Small Ruminant Research 127 (2015) 97–101

Contents lists available at ScienceDirect

Small Ruminant Research

journal homepage: www.elsevier.com/locate/smallrumres

Technical Note

Development of a zinc implant-based model for urolithiasis in goats

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ARTICLE INFO

Article history:
Received 14 January 2015
Received in revised form 17 April 2015
Accepted 22 April 2015
Available online 2 May 2015

Keywords:
Goat
Urolithiasis
Calculogenesis
Experimental model

ABSTRACT

Urolithiasis is an important disease of small ruminants and research efforts are often directed at prevention of disease using dietary modification. Studying urolithiasis for the comparison of urolith incidence across dietary treatments is challenging due to the sporadic development of naturally-occurring disease in populations and the difficulty in detection of subclinical stone formation. Ten, 1-year old Boer-cross nonpregnant doelings were fed a calculogenic diet. Four experiments were performed utilizing zinc discs of various sizes placed within the lumen of the urinary bladder. Undetected implant loss occurred in 25–50% of animals implanted with discs greater than 13 mm. One hundred percent of retained washers accumulated calculus material. The addition of suture material to the discs increased average disc weight gain from a mean of 0.03–1.9 mg/day to 1.5–46 mg/day across experiments. Analysis of calculus obtained revealed all stone material to be primarily composed of struvite, amorphous magnesium calcium phosphate or newberyite. This model may serve as the basis for experimental studies in females to provide candidate preventative strategies that can later be validated using clinical trials in large populations of at risk males.

1. Introduction

Urolithiasis is considered to be the most economically significant urinary tract disease of food and fiber animals, affecting intact and castrated male ruminants, swine and camelids. Urolithiasis is a common disease of animals fed high grain rations with low calcium to phosphorus ratios, with the most common stone compositions in this setting being struvite (magnesium ammonium phosphate) and apatite (calcium phosphate). Although medical and surgical treatments may be associated with positive short- and long-term outcomes (Ewoldt et al., 2006), they often carry a high cost and may result in the animal not being used for the intended purpose.

Prevention is an important strategy in managing this disease. One primary approach of preventing stone formation is achieving urinary acidification which reduces the likelihood of crystal formation in the bladder. Several investigators from different laboratories have recently published papers investigating dietary modification as a means of achieving urinary acidification (Stratton-Phelps and House, 2004; Jones et al., 2009; Grissett et al., 2012; Sprake et al., 2012), but none of these groups has directly measured the role of these interventions on the formation

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http://dx.doi.org/10.1016/j.smallrumres.2015.04.012
0921-4488/

or dissolution of stones or stone components. Major challenges in studying urolithiasis to test the effects of dietary modification on stone formation include the sporadic and unpredictable development of naturally-occurring disease as well as the difficulty in detecting subclinical spontaneously-occurring disease.

The development of a predictable and consistent model of urolithiasis in goats is a critical need in the study of dietary management for prevention this disease. While the pathogenesis of urolithiasis has not been systematically studied in goats, the matrix nucleation theory proposes that the presence of a nidus or matrix provides binding sites for crystalloids (Osborne and Kruger, 1984; Osborne et al., 1985). Several experimental models in laboratory rodents have been developed using an artificial nidus to initiate urolithiasis, including suture material (Portilla et al., 1999), calcium oxalate crystals, (Viel et al., 1999), zinc discs (Viel et al., 1999; Vermeulen et al., 1950), bacterial infection (Olson et al., 1989), mini-osmotic pumps providing oxalate (Khan et al., 1983), glass beads (Anand et al., 1994) paraffin, porcelain, chalk, charcoal, lead and uroliths (Vermeulen et al., 1950). Further, these artificially produced uroliths have been used in the study of treatment strategies for the dissolution of uroliths.

In rodents, zinc disc implantation has resulted in crystallization around the zinc disc, as well as the production of daughter stones not associated with the disc structure in 4–10 weeks (Vermeulen et al., 1950). More recently, it was shown that 10 days was sufficient implant time to determine the antiurolithiatic activity of certain compounds (Singh et al., 2010).

The objective of this study was to develop a zinc washer-based model of experimental urolithiasis in female goats to be used to study dietary preventative measures. Our hypothesis was that zinc washers would serve as a nidus to accumulate struvite crystals in goats fed a calculogenic diet.

2. Materials and methods

Procedures used in this study were approved by the Institutional Animal Care and Use Committee at Texas A&M University.

2.1. Animals and housing

Ten, 1-year old Boer-cross nonpregnant doelings, determined to be healthy based on physical examination, were utilized in these experiments. Initial body weights ranged from 22.7 to 29.5 kg. Goats were group housed in indoor stalls with wood shaving bedding.

2.2. Feed

The base of the study diet consisted of milo, dry distiller's grains, cottonseed meal and rice bran and was delivered to the goats in pelleted form at a rate of 3% of body weight. No additional forage source was available during the experimental periods and municipal water was available *ad libitum*. A partial dietary analysis including parameters of interest is shown in Table 1.

2.3. Implants

Four experiments were performed in succession using zinc washers of various sizes. Prior to each experimental period, the discs were weighed and labeled with their start weight. For Experiment 1, a Society of Automotive Engineers (SAE) #6 (6 mm) lock zinc washer[1] (initial weight: 0.11–0.14 g) was placed in each of 2 goats and a SAE #6 (10 mm) flat zinc washer[2] (initial weight: 0.41–0.69 g) placed in each of 4 goats. For Experiment 2, a SAE #10 (13 mm) flat zinc washer[3] (initial weight: 1.0954–1.1896 g) was placed in each of 8 goats. For Experiment 3, SAE #10 (13 mm) flat zinc washers[3] were concurrently placed into 8 goats. One implant of each of the following designs [see Fig. 1] was placed into each of 2 goats: zinc washer wrapped with USP 1 chromic catgut,[4] zinc washer wrapped with USP 2 polyester fiber suture,[5] zinc washer tied with 15 throws of USP 1 chromic catgut[4] and zinc washer tied with 15 throws of USP 2 polyester fiber suture[5] (initial weights: 1.1815–1.3959 g). For Experiment 4, a SAE #10 (13 mm) flat zinc washer[3] wrapped with USP 1 chromic catgut[4] (initial weight: 1.2831–1.3329 g) was placed in each of 6 goats.

Table 1
Selected parameters from dietary analysis of pelleted feed used as a total ration in all experiments.

Analyte	Value
Net energy	0.84 Mcal/lb
Crude protein	15.80%
Phosphorus	1.25%
Calcium	0.82%
Potassium	0.99%
Magnesium	0.34%
Sulfur	0.23%
Sodium	0.24%
Chloride	0.51%
DCAD (calc.)	70.50 mEq/kg

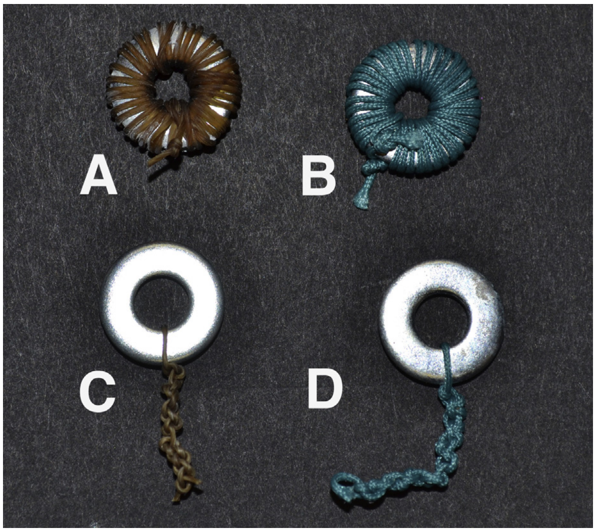

Fig. 1. SAE #10 (13 mm) flat zinc washer and suture combination designs for Experiment 3: catgut-wrapped washer (A), polyester-wrapped washer (B), washer with 15 throws of catgut (C), washer with 15 throws of polyester (D).

[1] Washers #6 Lock Washers – Zinc, The Hillman Group, Cincinnati, Ohio, 45231.

[2] Washers #6/M3.5 Flat Washers (SAE) – Zinc, The Hillman Group, Cincinnati, Ohio, 45231.

[3] Washers #10 SAE Flat Washers – Zinc, Blue Hawk, The Hillman Group, Cincinnati, Ohio, 45231.

[4] Catgut Chrom, B Braun Aesculap, Center Valley, Pennsylvania, 18034.

[5] Mersilene®, Ethicon, Somerville, New Jersey, 08876.