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Topical Review

Use of Purina Pro Plan Veterinary Diet UR Urinary St/Ox to Dissolve Struvite Cystoliths

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The objective of this study was to determine the efficacy of feeding the commercially available diet, Purina Pro Plan Veterinary Diets UR Urinary St/Ox, for the dissolution of struvite cystoliths in cats with naturally occurring disease. Twelve cats with clinical signs of lower urinary tract disease and cystoliths confirmed via radiographs were enrolled. The cats were fed the study diet ad libitum and assessed by abdominal radiographs weekly. Cats with cystoliths that resolved based on radiographs and confirmatory ultrasound examination were considered diet successes. Cats with no change in cystolith size after 2-6 weeks underwent cystotomy for stone removal, aerobic culture and antimicrobial susceptibility testing, and analysis. All cats accepted the study diet, and weight loss was not noted over the course of the study. Total cystolith dissolution was achieved by week 2 for 5 cats, which were presumed to have struvite cystoliths. All other cats underwent cystotomy for stone removal after radiographic evidence of cystoliths were still present at 2 weeks (1 cat with severe signs), 4 weeks (5 cats), or 6 weeks (1 cat). The cystoliths that were surgically removed were calcium oxalate (5 cats) and mixed (2 cats) and would not be expected to dissolve with this diet. Follow-up radiographs from 6 cats fed the diet long term (3 presumed struvite and 3 with other cystoliths removed surgically) were collected from 1 to 6 months after beginning the study and showed no evidence of cystolith recurrence.

While larger case numbers are needed, these results suggest that feeding Purina Pro Plan Veterinary Diets UR Urinary St/Ox can successfully dissolve cystoliths that are likely struvite and may lessen the risk of recurrence of struvite and calcium oxalate cystoliths.

Introduction

Feline lower urinary tract disease (FLUTD) includes a constellation of disorders including feline interstitial cystitis, cystolithiasis, urethral obstruction, and urethral plugs.[1,2] Cats with FLUTD present with signs of dysuria (difficult urination), hematuria, pollakiuria (increased frequency of urination), stranguria (straining), urethral obstruction, and/or periuria (inappropriate urination).[3] Cystolithiasis accounts for about 20% of the cases of FLUTD and may be treated by surgical removal of the cystoliths or by medical dissolution, depending on the type of stone.[4–6] Based on feline urolith submissions to the Minnesota Urolith Center, the most common cystoliths in order of frequency are struvite, calcium oxalate, urate containing stones, and mixed stones.[6,7]

Cystoliths form in urine environments where crystals precipitate out of solution and aggregate. There are a number of urine characteristics that influence cystolith formation that can be impacted by dietary manipulations. Most common include, urine volume, urine pH, and cystolith precursors.[4,6] Increasing water intake results in increased urine volume that encourages frequent urination and dilutes cystolith precursors within the bladder, all of which decrease the likelihood of crystal formation and aggregation.[4,8] Feeding canned food and increasing the dietary sodium chloride level are frequently employed methods to increase urine volume. Several studies have shown that increasing dietary sodium chloride in dry cat foods can increase water intake and urine volume, and decrease urine-specific gravity.[8–10] One study suggests that spot urine samples may not reflect the effect of high-sodium diets as accurately as 24-hour urine collection analysis.[10] Despite the success that has been reported with high-sodium diets, it has been suggested that high-sodium dry food diets are not a substitute for high-moisture foods ($>$ 75% moisture) when attempting to decrease urine concentration.[9]

Depending on the stone type, dietary manipulation of urine pH can have beneficial effects. The two most common radiodense cystoliths in cats are struvite and calcium oxalate.[7] Decreasing urine pH can aid in the dissolution of struvite cystoliths and lessen recurrence.[11] In contrast, while calcium oxalate stones cannot be dissolved by currently available diets, increasing urine pH and urine volume can be used to lessen recurrence.[9] Since these common cystoliths have dichotomous urine pH targets, it is also important to provide appropriate amounts of key mineral precursors such as magnesium, phosphorus, and calcium in the diet.[4]

At least 2 studies have documented the efficacy of commercially available low-magnesium, urine acidifying dry diets for the medical dissolution of struvite cystoliths.[11,12] In most cases, there was at least a 50% reduction in struvite stone size by 2 weeks and complete resolution by 4 weeks. Stones that did not dissolve with dietary therapy were removed surgically in both studies, and found to be ammonium urate, calcium oxalate, or calcium phosphate.[11,12]

In premarketing studies, the commercially available diet to be studied here (Purina Pro Plan Veterinary Diets UR Urinary St/Ox;

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Nestle Purina PetCare, St. Louis, MO) has been shown to maintain 24-hour urinary relative supersaturation for both struvite and calcium oxalate in the undersaturated and metastable ranges, respectively, which theoretically helps to minimize the risk of formation of these 2 types of cystoliths.[13] Feeding the test diet has also been shown to produce an average urine pH of 6.0-6.4, which is predicted to lessen struvite cystolithiasis, while not increasing the risk of calcium oxalate crystal formation.[14]

The primary objectives of this study were to use naturally affected cats to evaluate the clinical and laboratory findings associated with radiopaque cystoliths, determine the efficacy of feeding the test diet for the dissolution of suspected struvite cystoliths, and determine the rate of cystolith recurrence.

Materials and Methods

This study was approved by the Institutional Animal Care and Use Committee at Colorado State University (CSU). Local humane societies in north central Colorado were contacted to announce the study. Male or female, neutered or intact cats of any age were considered for entry into the study. Entry criteria included an episode of classic lower urinary tract signs (hematuria, dysuria, stranguria, pollakiuria, and/or periuria) recognized within the past 2 months, and/or radiographic evidence of cystolithiasis. Exclusion criteria included a history of being fed a diet formulated for the treatment of urinary tract disease within the last 3 weeks. Cats that qualified on clinical manifestations or radiographic evidence of radiopaque cystoliths, were transferred with permission to the Veterinary Teaching Hospital at CSU for performance of 2-view abdominal radiographs to determine if radiodense cystoliths without evidence of a nephrolith, ureterolith, or urethrolith were present. Cats that still qualified then had an abdominal ultrasound performed to evaluate the urinary system and to screen for abnormalities within the abdomen. A non-fasted, complete blood count and serum biochemical panel were performed. Urine was collected by cystocentesis for urinalysis and aerobic culture and antimicrobial susceptibility testing if possible; those that could not have urine collected by cystocentesis, had urinalysis alone performed on a voided urine sample. Cats were excluded from the study if they had evidence of radiolucent cystoliths, urine pH (measured via dipstick) less than 6.0 detected at the shelter, urinary masses, or other systemic diseases.

Experimental Design

The cats were housed in a gang room at the research study site to assure that only the test diet was fed and in an attempt to lessen stress. Water and the feline dry formulation of the test diet were offered ad libitum. Attitude, appetite, and clinical assessment was performed daily to evaluate for evidence of urinary obstruction. Cats with dysuria or stranguria had bladder palpation performed regularly, but as tolerated, to ensure they were not obstructed. Cats with aerobic urinary tract infections were retained in the study and administered appropriate antibiotics based on antimicrobial susceptibility testing. Body weight and abdominal radiographs for cystolith measurements were evaluated weekly. All cats assessed with significant discomfort, determined by a change in behavior or frequent episodes of stranguria and/or dysuria during their daily observations were administered buprenorphine (0.02 mg/kg, sublingual q 12 hours).

Cats with cystoliths that continued to decrease in size were radiographed until the cystoliths were not detectable for 2 sequential weeks. At that time, urinary system ultrasound was performed to corroborate complete resolution. These cats were defined as diet successes and were adopted, or returned to the shelter for adoption. Cystotomy was performed on cats with no change in cystolith size after 4 weeks, or if surgery was deemed medically necessary due to clinical signs. The cystoliths were analyzed for mineral content (University of Minnesota Cystolith Center, St. Paul, MN) and evaluated by aerobic culture and antimicrobial susceptibility testing. Those cats requiring a cystotomy were administered appropriate analgesia postoperatively, and when indicated, antibiotic therapy based on culture and antimicrobial susceptibility testing. Cats that refused the diet or lost $>15\%$ of their body weight over the course of the study were to be removed from the study and classified as "refused diet." Adoptive owners of each cat were offered the test diet and recheck radiographs and urinalyses at no charge.

Statistical Evaluation

The majority of the evaluations were descriptive. Cats with cystoliths that dissolved within 4 weeks were classified as "diet success" and dissolved cystoliths were presumed to be struvite. Cats with cystoliths analyzed as pure calcium oxalate or mixed cystoliths were classified as cystoliths not expected to dissolve on this test diet. Differences in age, urine pH, and urine-specific gravity for cats with presumed struvite calculi and those with calcium oxalate cystoliths were compared by Mann–Whitney test with significance defined as $P < .05$.

Results

A total of 4 neutered males and 8 spayed females were enrolled in the study (Table 1). The clinical history was available from the animal shelter for 10 of the 12 cats, with the most common clinical signs being hematuria (8 of 10 cats) and periuria (5 of 10 cats). The 12 cats ranged in age from 3 to 9 years of age with a median of 5 years (Table 1). All 12 cats were alert, had a body condition of 5 or greater, had a good appetite, and accepted the study diet. The most common clinical signs observed after the cats entered the study were hematuria, stranguria, pollakiuria, and periuria. The most common abdominal ultrasound findings on admission to the study were changes consistent with cystitis and chronic renal changes. One cat had hydronephrosis and hydroureter; this cat was bright, alert, and responsive, with no indication of obstruction or discomfort related to hydronephrosis and hydroureter, and so, was included in the study. Anaerobic and aerobic bacterial urine culture was performed on 9 cats on day 0 and were negative. Urine for culture could not be collected from 3 cats due to pollakiuria and insufficient bladder size; in these cases, the urinalysis performed on free catch urine showed no evidence of bacteriuria. The cat with hydronephrosis had urine collected for bacterial culture and antimicrobial susceptibility testing from the renal pelvis and urinary bladder and were negative for growth. One cat had perivulvar dermatitis, and was being administered amoxicillin-clavulanate on admission; this cat had the only complete blood cell count abnormalities of any of the cats, which included neutrophilia (19.6×10^9/L: normal range $= 4.0\text{-}14.0 \times 10^9$/L) and monocytosis ($2 \times 10^9$/L: normal range $= 0.0\text{-}0.8 \times 10^9$/L). Clinically significant biochemical panel abnormalities were not noted in any cat.

Overall, 42% (5 cats) were classified as diet successes and were classified as likely to have had struvite cystoliths. The cystoliths presumed to be struvite were resolved in 1 cat by week 1, and in the remaining 4 cats by week 2 (Table 1). Surgery was performed in the other 7 cats (58%) after feeding the diet