

Managing Calcium Oxalate Urolithiasis in Cats

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Prior to 1986, calcium oxalate disease was considered to be rare in cats. Since that time, the incidence has increased from 2 % in 1984 to almost 50% in 1999. This increase has been linked, although not clearly defined, with the consumption of magnesium restricted acidifying diets. Approximately 90% are found in the bladder. The remaining are found in the kidney and ureters. The mean age at diagnosis is 7.36 years. Males (57%) are more commonly affected than females (43%). The Burmese, Himalayan, and Persian breeds have an increased risk of developing calcium oxalate disease.

Urinary crystals form when the urine is supersaturated with respect to a specific mineral or mineral compound. Precipitation is a result of increasing supersaturation. The initial phase, or nucleation, of urolith formation involves the formation of a crystal nidus. This phase is dependent on supersaturation of urine with calcuogenic crystalloids. Factors that influence crystal formation include the extent of renal excretion of the crystalloid, the urine pH, urine temperature, the presence or absence of various inhibitory factors (e.g., citrate, pyrophosphate), and the presence of promoters of crystallization (e.g., dead cells, cellular debris, protein, bacteria or other crystals). Crystal growth depends on the ability of the nidus to remain within the urinary tract, the duration of supersaturation of the urine and the physical ultrastructure of the crystal. The actual rate of growth of the urolith depends on numerous factors including mineral composition and risk factors such as infection.

Risk factors that have been associated with calcium oxalate urolithiasis include hypercalciuria, hyperoxaluria, hypocitraturia, hypomagnesemia, acidosis, decreased macromolecular inhibitors, and urine volume. Increased urinary calcium excretion may result from increased intestinal absorption of calcium (excess dietary calcium, excess vitamin D, hypophosphatemia), decreased renal tubular reabsorption (furosemide and corticosteroids), or increased mobilization of calcium from body stores (acidosis, hyperparathyroidism, hyperthyroidism, excessive vitamin D). Diets high in animal protein have been associated with acidosis, increased urinary calcium and oxalate excretion, and decreased urinary citric acid excretion. Metabolic acidosis promotes skeletal mobilization of calcium and inhibits renal tubular reabsorption of calcium. Hypophosphatemia will stimulate the production of vitamin D and augment intestinal calcium absorption and urinary excretion of calcium. Excessive dietary oxalate (e.g., asparagus, broccoli, spinach, sardines, beet pulp, rice cakes) will increase the renal clearance of oxalate and risk of urolithiasis in humans, however, these are not typically ingredients utilized by the pet food industry. In humans, calcium oxalate stones have also been associated with excessive consumption of vitamin C. Vitamin C is metabolized to oxalic acid and excreted in urine. Pyridoxine increases the transamination of glyoxylate, to glycine. Therefore, pyridoxine deficiency increases the endogenous production and subsequent excretion of oxalate. Urinary citrate deficiency has been suggested to increase the risk of calcium oxalate in humans by increasing the availability of calcium ions to bind with oxalate. Citrate deficiency may be an inherited defect or arise secondary to acidosis, which promotes the renal tubular utilization of citrate. Recent research in dogs indicates that citrate supplementation does not alter the risk of calcium oxalate in dogs. Intravascular volume depletion and concentration of urine volume increases the risk of urine supersaturation with calcium and oxalate.

A tentative diagnosis of urolithiasis is made based upon the history, clinical signs, and physical findings. Initial signs suggestive of calcium oxalate urolithiasis include hematuria, pollakiuria, stranguria, dysuria, inappropriate urination (bathtubs, sinks, carpet etc), and urge incontinence. The cat often appears restless which may indicate discomfort. Partial or complete ureteral or urethral obstruction may occur suddenly or over a period



of weeks. Complete obstruction is characterized by depression, anorexia, lethargy, dehydration, hypothermia, and vomiting. In severe cases, the bladder or ureter may rupture providing a transient relief of signs followed rapidly by the development of uroabdomen and death.

The bladder should be palpated to evaluate its size (degree of distension), shape, contours, thickness of the bladder wall, pain, and masses or grating with the bladder lumen. Rarely in the cat is it possible to palpate cystic calculi because they are usually small.

The initial diagnostic evaluation should include a urinalysis with sediment examination, urine culture, and abdominal imaging. A CBC and biochemical profile should be obtained from cats that are sick or have urethral obstruction. The urine sample should be collected into a sterile collection container and refrigerated immediately unless analysis can be conducted within fifteen minutes. Abnormalities consistent with calcium oxalate urolithiasis include hematuria, proteinuria, pyuria, and crystalluria. The identification of crystals in the urine is dependent on the urine pH, temperature, and specific gravity. Absolutely fresh urine must be examined as crystals may form in urine that is allowed to stand and cool prior to examination (in-vitro crystallization).

Diagnostic imaging techniques include survey radiographs, ultrasound, contrast radiography, computed tomography (CT), and magnetic resonance imaging (MRI). Each of these studies has different capabilities and limitations, and often produce findings that are complementary. Confirmation of urolith location, number, density and shape requires plain abdominal radiography. Most uroliths greater than 3 mm in size can be visualized on plain abdominal radiographs. Ultrasound allows assessment of intra-luminal abnormalities not seen on survey radiographs, and is particularly useful for identifying partial or complete ureteral obstruction. Excretory urography can be utilized to try to identify a partial or complete ureteral obstruction. Using ultrasound guidance to inject contrast agent directly into the renal pelvis can facilitate the procedure. Double contrast cystography is used to evaluate the mucosal surface of the bladder and luminal contents. Contrast urethrocytography can detect uroliths greater than 1 mm in size. CT and MRI are advanced imaging techniques that provide the advantage of superb imaging capabilities however; they are expensive and have limited availability.

Determination of the mineral type can only be achieved by mineral analysis of the specimen. Uroliths need to be submitted in a clean dry container *without* preservatives or fluids. Specimens can be obtained by using aquarium fishing net to catch uroliths while the cat is voiding, by using a transurethral catheter, by voiding urohydropropulsion, or via surgery.

The only effective treatment for calcium oxalate disease is surgical removal of the uroliths. Surgery to remove calculi from the bladder or urethra is a straightforward procedure with which most veterinarians are familiar. However, controversy exists as how to most effectively manage ureterolithiasis. A recent abstract reported that 92% of cats with ureterolithiasis were azotemic at the time of presentation, 67% of cats had multiple uroliths, and 63% were affected bilaterally. Many authors have recommended unilateral nephrectomy to remove the obstructed ureter, however, the high probability of bilateral involvement, concurrent renal insufficiency and likelihood of reoccurrence, limit nephrectomy as a surgical option. Ureterotomy may be indicated for those cats with progressive hydronephrosis and an identifiable ureterolith. Post-operative complications include uroabdomen and ureteral stricture. Alternatively, partially obstructing uroliths can be managed conservatively. The ureterolith will pass into the bladder in 30% of cats managed conservatively.

Lithotripsy involves the use of externally applied sound waves, direct laser light vaporization or an electric spark to crumble the urolith. Although commonly used in human medicine, lithotripsy has not been established as a routine procedure in the cat.

Most calcium oxalate uroliths will reoccur. Therefore, prevention of recurrence is an important aspect of the medical plan. The risk of developing urolithiasis can be evaluated by the relative supersaturation (RSS) methodology (the activity product of a urolith for a given sample of urine divided by the known thermodynamic

solubility product for that urolith). This technique was first applied to humans in the late 1960s, and it now considered the gold standard technique for urine evaluation in human patients. This methodology has since been developed and validated for use in cat and dog urine. RSS requires a complete 48-hour urine collection. The urine is analyzed for the concentration of 12 urinary constituents, as well as urine pH and USG. Together, this information is evaluated by computer analysis to determine the possible interaction that can occur between the ions in urine. The end result is a value that can be used to predict whether specific uroliths are likely to develop, grow or dissolve. This methodology is then applied to evaluate the effect of any given nutrient of diet on the risk of forming calcium oxalate stones. If the RSS value for calcium oxalate is between 1 and 12, the urine is considered to be metastable, and new calcium oxalate stones are unlikely to form, although pre-existing calcium oxalate stones may grow.

Nutritional recommendations include a diet that is high in moisture with reduced quantities of protein, calcium, oxalate, vitamin C, and vitamin D. The diet should not be restricted in phosphate, magnesium, or pyridoxine, and should produce a urine with an RSS value < 12. In addition, the diet should not predispose the patient to the development of struvite urolithiasis. Excessive dietary calcium and dietary oxalate should be avoided. However, absolute restriction of dietary calcium should be avoided unless intestinal hyperabsorption of calcium is documented. In addition, a reduction in dietary calcium should be accompanied with a concurrent reduction in oxalate, as reducing consumption of only one of these constituents will increase the availability of the other constituent for intestinal absorption. Traditionally, excessive dietary sodium has been associated with increased urinary excretion of calcium. However, recent evidence suggests that the effect of sodium on increasing calcium excretion may be countered by the positive effect that excess sodium has on urine dilution and volume. Therefore, a moderate dietary intake of sodium is recommended. Magnesium has been reported to be an inhibitor of calcium oxalate crystallization in humans, and there have been concerns that the severely magnesium restricted diets utilized to prevent struvite urolithiasis may have increased the risk of cats developing calcium oxalate stones. Therefore, the diet of the cat with calcium oxalate should contain an adequate, but not excessive concentration of dietary magnesium. Urinary citrate was considered to be an important inhibitor of calcium oxalate crystallization, however, research in dogs has shown that oral supplementation with potassium citrate fails to reduce the risk of calcium oxalate formation, and indeed, may actually increase the risk of struvite formation. It was initially reported that calcium oxalate stones form in acidic urine, and hence an alkaline urine was suggested to minimize reoccurrence. However, research suggests that calcium oxalate stones can actually form in urine ranging from a pH of 4.8 to 7.4. Therefore, urine pH manipulation alone cannot reliably prevent calcium oxalate reoccurrence. In addition, alkaline urine may increase the risk of struvite urolithiasis. Studies have also shown that the ideal urine pH range in cats for managing both calcium oxalate and struvite urolithiasis is actually 6.0-6.5. Hydrochlorothiazide has been recommended in dogs and humans to reduce renal calcium excretion. However, there have not been any studies to evaluate the effect of hydrochlorothiazide on urinary calcium excretion in the cat.

REFERENCES

1. Adin CA, Gregory CR, Kyles AE et al. Diagnosis and treatment of ureterolithiasis in cats. Abstract; UC Davis Urological Colloquium May 4-6, 2000.
2. Lekcharoensuk C, Osborne CA, Lulich JP et al. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2001;219:1228-1237
3. Smith BHE, Stevenson AE, Markwell PJ. Urinary relative supersaturations of calcium oxalate and struvite in cats are influenced by diet. *J Nutr* 1998;128:2763S-2764S