) calcium oxalate, and with hypercalciuria or hypocitraturia

Source: Renal and ureteric stones: Assessment and management. Available at: https://www.nice.org.uk/guidance/ng118/chapter/Recommendations#preventingrecurrence. Accessed on: 14/11/2023.

Fluid and dietary management

Dietary therapy holds promise for reducing recurrent kidney stone formation. Awareness and optimized food choices can mitigate the prevalence of renal stone disease, particularly in India where high protein and carbohydrate consumption prevails. Adequate fluid intake, especially water, and dietary modifications are crucial preventive measures. Avoiding oxalate-rich foods, reducing animal protein intake, and adding milk to oxalate-containing beverages are advised.[6,30,31]

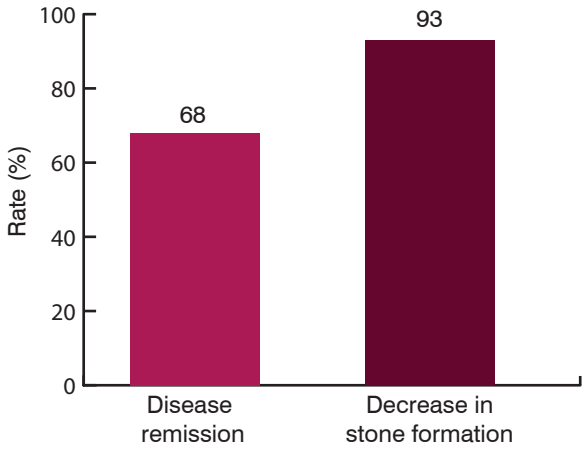
Urinary alkalization for dissolution of renal calculi

Urinary alkalization, achieved through alkali administration, is a clinically established treatment approach for stone dissolution.[32-34] Potassium citrate, a preferred alkalizing agent due to low sodium load, not only raises urine pH but also increases urinary citrate, inhibiting stone formation, making it beneficial for patients with Ca-oxalate, cystine, and uric acid stones.[35-37]

Effectiveness of long-term potassium citrate therapy

In a retrospective cohort study by Robinson *et al,*[38] patients with nephrolithiasis showed a significant and durable change in urinary metabolic profiles with potassium citrate therapy. Within 6 months of treatment onset, there was a notable increase in urinary pH (5.90 to 6.46) and urinary citrate (470 to 700 mg/day). Stone formation rate significantly decreased from 1.89 to 0.46 stones per year, resulting in a 68% remission rate and a 93% decrease in stone formation rate (Figure 4). Changes in urinary metabolic profiles were sustained for as long as 14 years of treatment. The study affirmed the long-term efficacy of potassium citrate therapy for recurrent nephrolithiasis.

Figure 4: Efficacy of potassium citrate therapy in patients with recurrent nephrolithiasis[38]



Combination therapy with potassium citrate, magnesium citrate and vitamin B6

The property of magnesium to enhance calcium oxalate solubility suggests its potential in slowing calcium oxalate crystal growth, proposing a preventive role against stone recurrence.[39,40] Vitamin B6 deficiency is linked to increased oxalate production and excretion, while its intake inversely associates with stone formation risk.[41] In this context, a 3-year prospective study by Reddy and colleagues[42] involving 247 Indian patients with hypocitraturia- and hyperuricosuria-induced recurrent calcium oxalate and calcium phosphate stones showed that long-term treatment with potassium magnesium citrate and vitamin B6 prophylaxis yielded a sustained increase in 24-hour urinary citrate excretion (from 221 mg/dL to 604.04 mg/dL at 6-month follow-up), elevated urinary pH (from 5.62 to 6.87), and reduced the stone recurrence rate (from 3.23 to 0.35 per patient per year).

Conclusion

Nephrolithiasis, or kidney stone, has gradually become a universal problem transcending geographical and cultural boundaries. Acute flank pain (renal colic) is the most common symptom associated with nephrolithiasis. Medical management involves dietary modifications, disease-specific treatment, symptomatic relief, and medical expulsive therapy. Tamsulosin is effective in medical expulsive therapy and increases the passage rate for stones up to 10 mm. Furthermore, Drotaverine, a directly acting, smooth muscle antispasmodic agent provides quick and effective pain relief for renal and ureteral colic. Lastly, citrate salts, particularly potassium citrate, play a crucial role in preventing new stone formation, reducing stone size, and maintaining stability, especially in oxalate-containing stones, thereby lowering recurrence of calcium oxalate and phosphate urolithiasis.

References

1. Nojaba L, Guzman N. Nephrolithiasis. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559227/. Accessed on 14/11/2023.
2. Patti L, Leslie SW. Acute Renal Colic. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431091/. Accessed on 14/11/2023.
3. Dash A, Maiti R, Akantappa Bandakkanavar TK, *et al.* Intramuscular drotaverine and diclofenac in acute renal colic: a comparative study of analgesic efficacy and safety. *Pain Med*. 2012;13(3):466-71.
4. Kanwal M, Anwar S, Majeed S, *et al.* Assessing the Efficacy of Combined Therapy of Drotaverine and Ketorolac as Compared to Ketorolac Alone in Decreasing the Intensity of Renal Colic at PIMS Emergency. *Middle East Journal of Applied Science & Technology.* 2021;4(2):43-54.
5. Alelign T, Petros B. Kidney Stone Disease: An Update on Current Concepts. *Adv Urol.* 2018;2018:3068365.
6. Guha M, Banerjee H, Mitra P, *et al.* The Demographic Diversity of Food Intake and Prevalence of Kidney Stone Diseases in the Indian Continent. *Foods.* 2019;8(1):37.
7. Liu Y, Chen Y, Liao B, *et al.* Epidemiology of urolithiasis in Asia. *Asian J Urol.* 2018;5(4):205-214.
8. Singh S, Gupta S, Mishra T, *et al.* Risk Factors of Incident Kidney Stones in Indian Adults: A Hospital-Based Cross-Sectional Study. *Cureus*. 2023;15(2):e35558.
9. Baatiah NY, Alhazmi RB, Albathi FA, *et al.* Urolithiasis: Prevalence, risk factors, and public awareness regarding dietary and lifestyle habits in Jeddah, Saudi Arabia in 2017. *Urol Ann.* 2020;12(1):57-62.
10. Thakore P, Liang TH. Urolithiasis. [Updated 2020 Nov 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559101/. Accessed on 14/11/2023.
11. Portis AJ, Sundaram CP. Diagnosis and initial management of kidney stones. *Am Fam Physician.* 2001;63(7):1329-38
12. Managing patients with renal colic in primary care: Know when to hold them. Available at: https://bpac.org.nz/bpj/2014/april/docs/BPJ60-colic.pdf. Accessed on 14/11/2023.
13. Vinod KM, Ashish D. Oral drotaverine and aceclofenac combination versus aceclofenac alone for postoperative pain relief: a prospective randomized clinical trial. *Indian Journal of Pharmacy Practice.* 2013;6(4):18-21.
14. 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;92(1):92-6.
15. Porwal A, Mahajan AD, Oswal DS, *et al.* Efficacy and Tolerability of Fixed-Dose Combination of Dexketoprofen and Dicyclomine Injection in Acute Renal Colic. *Pain Research and Treatment.* 2012;2012:295926.
16. Shafi H, Moazzami B, Pourghasem M, *et al.* An overview of treatment options for urinary stones. *Caspian J Intern Med.* 2016 Winter; 7(1): 1-6.
17. Bos D, Kapoor A. Update on medical expulsive therapy for distal ureteral stones: Beyond alpha-blockers. *Can Urol Assoc J.* 2014;8(11-12):442-445.
18. Scales CD Jr, Tasian GE, Schwaderer AL, *et al.* Urinary Stone Disease: Advancing Knowledge, Patient Care, and Population Health. *Clin J Am Soc Nephrol.* 2016;11(7):1305-1312.
19. Surgical management of stones: American urological association/ endourological society guideline. Available at: www.imop.gr/sites/default/files/giannakopoulos_2_0.pdf. Accessed on: 14/11/2023.
20. Turk C, Petrık A, Sarica K, *et al.* EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis. *European Urology.* 2016;69:468-474.
21. Cervenakov I, Fillo J, Mardiak J, *et al.* Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker--Tamsulosin. *Int Urol Nephrol* 2002;34:25-9.
22. Porpiglia F, Ghignone G, Fiori C, *et al.* Nifedipine versus Tamsulosin for the management of lower ureteral stones. Fontana *et al. J Urol* 2004;172:568-71
23. Lipkin M, Shah O. The Use of Alpha-Blockers for the Treatment of Nephrolithiasis. *Rev Urol.* 2006;8(Suppl 4):S35-S42.
24. Rivard R. Tamsulosin: Ureteral stones (distal). Hosp Pharm. 2015;50(1):31-33.
25. Arrabal-Martin M, Valle-Diaz de la Guardia F, Arrabal-Polo MA, *et al.* Treatment of ureteral lithiasis with Tamsulosin: literature review and metaanalysis. *Urol Int.* 2010;84(3):254-9.
26. Guidelines on Urolithiasis. European Association of Urology 2023. Available at: https://uroweb.org/guidelines/urolithiasis. Accessed on 14/11/2023.
27. De Sio M, Autorino R, Di Lorenzo G, *et al.* Medical expulsive treatment of distal-ureteral stones using Tamsulosin: a single-center experience. *J Endourol* 2006;20:12-6.
28. Speakman M. Efficacy and safety of Tamsulosin OCAS. *BJU international* 2006;98(2): 13-17.

Continued on page 13...