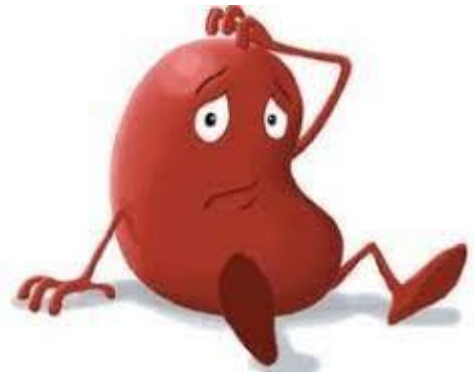
Dr Mohsen Mohammadrahimi

Assistant professor
department of urology
Tabriz university of Medial Sciences

medical management of renal calculi



Medical expulsive therapy

- Medical expulsive therapy should only be used in informed patients if active stone removal is not indicated

- Treatment should be discontinued if complications develop (infection, refractory pain, deterioration of renal function)

- Several drug classes are used for MET

- When using α-blockers for MET, possible side effects include retrograde ejaculation and hypotension

- α-blockers
- calcium-channel inhibitors (nifedipine)
- Phosphodiesterase type 5 inhibitors (PDEI-5) (tadalafil)
- pass stones with fewer colic episodes than those not receiving such therapy
- Based on studies with a limited number of patients no recommendation for the use of PDEI-5 o corticosteroids in combination with α-blockers in MET can be made

- Tamsulosin showed an overall superiority to nifedipine for distal ureteral calculi

- There are small trials of uncertain quality suggesting tadalafil alone or in combination with tamsulosin may be beneficial for ureteric stone passage

Summary of evidence	LE
Medical expulsive therapy seems to be efficacious for treating patients with ureteral stones who are amenable to conservative management. The greatest benefit might be among those with > 5 mm (distal) ureteral stones.	1a
Insufficient data exist to support the use of PDEI-5 or corticosteroids in combination with α-blockers as an accelerating adjunct.	2a
α-blockers increase stone expulsion rates in distal ureteral stones > 5 mm.	1a
A class effect of α-blockers has been demonstrated.	1a

Recommendation	Strength rating
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm.	Strong

General considerations for recurrence prevention

Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day
	Circadian drinking
	Neutral pH beverages
	Diuresis: 2.0-2.5 L/day
	Specific weight of urine: < 1010 g/day
Nutritional advice for a balanced diet	Balanced diet*
	Rich in vegetables and fibre
	Normal calcium content: 1-1.2 g/day
	Limited NaCl content: 4-5 g/day
	Limited animal protein content: 0.8-1.0 g/kg/day
Lifestyle advice to normalise general risk factors	BMI: Retain a normal BMI level
	Adequate physical activity
	Balancing of excessive fluid loss

calcium phosphate stones

- Hyperparathyroidism and RTA are common causes of calcium phosphate stone formation.

- Although most patients with primary HPT require surgery, RTA can be corrected pharmacologically

- If primary HPT and RTA have been excluded, pharmacotherapy for calcium phosphate calculi depends on effective reduction of urinary calcium levels using thiazides
- If urine pH remains constantly > 6.2, urinary acidification with L-methionine may be beneficial
- however, it is not commonly used and needs monitoring for systemic acidosis development
- For infection-associated calcium phosphate stones, it is important to consider the guidance given for infection stones

Summary of evidence	LE
Thiazide is beneficial in case of hypercalciuria.	1a
Acidification of urine can be beneficial in case of high urine pH.	3-4

Recommendations	Strength rating
Prescribe thiazide in case of hypercalciuria.	Strong
Advise patients to acidify their urine in case of high urine pH.	Weak

Cystine stones

- General preventative measures for fluid intake and diet are recommended
- A diet low in methionine may theoretically reduce urinary excretion of cysteine
- however, patients are unlikely to comply sufficiently with such a diet

- A restricted intake of sodium is more easily achieved and is more effective in reducing urinary Cystine

- Patients are usually advised to avoid sodium consumption > 2 g/day

- A high level of diuresis is of fundamental importance, aiming for a 24-hour urine volume of > 3 L

- A considerable fluid intake evenly distributed throughout the day is necessary

Pharmacological treatment of cystine stones

- The main therapeutic option for avoiding cystine crystallisation is to maintain urine pH >> 7.5, to improve cysteine solubility and ensure appropriate hydration with a minimum of 3.5 L/day in adults, or 1.5 L/m2 body surface area in children

- Free cystine concentration can be decreased by reductive substances, which act by splitting the disulfidebinding of cysteine.

- Tiopronin is currently the best choice for cystine reduction

- However, side effects often lead to treatment termination, for example when nephrotic syndrome develops or when there is poor compliance, especially with long-term use

After carefully considering the risk of early tachyphylaxis, put into place a dose-escape phenomenon for long-term use, and recurrence risk, tiopronin is recommended at cysteine levels > 3.0 mmol/day or in the case of recurring stone formation, notwithstanding other preventive measures

Summary of evidence	LE
Increasing fluid intake so that 24-hour urine volume exceeds 3 L is used to dilute the cystine.	3
Alkaline citrates 3-10 mmol two or three times daily can be used to achieve pH > 7.5.	3
Tiopronin, 250-2,000 mg/day can be used to reduce stone formation in patients with cysteine excretion, > 3 mmol/day, or when other measures are insufficient.	3

Recommendations	Strength rating
Therapeutic measures	
Urine dilution Advise patients to increase their fluid intake so that 24-hour urine volume exceeds 3 L.	Strong
Alkalinisation Prescribe potassium citrate 3-10 mmol two or three times daily, to achieve pH > 7.5 for patients with cystine excretion < 3 mmol/day.	Strong
Complex formation with cystine For patients with cystine excretion, > 3 mmol/day, or when other measures are insufficient: prescribe in addition to other measures tiopronin, 250-2,000 mg/day.	Strong

Calcium oxalate stones

- General preventive measures are recommended for fluid intake and diet.

- Hyperoxaluric stone formers should consume foods with low oxalate content, whereas hyperuricosuric stone formers benefit from daily dietary reduction of purine

4.4.4 *Summary of evidence and guidelines for pharmacological treatments for patients with specific abnormalities in urine composition (based on 24-hour urine samples)*

Summary of evidence	LE
Thiazide + alkaline citrates can reduce stone formation.	1a
Oxalate restriction is beneficial if hyperoxaluria is present.	2b
Alkaline citrates can reduce stone formation in enteric hyperoxaluria.	4
Calcium supplement can reduce stone formation in enteric hyperoxaluria.	2
A diet reduced in fat and oxalate can be beneficial in reducing stone formation.	3
Alkaline citrates and sodium bicarbonate can be used to if hypocitraturia is present.	1b
Allopurinol is first-line treatment of hyperuricosuria.	1a
Febuxostat is second-line treatment of hyperuricosuria.	1b
Avoid excessive intake of animal protein in hyperuricosuria.	1b
Restricted intake of salt is beneficial if there is high urinary sodium excretion.	1b

Recommendations	Strength rating
Prescribe thiazide + alkaline citrates in case of hypercalcuria.	Strong
Advise oxalate restriction if hyperoxaluria is present.	Weak
Offer alkaline citrates in enteric hyperoxaluria.	Weak
Offer calcium supplement in enteric hyperoxaluria.	Weak
Advise reduced dietary fat and oxalate in enteric hyperoxaluria.	Weak
Prescribe alkaline citrates and sodium bicarbonate in case of hypocitraturia.	Strong
Prescribe allopurinol in case of hyperuricosuria.	Strong
Offer febuxostat as second-line treatment of hypericosuria.	Strong
Avoid excessive intake of animal protein in hypericosuria.	Strong
Advise restricted intake of salt if there is high urinary sodium excretion.	Strong

Uric acid and ammonium urate stones

- General preventive measures are recommended for fluid intake and diet
- Hyperuricosuric stone formers benefit from purine reduction in their daily diet
- For uric acid stones, allopurinol may change the stone composition distribution in patients with gout to a pattern similar to that in stone formers without gout

Summary of evidence	LE
Alkaline citrates can be beneficial to alkalinise the urine in urate stone formers.	3
Allopurinol can be beneficial in hyperuricosuric urate stone formers.	1b

Recommendations	Strength rating
Prescribe alkaline citrates to alkalinise the urine in urate stone formers.	Strong
Prescribe allopurinol in hyperuricosuric urate stone formers.	Strong

Struvite and infection stones

- General preventive measures are recommended for fluid intake and diet
- Specific measures include

  - Complete surgical stone removal
  - short- or long-term antibiotic treatment
  - urinary acidification using
  - methionine or ammonium chloride,
  - and advice to restrict intake of urease

For severe Infections

- acetohydroxamic acid may be an option
- however, it is not licensed/available in all European countries
- Eradication of infection after complete stone removal is desirable
- The evidence regarding the duration of post-operative antibiotic administration is inconclusive

Summary of evidence	LE
Removing the stone material as completely as possible with surgery can reduce ongoing infection.	3
Antibiotics are beneficial after complete stone removal.	3
Ammonium chloride, 1 g, two or three times daily, can ensure urinary acidification to prevent recurrent infection.	3
Methionine, 200-500 mg, one to three times daily, can be used as an alternative to ammonium chloride, to ensure urinary acidification.	3
Urease inhibitors in case of severe infection are occasionally used (if licensed).	1b

Recommendations	Strength rating
Surgically remove the stone material as completely as possible.	Strong
Prescribe antibiotics in case of persistent bacteriuria.	Strong
Prescribe ammonium chloride, 1 g, two or three times daily to ensure urinary acidification.	Weak
Prescribe methionine, 200-500 mg, one to three times daily, as an alternative, to ensure urinary acidification.	Weak

Primary hyperoxaluria

Patients with primary hyperoxaluria (PH) should be referred to specialised centres, as successful management requires an experienced interdisciplinary team.

- The main therapeutic aim is to reduce endogenous oxalate production, which is increased in patients with PH

- In approximately one-third of patients with PH type I, pyridoxine therapy normalises or significantly reduces urinary oxalate excretion

The goal of adequate urine dilution is achieved by adjusting fluid intake to 3.5-4.0 L/day in adults (children 1.5 L/m2 body surface area) and following a circadian drinking regimen

- Therapeutic options for preventing calcium oxalate crystallisation include

  - hyperdiuresis
  - alkaline
  - citrates
  - Magnesium

- in end-stage renal failure, PH requires simultaneous liver-kidney transplantation.

❖ Treatment regimens are:

- pyridoxine in PH type I: 5-20 mg/kg/day according to urinary oxalate excretion and patient tolerance
- alkaline citrate: 9-12 g/day in adults, 0.1-0.15 mq/kg/day in children
- magnesium: 200-400 mg/day (no magnesium in the case of renal insufficiency)

Summary of evidence	LE
Pyridoxine can reduce the urinary oxalate excretion in primary hyperoxaluria.	3

Recommendation	Strength rating
Prescribe pyridoxine for primary hyperoxaluria.	Strong

Enteric hyperoxaluria

- restricted intake of oxalate-rich foods
- restricted fat intake
- calcium supplementation at meal times to enable calcium oxalate complex formation in the intestine
- sufficient fluid intake to balance intestinal loss of water caused by diarrhea
- alkaline citrates to raise urinary pH and citrate.

Summary of evidence	LE
Alkaline citrates can be beneficial to replace citrate loss and raise urine pH.	3
Calcium supplements with meals can enable calcium oxalate complex formation in the intestine.	2
Reduction in dietary fat and oxalate can be beneficial in intestinal malabsorption.	3

Recommendations	Strength rating
Prescribe alkaline citrates for enteric hyperoxaluria.	Weak
Advise patients to take calcium supplements with meals.	Weak
Advise patients to follow a diet with a low fat and oxalate content.	Weak