Aetiology and prevention of recurrent renal calculi

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Factors that have the greatest impact on prevention of stone disease include advising patients to drink plenty of fluids, adopt a healthy lifestyle, reduce their risk of obesity and control diabetes and blood pressure.

Nephrolithiasis is a condition in which organic and inorganic masses form within the urinary tract. Stone formation may occur when the urinary concentration of crystals (eg calcium, oxalate and uric acid) is high and when the concentration of substances that inhibit stone formation (eg citrate) is low (Figure 1).1

**PREVALENCE AND EPIDEMIOLOGY OF KIDNEY STONES**

Kidney stones may present at any age; however, young and middle-aged adults are more commonly affected, especially in hot climates.2 The typical presentation is mainly in the working age group (between 20 and 60 years of age).3,4

Lifetime prevalence is 13 per cent for men and 7 per cent for women.1 In recent years the incidence of stone presentation has been increasing in the UK. In 2008–09, about 80000 patients presented to hospital with kidney stones. This figure represents a 60 per cent increase in hospital attendance as a result of stone disease since 2003.5

The recurrence rate is about 50 per cent within 5–10 years and 75 per cent within 20 years. In developed countries a rapid increase in stone disease has occurred over the past 30 years, especially in women, in whom the incidence is now almost equal to that of men.6 Following an initial stone event, the five-year recurrence rate in the absence of specific treatment is 35–50 per cent.7

Urinary tract stones can be classified according to composition, location, size, aetiology, radiological characteristics and risk of recurrence (Figure 2).8,9 About 80 per cent of patients predominantly have calcium oxalate and/or calcium phosphate stones. Uric acid and struvite stones each account for 5–10 per cent and cystine stones are quite rare.10

**AETIOLOGY OF STONE FORMATION**

The causes of stone formation can be divided into anatomical, genetic, pathological and...
Large observational studies have shown that low fluid intake, low calcium intake and high fructose intake increase the risk of stone formation. Stones usually form when conditions favour separation of crystals out of the urine; many patients may have low urine volume and one or more biochemical abnormalities in the urine or blood. The most common abnormality is hypercalciuria; other abnormalities include hypercalcaemia, hyperuricaemia, hyperuricosuria, hyperoxaluria, hypocitraturia, and either low or high urine pH.

Anatomical abnormalities that occur along the urinary tract are key factors in preventing adequate flow of urine. This disturbance in flow favours the deposition of crystals and promotes stone formation. Wherever there is a change in the normal anatomical structure of the urinary tract, stone formation should be suspected, as in horseshoe kidney, medullar sponge kidney and a calyceal diverticulum.

The flow of urine from the kidney would be hindered in pelviureteric junction obstruction, ureteric stricture and a ureterocele. Bladder stones may occur in long-standing bladder outflow obstruction caused by benign prostatic hyperplasia or a urethral stricture.

Stones retrieved from first-time formers and recurrent stones should be analysed. Repeat stone analysis is required when the patient is under pharmacological prevention, when there is early recurrence after intervention with complete stone clearance, and when there is late recurrence after a prolonged stone-free period.

The European Association of Urology guidelines recommend general preventive measures that can be adopted by all stone formers regardless of their individual risk factors. These modifications focus on encouraging fluid intake, altering dietary habits and changing lifestyle. Patients at high risk of recurrence may need specific prophylaxis, which is usually pharmacological management based on stone analysis.

Changing the lifestyle with focus on a balanced diet and exercise is essential, as a raised body mass index, diabetes mellitus and hypertension add to the risk of stone formation. Increasing fluid intake reduces the risk of stone formation.

The effect of fruit juices is mainly determined by the presence of citrate or bicarbonate. Maintaining a balanced diet with contributions from all food groups and without any excesses is essential. The fibre content in fruits and vegetables is beneficial and this should be encouraged, but a vegetarian diet may increase the urinary pH due to the alkaline content. Intake of oxalate-rich products should be avoided to prevent high oxalate excretion.
Patients with calcium oxalate stones are advised to avoid excessive intake of vitamin C as it is a precursor of oxalate. The excessive consumption of animal protein may favour stone formation by causing low urine pH, hypocitraturia, hyperoxaluria and hyperuricosuria.

The daily sodium intake should be within 3–5g. Excessive intake alters the urine composition and results in increased calcium excretion by reduced tubular reabsorption, bicarbonate loss leads to reduced citrate content in the urine, with a potential risk of sodium urate crystal formation. Recent evidence confirmed an inverse relationship between dietary calcium and stone formation. The daily calcium requirement is 1–1.2g/day. Restriction of animal protein and sodium may reduce the risk of calcium stone formation. The only condition where calcium supplements are recommended is in enteric hyperoxaluria, as the additional calcium is taken with meals to bind intestinal oxalate.

Pharmacological prevention of stone formation
In patients who are at high risk of developing recurrence, pharmacological treatment is necessary. This treatment is guided by urine chemistry. In patients with hypercalciuria, thiazide diuretics may reduce calcium excretion by 50 per cent.

In hypocitraturia, potassium citrate is indicated and used as a urine alkalinising agent. The addition of amiloride may increase citrate excretion. The use of agents such as citrate or bicarbonate to alkalinise the urine increases the solubility of uric acid, cystine and calcium oxalate stones. The doses are titrated to reach an ideal urine pH of 7. Higher pH may lead to the formation of calcium phosphate stones, particularly in the presence of hypercalciuria.

An elevated level of uric acid in the urine or hyperuricosuria is suspected to increase the possibility of calcium oxalate stone formation. One third of patients with calcium oxalate stones have elevated levels of uric acid in the urine. Lowering the level of uric acid would benefit this group of patients. Treatment with allopurinol, which is a xanthine oxidoreductase inhibitor, has been shown to reduce the rate of stone recurrence. A newer medication of the same xanthine oxidoreductase group, febuxostat, is effective in reducing the serum urate levels, especially in patients with hyperuricemic gout.

In patients with enteric hyperoxaluria, patients are encouraged to increase their fluid intake, restrict dietary oxalate and increase calcium intake. In patients with a short bowel, the increase in water intake may lead to diarrhoea without improving urine dilution. A solution containing glucose and electrolytes may have a better effect than plain water. Staghorn calculi caused by struvite stones are associated...
KIDNEY DISEASE

BOX 4. Specific measures to prevent stone disease

- Small urine volume
  - increase fluid intake
  - urine volume >2.5 litres/day
- High sodium excretion
  - restrict salt intake
- Hyperoxaluria
  - restrict oxalate intake
- Urea level indicates high animal protein intake
  - balanced consumption of animal protein
- Hypocitraturia leads to reduced solubility of calcium salts
  - increase fruit and vegetable intake
  - citrate supplementation
- Hypercalciuria
  - restrict dietary salt and sugar
  - thiazide +/- amiloride
- Low urine pH leads to reduced solubility of calcium oxalate, uric acid and cystine
  - alkalinisation of the urine with citrate or bicarbonate (avoid in calcium phosphate stones)

with urinary tract infections and are formed in alkaline urine. This condition is managed by sending the urine for culture and sensitivity, stone clearance, analysis and antibiotics.

CONCLUSION

Kidney stone disease is a multifactorial and complex disorder that causes a large degree of pain and discomfort to patients. Most patients are young and in the working age group. This poses an economic burden on the individual and the healthcare system. The adequate management of stone disease requires vigilant and comprehensive assessment and planning, as a small obstructing stone can be life-threatening if it is obstructing and causing sepsis.

Endourological management of stones and medical assessment and advice to the patient is usually undertaken in specialist centres. However, it is the responsibility of every healthcare professional to advise patients to drink plenty of fluids, adopt a healthy lifestyle, reduce their risk of obesity and control diabetes and blood pressure, as these factors have the greatest impact on prevention.

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REFERENCES