BAPEN
Putting patients at the centre of good nutritional care

Managing Kidney Stones and Nephrocalcinosis in Patients with a Short Bowel

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Patients with a short bowel are at increased risk of uric acid and calcium oxalate stones, and also of progressive kidney damage caused by asymptomatic nephrocalcinosis. These complications are both preventable and treatable. Most of our understanding of the topic is based on case reports.

Key points

1. Uric acid kidney stones do not show on a plain abdominal radiograph (radiolucent) while calcium oxalate ones do (radio-opaque). Both types of stone may present with renal colic, recurrent pyelonephritis, or reduced renal function with hydronephrosis.
2. Uric acid stones form in acidic concentrated urine, typically in patients with a small bowel stoma (jejunostomy or ileostomy).
3. Treatment of uric acid stones with alkali and increased rehydration solutions (oral or intravenous) to increase urine output can result in complete dissolution of existing stones and prevent recurrence.
4. 'Enteric Hyperoxaluria' describes a high urinary excretion of oxalate that results in patients after an ileal resection/bypass (includes short bowel – jejunum in continuity with a functioning colon – who have about a 25% incidence of calcium oxalate renal stones) or ileal disease (e.g. coeliac disease or intestinal lymphangiectasia).
5. The causes of enteric hyperoxaluria include bile salt malabsorption, fat malabsorption, increased dietary oxalate, reduced calcium intake and treatment with high-dose phosphate supplements.
6. Enteric hyperoxaluria increases the risk of discrete calcium oxalate renal stones.
7. Enteric hyperoxaluria can also cause nephrocalcinosis – calcium oxalate deposition in the kidney parenchyma – without renal stone formation. This can cause a progressive deterioration of renal function without pain and without abnormalities on urine dipstick testing.
8. Treatment of enteric hyperoxaluria currently requires restriction of dietary oxalate and 'oxalate binder' therapy, plus citrate supplementation if hypocitraturic.
9. Calcium intake must not be restricted as this increases the risk of renal stones and a supplement may be helpful.
10. Therapy with oxalate-degrading enzymes and biotherapy with oxalate-degrading bacteria may prove to be effective in the future.

Explanations

1. Formation of renal stones occurs when the urine is supersaturated with the relevant chemicals (uric acid or calcium oxalate) and is more likely when existing crystals initiate crystal formation (nucleation) and when low urine flow or urinary stasis permits adherence of the crystal to the uroepithelium. Renal stones can grow in situ and, on occasions, grow to fill the entire collecting system ('staghorn calculi'). Renal stones cause renal colic when they become stuck in the ureter. CT urography without contrast is the most common first-line investigation for renal colic. Renal stones can also increase the risk of upper urinary tract infection, which may be refractory to treatment unless the stones are removed. Obstruction by renal stones can also cause an acute kidney injury, which is reversible if the stones are removed or, if the obstruction persists, a degree of chronic kidney disease may persist.

2. Uric acid, derived from purine metabolism, is highly soluble in alkaline urine, but highly insoluble in acidic urine, so urine pH is the major determinant of uric acid stone formation. Patients who lose much bicarbonate from a small bowel stoma form very acidic urine, and if their fluid losses are also high, form very concentrated urine, which further increases uric acid supersaturation.

3. Patients with uric acid stones should be offered treatment with alkali supplements (potassium citrate or sodium bicarbonate) often as an oral rehydration solution, and antimotility medication (e.g. loperamide) to reduce stomal output. Dietary purine restriction and allopurinol are pointless if the urine remains acidic and unnecessary if dilute, neutral pH urine can be achieved. Therapy can be monitored using urine pH dipsticks at home.

4. Oxalate is absorbed by transporters in the colonic lumen. Its bioavailability is highly dependent on luminal calcium concentration (usually calcium and oxalate form an insoluble complex): bile salt malabsorption results in bile acids binding calcium and thus increasing oxalate bioavailability. Bile salts can also increase colonic permeability to oxalate. An altered colonic microbiome – in particular, absence of oxalate-degrading bacteria such as Oxalobacter formigenes – can contribute to calcium oxalate stone formation.

5. Any disorder that increases the concentration of bile salts or reduces luminal calcium excretion can cause enteric hyperoxaluria. Lipid malabsorption can result in calcium binding to free fatty acids, so more free oxalate is available in the lumen to be absorbed. Lipid malabsorption from causes other than ileal disease/resection/bypass also give rise to enteric hyperoxaluria (e.g. chronic pancreatitis or Orlistat® therapy). In addition, two inhibitors of calcium oxalate crystallisation – magnesium and citrate – may be reduced.

6. Biochemical investigation of patients with suspected enteric hyperoxaluria requires measurement of oxalate, calcium, magnesium, creatinine, and citrate from 24-hour urine collections. Measurement of creatinine on serial samples allows assessment of the completeness of urine collections – 24-hour creatinine excretion remains constant within individuals so long as their muscle mass remains stable.

7. It is not clear why enteric hyperoxaluria causes kidney stones in some patients but nephrocalcinosis in others. Nephrocalcinosis does not necessarily show up on X-ray, CT or ultrasound, and does not cause haematuria or proteinuria. Most cases are diagnosed by renal biopsy, which should be actively if there is an unexplained progressive fall in eGFR. Early diagnosis is essential to allow treatment to prevent progression to end-stage renal failure (chronic kidney disease stage 5).

8. Restriction of dietary oxalate intake is the recommended and logical treatment for enteric hyperoxaluria, but is complicated by the fact that many foods of vegetable origin contain high or moderate amounts of oxalate. Avoidance of the classic very-high-oxalate foods (e.g. rhubarb, spinach and beetroot) is not enough, those foods/drinks with a moderate oxalate content (e.g. tea), but consumed in a moderate/large amount, need also to be restricted. Specialist dietetic input is important. An oxalate binder is something that chemically binds oxalate in the gut lumen (e.g. calcium salts, lanthanum, sevelamer, and some bile acid sequestrants). Commonly used are calcium supplements taken with meals or bile acid sequestrants (e.g. cholestyramine), if tolerated.

9. It may seem illogical to give calcium supplements to patients whose stones are made of a calcium salt; however, changes in dietary calcium have major effects on oxalate absorption but minor, if any, effects on urinary calcium excretion.

10. Trials with oxalate-degrading enzymes in formulations designed to reach the colon have shown some reduction in oxalate excretion, but up to 10 capsules per day were required. If a formulation can be designed that is well tolerated and results in complete degradation of oxalate in the gut lumen (to carbon dioxide), then this would transform treatment of enteric hyperoxaluria.

Suggested reading:

- Coe FL. (1983). Uric acid and calcium oxalate nephrolithiasis. Kidney Int.; 24(3): 392-403.
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- Lumlertgul N, *et al.* (2018). Secondary Oxalate Nephropathy: A Systematic Review. Kidney Int Rep.; 3(6): 1363-1372.
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