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A NEW PORCINE MODEL OF ENTERIC HYPEROXALURIA MIMICS EFFECTS OF HIGH OXALATE ABSORPTION IN HUMANS

Kristina L Penniston, David A Bennett, Leema M John, Elizabeth L Zars, Thomas D Crenshaw, Madison, WI*

INTRODUCTION AND OBJECTIVES: 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; Patel *et al*, 2012). In an effort to emulate enteric hyperoxaluria, a more common condition in humans, we examined whether pigs would respond similarly to an oxalate-rich diet.

METHODS: With IACUC approval, we randomized 32 gilts (adult, virgin sows) to 1 of 3 dietary treatments: high-oxalate/normal-calcium; high-oxalate/low-calcium; or normal-oxalate/low-calcium. Oxalate was provided as sodium oxalate. A fourth group was fed the usual adult sow diet. The high- and normal-oxalate diets provided approx. 8,100 and 1,110 mg oxalate/d, respectively. The normal- and low-calcium diets provided 13,000 and 4,000 mg calcium/d respectively. Animals were treated up to 21 d. Foley catheters were inserted for 24-h urine collections. Fecal "grab" collections were made at time points throughout the intervention. Animals were sacrificed at various time points. Urinary oxalate excretion from 24-h urine collections and fecal oxalate was compared within and between groups.

RESULTS: Gilts fed the high-oxalate diets achieved the highest urinary oxalate excretion (figure); this effect was significantly potentiated when dietary calcium was reduced. Fecal oxalate excretion, presumably representing unabsorbed gastrointestinal oxalate, was highest in the high-oxalate/normal-calcium treated gilts and lower in those with reduced calcium. H&E and Yasue staining revealed crystals in cortical and medullary regions of renal tubules (which were birefringent upon polarization), inflammation, and fibrosis in oxalate-treated gilts. No such sequelae were observed in gilts fed the normal adult sow diet.

CONCLUSIONS: Adult female pigs, closely related to humans for renal function and urinary tract physiology, are useful in studying hyperoxaluria and oxalate-related pathologies. We have previously defined dietary methods that induce increased endogenous oxalate synthesis and now, in the current study, enteric hyperoxaluria. Pigs demonstrate similar renal pathology to humans who have hyperoxaluria and can be made to form calcium oxalate stones via methods that increase either oxalate synthesis or absorption. Work is underway to further characterize the effects of hyperoxaluria and oxalosis in this porcine (swine) model and to identify specific calcium oxalate-related human conditions for which future porcine studies may be designed.

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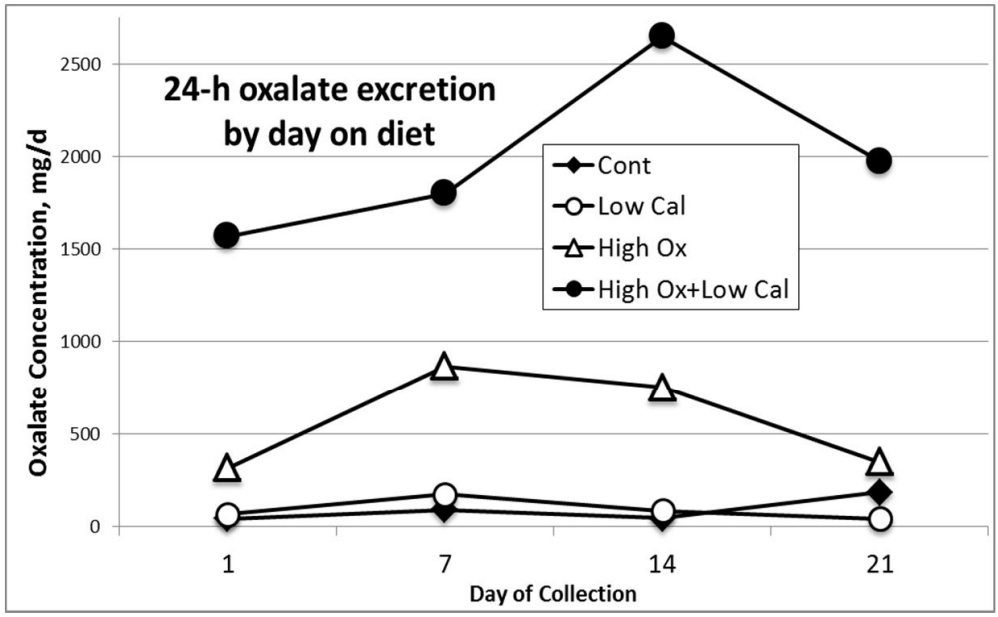

Day 1:
Control v. high oxalate, P=0.041
Control v. high oxalate/low calcium, P<0.0001
Low calcium v. high oxalate/low calcium, P=0.028
High oxalate v. high oxalate/low calcium, P=0.013

Day 7:
Control v. high oxalate/low calcium, P=0.004
Low calcium v. high oxalate/low calcium, P<0.0001
High oxalate v. high oxalate/low calcium, P<0.0001

Day 14:
Control v. low calcium, P=0.009
Control v. high oxalate, P=0.010
Control v. high oxalate/low calcium, P<0.0001
Low calcium v. high oxalate, P<0.0001
Low calcium v. high oxalate/low calcium, P<0.0001
High oxalate v. high oxalate/low calcium, P=0.022

Day 21:
Control v. high oxalate/low calcium, P=0.018
Low calcium v. high oxalate, P=0.005
Low calcium v. high oxalate/low calcium, P<0.0001
High oxalate v. high oxalate/low calcium, P=0.012