Moans, Groans and Kidney Stones!

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Kidney stones once thought to be a problem seen mainly in adults, is becoming increasingly prevalent in children. In 2007, Vandervoort K reported a 5-fold increase in the incidence of pediatric urolithiasis in the past decade. Hospital records show a 1 in 1,000 to 1 in 7,600 hospital discharges, a rate that is 2-4% that of adults. This is largely thought to be the result of changing lifestyles and dietary habits of children.

Symptoms:

In young children the symptoms are largely non-specific with irritability and excessive crying, fever, nausea and vomiting. Some children can present with hematuria, mostly painful and older children and adolescents can present with the typical pain starting from the flank and radiating to the groin, with hematuria. About 30% of children can present with a concomitant urinary tract infection.

Etiology and Pathogenesis:

Although many inherited diseases such as hyperoxaluria and cystinuria (both autosomal recessive) are associated with kidney stones, most stones in children are idiopathic.

Urine is a delicate balance between the solvent (liquid) and the solute (solids). If the concentration of the solute exceeds that of the solvent, it promotes crystallization and the formation of stones. The term supersaturation is used to describe the pathogenesis of stone formation. Supersaturation is the ratio of the urinary calcium oxalate or calcium phosphate concentration to its solubility. At levels of supersaturation below 1, crystals
dissolve and no stones are formed. However at levels above 1, crystals grow, promoting stone formation.

Stones develop because of an imbalance between the inhibitors and promoters of stone formation. In general, factors such as adequate fluid intake, pH (mostly alkaline), citrate, magnesium and a normal renal anatomy, inhibit stone formation. There are a few endogenous inhibitors in the urine: Nephrocalcin is one such inhibitor of stone formation, which is generally absent in the urine of children who have kidney stones. The promoters of stone formation include dehydration, hypercalcemia, loop diuretics, high salt intake, high protein intake, high phosphorus intake, hypercalciuria, hyperoxaluria, cystinuria, hyperuricemia, urinary tract infections, abnormal renal anatomy and certain medications.

In recent years a number of articles have emerged on the lithogenic potential of dietary protein. Animal proteins are high in sulfur-containing amino acids cysteine and methionine. Oxidation of sulfur to sulphate generates an acid load that aggravates calcium mobilization from bones. High purine content in animal protein increases uric acid burden. Urinary oxalate levels increase with high protein intake as well.

High salt intake predisposes to stone formation as it causes hypercalciuria. Sodium and calcium are excreted in parallel in the proximal tubule and therefore excretion of a high sodium load results in hypercalciuria.

More than 80% of stones in children are made up of calcium (either calcium oxalate or calcium phosphate). About 7% stones are uric acid stones, 12% struvite (formed as a result of infection mostly in children with an abnormal urinary anatomy) and 1% of stones are cystine stones.

10-15% of oxalate is from dietary sources and the rest is the end product of metabolism that involves glycolate and ascorbic acid. Oxalate is primarily excreted in the kidneys. Increased oxalate excretion may be caused by metabolic errors (primary hyperoxaluria) or by increased oxalate absorption as seen in GI disorders such as IBD, pancreatitis or small bowel resection or excessive intake of oxalate precursors (eg. Vitamin C). Poisoning by ethylene glycol (anti-freeze) also results in oxalate stones.

Cystinuria is a defect in the transport of cysteine by the intestinal mucosa and proximal renal tubular epithelium. Urinary pH <7.0 reduces cystine solubility and favors crystallization. Urine turns purple in the presence of cyanide nitroprusside. These stones are opaque because of their sulphur content. This disorder is very different from cystinosis which is a systemic disorder and does not result in stones.

Infectious, or struvite stones are an unusual type of stone that develops following change in the urinary composition caused by the urease-producing bacteria that
catalyze the breakdown of urea into ammonium. The very alkaline urine with very high concentrations of ammonium form Magnesium-ammonium-phosphate (struvite) stones. These stones typically form staghorn calculi that fill the entire collecting system.

Medications that are implicated in stone formation are loop diuretics (furosemide), protease inhibitors notably indinavir, sulphamethoxazole, acetazolamide and topiramide.

Melamine is a food additive added to give a false appearance of higher protein content in food quality tests. 1% of children exposed to milk contaminated with melamine were found to have nephrolithiasis diagnosed by ultrasound. None of the children were symptomatic. All patients responded to conservative management of fluids and alkalinization of urine.

**Evaluation:**

At the initial visit it is very important to ask for history of gross hematuria, any pain, malabsorption, recurrent UTIs, diet and family history. Physical exam should include assessment of growth, evidence of spina bifida and any metabolic disease. An initial set of laboratory tests should include electrolytes, BUN, creatinine, uric acid, calcium, phosphorus and a complete urine analysis. A spot urine calcium and urine creatinine ratio may also be useful to detect hypercalciuria (normal <0.2). Other ratios can be obtained based on degree of suspicion. Normative values for children can be found in Gillespie R.S et al. *Pediatrics in Review* 2004 25: 131-139

An astute physician can do a urine microscopy in the office setting. Calcium oxalate crystals are either enveloped shaped (calcium oxalate dihydrate) or dumbbell shaped (calcium oxalate monohydrate), calcium phosphate crystals are described as coffin-shaped and cystine crystals are hexagonal.

After the initial visit, it is important to order 24 hour urine collections on a regular diet for a comprehensive assessment of stone risk that include calcium, oxalate, citrate, uric acid, creatinine, sodium, phosphate, pH and volume (www.litholink.com or www.questdiagnostics.com)

We also advice all patients to bring in the 3 day food diary to make an overall assessment of their protein, sodium, calcium and phosphorus intake and to check if there are any glaring dietary excesses.

If the stone can be obtained a stone analysis is very useful.
Imaging:

A KUB can detect radiopaque stones and up to 60% of stones are radiopaque. In general calcium phosphate stones have the greatest density followed by calcium oxalate and triple phosphate. Uric acid stones are entirely radiolucent.

A renal ultrasound is the most common modality especially if patient is asymptomatic. Stones are hyperechoic and show evidence of ‘shadowing’. Ultrasound has the advantage of no ionizing radiation and can detect large stones and urinary tract obstruction easily. However small stones and ureteral stones are poorly visualized.

CT Urogram is a non-contrast spiral CT of the kidney-ureter-bladder. This is the standard of care for symptomatic patients as it detects most stones of significant size. It can also provide information about the stone’s composition by giving the density. It is associated with significant radiation but much less so than a CT abdomen.

Certain low density stones ie uric acid and crystals from indinavir are difficult to visualize by any modality.

Management:

There are 3 important aspects to managing a patient with kidney stones: Dietary, Medical and surgical

Dietary: A review of food diary is performed and the management guidelines are given. Fluid intake is increased to about 2 liters per day or to obtain a urine output of 35cc/kg/day. Increase in intake of citrate rich fluids is advised and this includes orange juice and sugar-free lemonade. Recommended dietary allowance for calcium and protein is advised and children are not restricted on calcium or protein. However advice on limiting intake of red meat to 1-2 times/week is given. Sodium intake should be limited to less than 2-2.5gms/day. Children are taught and encouraged to read labels. Processed foods must be avoided. Recommendations for limiting consumption of foods containing high amounts of oxalate ie spinach, strawberries, nuts, cocoa and brewed tea, is advised.

Medical: The goal of medical management is to increase the solubility of the offending agent either by changing urine pH and/or by having it bind to another agent that increases solubility. Increase fluid intake increases urinary volume and dilutes stone forming compounds making them less likely to precipitate. Most stones benefit from urinary alkalinization with either citrate, bicarbonate or acetazolamide. The only stone that does not require alkalinization is triple phosphate stone.
**Surgical:** in general stones <5mm pass spontaneously in children and do not require surgical management. Stones greater than 5mm may require either ureteroscopy in conjunction with holmium laser lithotripsy and stone basketing or ESWL. Percutaneous nephrolithotomy is reserved for patients with large stone burden and lower pole stones. This procedure is more invasive with potential for parenchymal injury and high rate of bleeding and longer duration of hospital stay.

**Conclusion:**

Overall the incidence of renal stones in children is increasing. Most stones tend to be calcium oxalate or phosphate. It is very important to determine the metabolic abnormalities causing the stone by performing a 24 hour urine collection when possible to assess the stone risk profile. The major metabolic abnormalities are hypercalciuria, hypocitraturia and hyperoxaluria.

Since the risk of recurrence of stones is as high as 40%, preventing recurrence by addressing factors causing the stone are of paramount importance. An excellent team of nephrologists, urologist and dieticians is needed to diagnose, evaluate and manage children with kidney stones. At Cedars Sinai Medical Center, Pediatric Nephrology and Pediatric Urology maintain a joint clinic once a month where children with renal stones can be seen by the team that includes specially trained renal dietitians.

For questions regarding kidney stones or any pediatric nephrology issues please email me at Dechu.puliyanda@cshs.org.

**References:**


