

FREQUENTLY ASKED QUESTION SERIES

Center for Companion Animal Studies

Updated May 15, 2013

Does intravesical infusion of glycosaminoglycans lessen the potential for repeat obstruction in male cats with suspected idiopathic cystitis?

Feline idiopathic cystitis (FIC) is a common condition affecting an estimated 250,000 to 500,000 cats in the United States each year (1). There have been many theories as to the cause of FIC in cats and it is likely the syndrome is multifactorial (2). Many cats develop hematuria and some develop urethral plugs that can result in urethral obstruction which is over-represented in males because of the narrow penile urethra (2,3). Urethral obstruction in cats can be life-threatening and expensive to manage, thus, avoiding repeated obstruction is desirable as euthanasia of these cats is often chosen by the owners (4). Repeat urethral obstruction rates in toms vary by the report and the cause of obstruction but were 36% and 58%, respectively, in two recent studies (4,5).

A defective glycosaminoglycan (GAG) layer lining the urinary bladder mucosa has been proposed as both a cause and effect of FIC in cats and people (2,6). Urothelial permeability increases with defects in surface GAGs which could lead to increased contact of urine to bladder wall tissues and result in induction of immune-mediated or neurogenic inflammation, mast cell activation, and sensory afferent nerve stimulation (2). Abnormalities in urinary system GAGs have been documented in cats with FIC (6-8). Exogenously administered GAGs adhere to damaged bladder uroepithelium and promising data exist for their use in experimental models and human interstitial cystitis, particularly when administered by intravesical infusion (9-12). Recently, a new formulation of GAGs for intravesical administration (A-CYST, Dechra Veterinary Products, Overland Park, KS) was introduced into the veterinary market in the United States and was shown to be safe when administered parenterally several times to normal research cats (13).

A pilot study was just completed at CSU and is currently in review for publication. In this study, the medical management for blocked toms was provided free of charge to the owners to encourage case recruitment. The primary care veterinarians and veterinary nurses at the Veterinary Teaching Hospital were provided the protocol and client consent forms that were approved by the Institutional Animal Care and Use Committee. The clinicians and veterinary nurses in the Critical Care Unit were asked to use standardized protocols as consistently as possible amongst patients. Protocols provided included those for pain scores, sedation (or anesthesia) for urinary catheter placement, sterile saline lavage to remove sediment from the bladder after the initial catheter placement, intravenous fluid therapy, buprenorphine analgesia, and for phenoxybenzamine administration. In addition, all cats were fed a canned urinary diet

when the appetite returned. Deviations from the suggested protocols were noted and ultimately the major difference in the management of the two groups of cats was whether or not intravesical GAG infusions (versus saline control) were performed.

Intravesical A-CYST infusion protocol

- Use scanning ultrasound to rule out stones and masses.
- Submit urine and blood samples.
- Relieve obstruction and place an indwelling urinary catheter.
- Lavage the bladder with body temperature sterile saline until clear.
- Instill 2.5 ml of A-CYST followed by 1 ml of sterile saline.
- Clamp the urinary catheter for one hour to ensure the retention of A-CYST.
- Palpate the bladder gently every 20 minutes to monitor for over-distension.
- Unclamp the catheter and continue closed system collection of urine.
- Repeat the infusion at 12 and 24 hours.
- Remove the urinary catheter at 36 hours.
- Observe for repeat obstruction by Day 7.

Outcomes assessed included urinalysis at day 0, 3, and 7, aerobic bacterial urine culture at day 0 and 7, daily standardized pain scoring while hospitalized and at recheck on days 3 and 7, and incidence of repeat urethral obstruction within the 7-day follow-up period. Repeat urethral obstruction occurred within the seven day observation period in three of seven placebo treated cats and none of the seven GAG infused cats. Owners of two of three cats with repeat obstruction allowed cross over into the GAG treatment group and repeated obstruction was not observed. When the two placebo treated cats that crossed over were included in the GAG infusion group, the overall repeat obstruction rates were three of seven (42.9%) placebo treated cats and 0 of nine (0%) GAG infused cats ($p = 0.06$). No adverse effects relating to A-CYST were observed.

The repeat obstruction rate of 42.9% in the placebo group was similar to the 58% repeat obstruction rate in the placebo group of a recent study assessing lidocaine and sodium bicarbonate delivered by intravesical infusion (5). However in contrast to the 0% repeat obstruction rate in the GAG infused cats described here, the repeat obstruction rate in the lidocaine and sodium bicarbonate infused cats in the other study was 57%. While the studies should not be directly compared, the information gathered in the study described here suggests that intravesical infusion of this product using this protocol may lessen the potential for repeat obstruction in males with urethral obstruction suspected to be related to FIC. A study with larger numbers of cats per group should be considered to further evaluate for a treatment effect associated with intravesical infusion of the GAG product. However, the results of this study suggest the use of A-CYST in this protocol was safe and potentially effective for lessening repeat urethral obstruction in the short term.

References:

1. Kalkstein TS, Kruger JM, Osborne CA. Feline idiopathic lower urinary tract disease: part I. Clinical manifestations. *Compend Contin Educ Pract Vet* 1999;21:15–26.
2. Kruger, JM, CA Osborne, and JP Lulich. Changing paradigms of feline idiopathic cystitis. *Vet Clin Small Anim* 2008;39:15.
3. Defauw PA, Van de Maele I, Duchateau L, Polis IE, Saunders JH, Daminet S. Risk factors and clinical presentation of cats with feline idiopathic cystitis. *J Feline Med Surg.* 2011;13:967-975.

4. Gerber B, Eichenberger S, Reusch CE. Guarded long-term prognosis in male cats with urethral obstruction. *J Feline Med Surg.* 2008;10:16-23.
5. Zezza L, Reusch CE, Gerber B. Intravesical application of lidocaine and sodium bicarbonate in the treatment of obstructive idiopathic lower urinary tract disease in cats. *J Vet Intern Med.* 2012;26:526-531.
6. Pereira DA, Aguiar JA, Hagiwara MK, Michelacci YM. Changes in cat urinary glycosaminoglycans with age and in feline urologic syndrome. *Biochim Biophys Acta.* 2004 ;1672:1-11.
7. Press SM, Moldwin R, Kushner L, et al. Decreased expression of GP-51 glycosaminoglycan in cats afflicted with feline interstitial cystitis. *J Urol* 1995;153 (Suppl 4):288A.
8. Westropp JL, Kass PH, Buffington CAT. Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res* 2006;67:731-6.
9. Bassi PF, Costantini E, Foley S, Palea S. Glycosaminoglycan therapy for bladder diseases: emerging new treatments. *European Urology Supplements.* 2011;10:451-455.
10. Nickel, JC, et al. A real-life multicentre clinical practice study to evaluate the efficacy and safety of intravesical chondroitin sulphate for the treatment of interstitial cystitis. *BJUI* 2008;103:56.
11. Nickel JC, Egerdie RB, Steinhoff G, Palmer B, Hanno P. A multicenter, randomized, double-blind, parallel group pilot evaluation of the efficacy and safety of intravesical sodium chondroitin sulfate versus vehicle control in patients with interstitial cystitis/painful bladder syndrome. *Urology.* 2010;76:804-809.
12. Nordling, J and A van Ophoven. Intravesical glycosaminoglycan replenishment with chondroitin sulphate in chronic forms of cystitis. *Drug Research* 2008;58:328.
13. Veir JK, Webb CB, Lappin MR. Systemic effects of a commercial preparation of chondroitin sulfate, hyaluronic acid and N acetyl-D-glucosamine when administered parenteral to healthy cats. *Int J Applied Vet Res* In press, 2013.