

A New Porcine Model of Enteric Hyperoxaluria Mimics Effects of High Oxalate Absorption in Humans

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Introduction & Objective

INTRODUCTION

Adult swine can be made to manifest hyperoxaluria and calcium oxalate stone formation with a diet enriched with **hydroxyproline**, an oxalate precursor, to emulate Primary Hyperoxaluria

- Sivalingam et al, 2013 J Endourol
- Patel et al, 2012 J Endourol

Enteric hyperoxaluria, however, is a more common cause of calcium oxalate stones

OBJECTIVE

In a effort to model enteric hyperoxaluria, we fed high amounts of oxalate to pigs and examined urinary oxalate excretion

Animals & Diets

- With IACUC approval, adult virgin sows ($n=32$), Large White x Landrace crossbred, were randomized to dietary treatment:

- Normal oxalate, normal calcium
Calcium-to-oxalate ratio (mg/mg), 13.0
- Normal oxalate, low calcium
Calcium-to-oxalate ratio (mg/mg), 4.0
- High oxalate, normal calcium
Calcium-to-oxalate ratio (mg/mg), 1.6
- High oxalate, low calcium
Calcium-to-oxalate ratio (mg/mg), 0.50



(treatment group 1 was the sows' usual diet and therefore served as control)

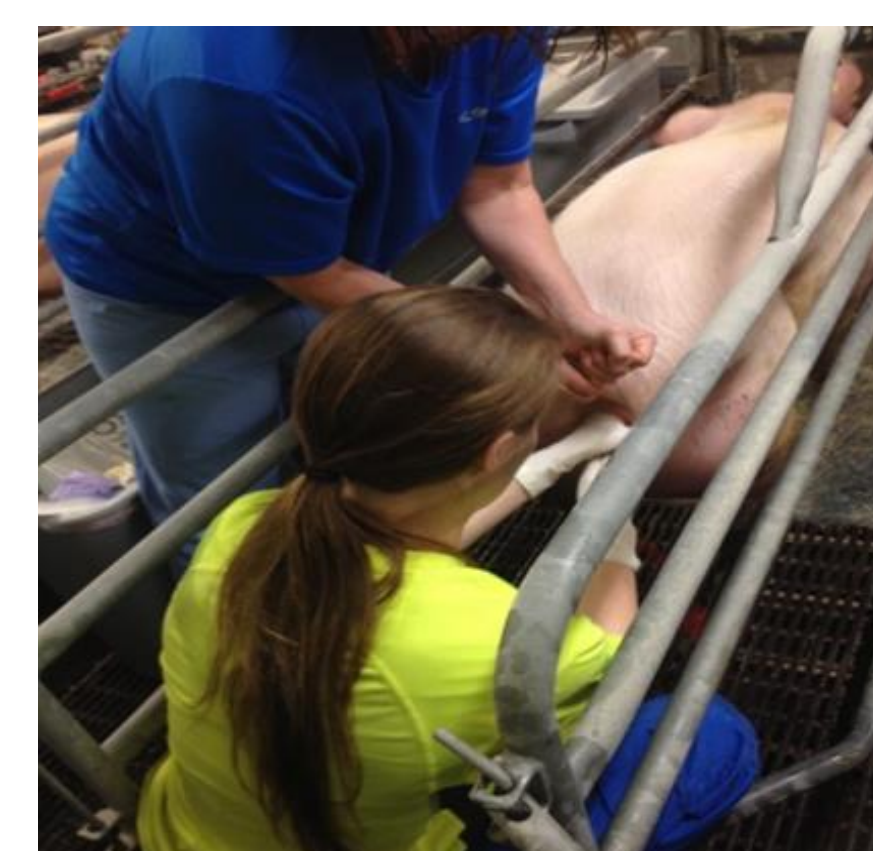
Methods

Feeding & Housing

- Animals were housed at the Swine Research & Teaching Center at UW-Madison
- Diets were mixed at the SRTC
 - For the high oxalate treatments (diets 3 and 4), **sodium oxalate was added to sows' basal diet at a 5% concentration** providing an **additional 7,000 mg oxalate daily**
 - No oxalate was added to diets 1 and 2 (basal oxalate content was 1,000 mg)
 - For the reduced calcium diet (diet 2), the mineral pre-mix was altered to reduce calcium by 70%
- Sows received 2 kg feed/d for up to 21 days; water access was not limited
- Sows were housed in rooms containing up to 12 sows; sows within rooms were individually crated (per usual)
- Sows were 9 months and 140 ± 9.6 kg at start
- For 24-h urine, Foley catheters were inserted at staggered time points during the intervention



SRTC
Swine Research & Teaching Center

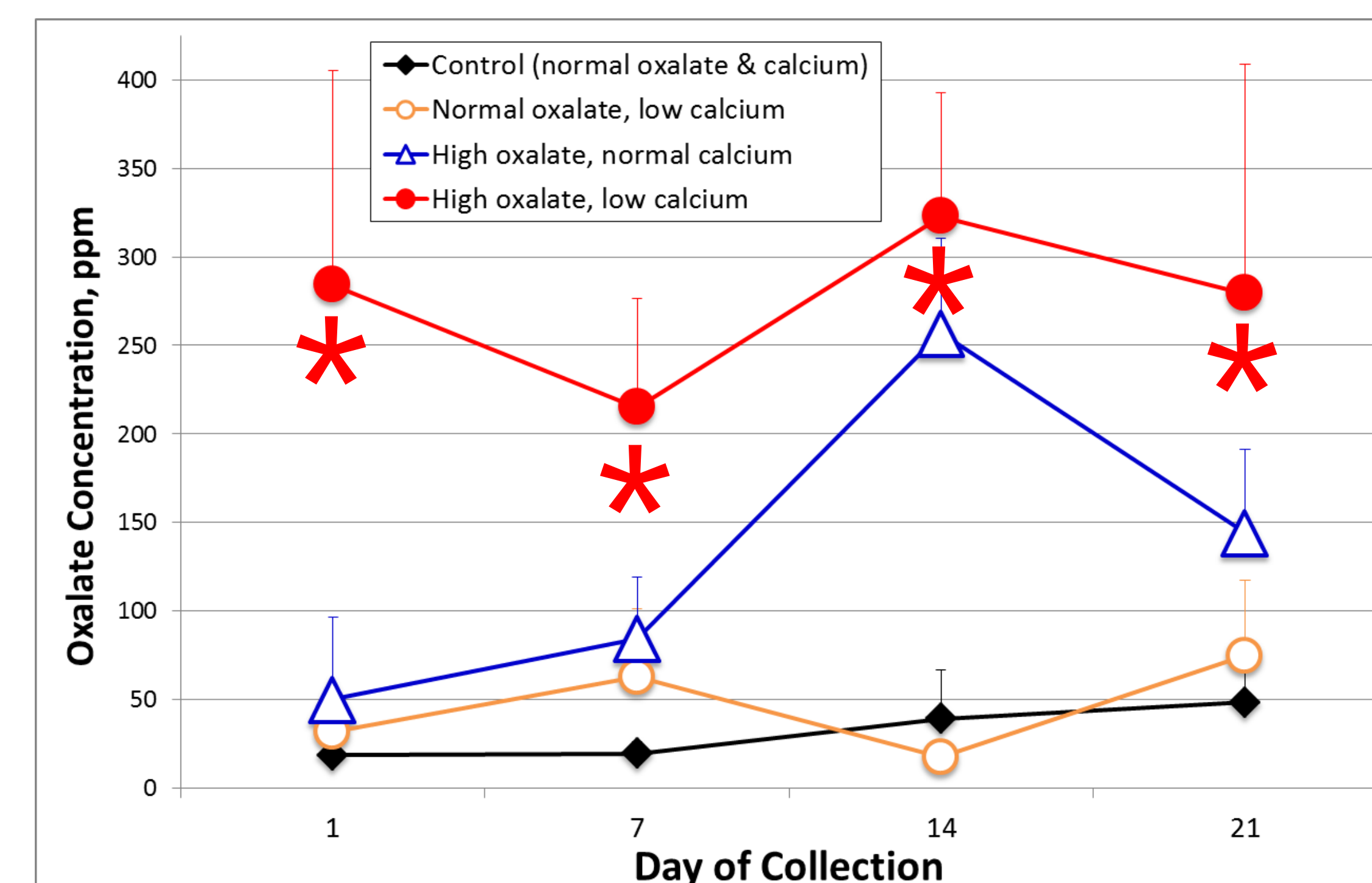


Outcome measures

- Urinary oxalate (ion chromatography)
- Fecal oxalate (ion chromatography)

Results

FIG. 1. 24-h urinary oxalate excretion by diet group at time points through 3 weeks



High oxalate, low calcium diet (diet 4)

- Urinary oxalate excretion was the highest of all groups; high oxalate excretion began within 24 hours of diet intervention
- When accounting for urine output (7.8 ± 0.7 L per day), mean urinary oxalate excretion approached 3,000 mg/d (14 d time point above)

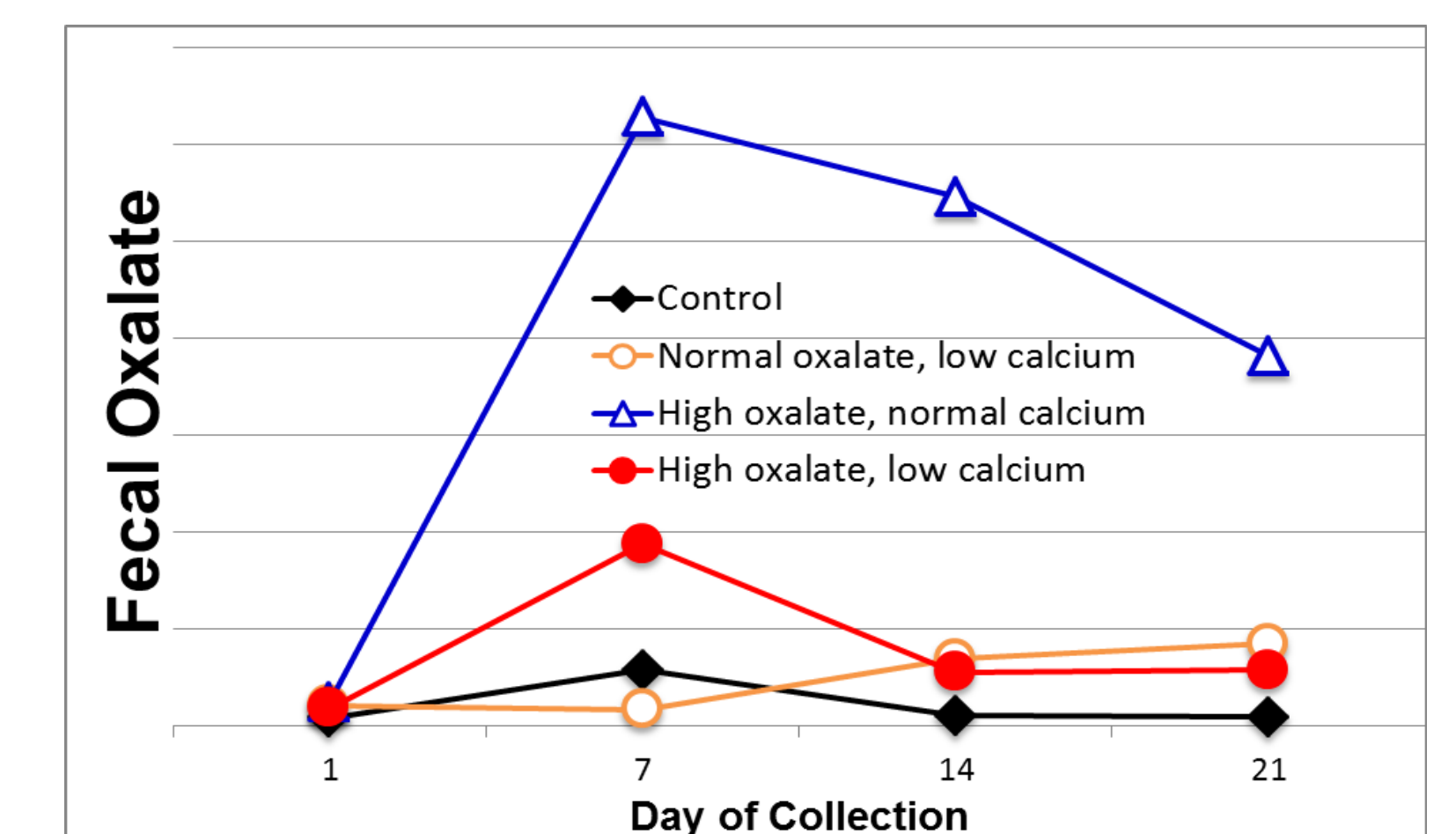
High oxalate, normal calcium diet (diet 3)

- Compared to the high oxalate diet with reduced calcium, urinary oxalate excretion was significantly lower at all time points ($P < 0.02$) in sows with ample calcium
- Urinary oxalate (ppm) was lower by 82, 61, 20, and 48% on days 1, 7, 14, and 21, respectively

Normal oxalate, low calcium diet (diet 2)

- Urinary oxalate excretion tended to be higher (fig. 1, orange circles) than in the control diet group (fig. 1, black diamonds) at 3 of 4 time points, but this was not significant ($P = 0.07$ or higher)

FIG. 2. Fecal oxalate excretion, trend



Fecal analysis was done by ion chromatography on fecal "grab" collections. Total fecal output was not assessed; total fecal oxalate cannot therefore be calculated

Relative to sows in the other groups, sows fed the **high oxalate diet with ample (normal) calcium** (diet group 4), excreted more fecal oxalate

This would explain their lower urinary oxalate excretion (fig. 1) even though they were fed the same amount of oxalate ($>8,000$ mg/d) as sows in the high oxalate, low calcium diet group

Discussion

- Renal anatomy and physiology similar to humans
- Gastrointestinal tract anatomy, morphology, physiology, and functionality is the same



- We have shown previously that adult pigs can be fed hydroxyproline, an oxalate precursor
 - They exhibit high urinary oxalate excretion and calcium oxalate stone formation due to **enhanced oxalate biosynthesis** (as in Primary Hyperoxaluria)
- In the present study, we show that pigs can be fed oxalate, such as humans consume in foods
 - They exhibit high urinary oxalate excretion due to **higher oxalate absorption**, which is significantly potentiated with reduced calcium (as in enteric hyperoxaluria)

Swine are a good platform for studying dietary prevention of kidney stones