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K-STATE Research and Extension

CATTLEMEN'S DAY 2025

Nutrikinetic Evaluation and Modeling of 25-Hydroxyvitamin D_3 in Beef Cattle

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Abstract

Two studies were designed to evaluate serum 25-hydroxyvitamin D_3 [25(OH)D_3] status in beef cattle when 1) fed diets with supplemental 25(OH)D_3 or calcidol (Hy-D, DSM Nutritional Products, Plainsboro, NJ) and 2) administered as a single dose of calcidol solution (Hy-D, DSM Nutritional Products) to cannulated heifers for nutrikinetic evaluation and predictive modeling simulations. In experiment one, high-risk heifer calves were assembled in Dickson, TN, for transport to Manhattan, KS. One of four dietary treatments was used for each pen in the trial: 1) no supplemental vitamin D_3 or calcidol (CON); 2) 3,000 IU supplemental vitamin D_3/head/day (D3); 3) 0.5 mg calcidol/head/day (HyD Low); or 4) 1.0 mg calcidol/head/day (HyD High) for 60 days. Blood samples were collected from each heifer prior to transport (day -1), on arrival (day 0), and on days 14, 31, and 60 of the dietary treatment period. Data were analyzed using the GLIMMIX procedure of SAS using animal as experimental unit and treatment as a fixed effect. On days 14, 31, and 60, calves fed the HyD High or the HyD Low had greater ($P < 0.001$) serum 25(OH)D_3 concentrations than calves fed the CON or D3 treatments. In experiment two, eight cannulated crossbred heifers were randomly assigned to one of two treatments: 1) 3 mg/600 lb body weight (BW) calcidol; or 2) 5 mg/600 lb BW calcidol in a single dose administered via rumen cannula at hour 0. Serial blood samples were collected at baseline through to 70 days. The elimination half-life ($t_{1/2}$) of calcidol was determined to be an average of 7.1 days and the area under the change in the concentration time curve from time 0 to last time point that measured above the baseline concentration post-dose ($AUC_{0\text{-last}}$) averaged 33 days. Non-parametric dosing simulations using nutrikinetic parameters suggest that administration of two 5 mg oral doses of calcidol with daily feeding of 1 mg would result in a rapid and sustained increase in serum 25(OH)D_3. However, simulations should be confirmed *in vivo* before implementation.

Introduction

Vitamin D is critical to the normal development and growth of all cattle. Recent reports have shown a positive role for vitamin D in immune function of dairy cattle. Despite the role of vitamin D in growth and health, it has been largely ignored in beef cattle because it is commonly assumed that cattle on pasture or in a feedyard receive adequate vitamin D either from photoconversion of 7-dehydrocholesterol to vitamin D_3 in the skin or ingestion of vitamin D_2 from forages. The 25-hydroxyvitamin D_3 (25(OH)D_3)

[1] DSM Nutritional Products, Plainsboro, NJ

is the best indicator of vitamin D status in cattle. Serum 25(OH)D_3 concentrations above 20 ng/mL have generally been considered adequate for beef cattle; whereas concentrations less than 10 ng/mL are representative of deficiency and put cattle at risk for rickets and weak bones. Two experiments were conducted to evaluate serum 25-hydroxyvitamin D_3 [25(OH)D_3] status in beef cattle where heifers received supplemental calcidol through different administrations. Heifers in experiment one were fed diets with supplemental calcidol (HyD; DSM Nutritional Products, Plainsboro, NJ) as a top dress. Heifers in experiment two received a single dose of calcidol solution (HyD; DSM Nutritional Products, Plainsboro, NJ) through rumen cannula to evaluate nutrikinetics of calcidol to be used for predictive modeling simulations.

Experimental Procedure

Experiment 1

Ninety-six high-risk receiving heifer calves (489 ± 37.4 lb) were assembled from auction markets near Dickson, TN, and transported (~12 hours) to Manhattan, KS. Blood samples were taken via jugular vein with an 18 g needle from heifer calves at pre-transport (day -1), on arrival (day 0), and on days 14, 31, and 60 of the treatment period. Blood was collected into an 8.5 mL serum separator blood tube for analysis of serum 25(OH)D_3 concentrations. Calves were fed a corn-based receiving diet (Table 1) and administered one of four dietary treatments: 1) no supplemental vitamin D_3 or calcidol (CON, n = 24); 2) 3,000 IU supplemental vitamin D_3/head/day (D3, n = 24); 3) 0.5 mg calcidol/head/day (HyD Low, n = 24); or 4) 1.0 mg calcidol/head/day (HyD High, n = 24) for 60 days.

Experiment 2

Eight cannulated, crossbred beef heifer calves (initial body weight (BW) 637 ± 98 lb) were used for the evaluation of a calcidol solution (HyD, DSM Nutritional Products, Plainsboro, NJ). Heifers were weighed on day 0 of the trial to calculate the dose to be administered. Heifers were bled via jugular vein with an 18 g needle and blood was collected into an 8.5 mL serum separator blood tube for baseline analysis of circulating 25(OH)D_3. Following the initial blood draw, calcidol dose was administered via ruminal cannula through a syringe and line of 12 g plastic tubing. Following the dose administration, the line was flushed with 35 mL of distilled water and 35 mL of air. Heifers were randomly assigned to one of two treatments: 1) 3 mg/600 lb kg BW of calcidol (n = 4); and 2) 5 mg/600 lb BW of calcidol (n = 4). All eight heifers were used in the nutrikinetics trial. Remaining blood samples were taken at hours 2, 4, 6, 8, 12, and 24, and on days 2, 3, 5, 7, 10, 14, 21, 28, 35, 42, 49, 56, 63, and 70 post initial pulse dose. Serum was separated by centrifugation at 3,000 rpm for 12 minutes and placed into 2 ml cryovials. Samples were frozen at -4°F until analysis by High Performance Liquid Chromatography coupled with tandem mass spectrometry (DSM Nutritional Products, Belvidere, NJ).

Results and Discussion

Experiment 1

Serum 25(OH)D_3 concentrations in heifers on arrival averaged 12 ± 3.1 ng/mL and were considered suboptimum. Heifer calves fed HyD Low or HyD High had increased serum 25(OH)D_3 levels ($P < 0.001$) from day 14 to 60 compared with heifer calves fed CON or D3 dietary treatments (Figure 1).

Experiment 2

The maximum concentration from calcidol pulse dose was reached in 48 hours (Figure 2). The half-life ($t_{1/2}$) ofcalcidol was determined to be an average of 7.1 days. Calcidol pulse dose remained circulating in the serum for approximately 33 days. Modeling simulations were used to predict circulating 25(OH)D_3 concentrations in various scenarios. Non-parametric superposition was used from applying non-compartmental analysis from the single dose of 5 mg/600 lb BW of calcidol on nutrikinetics evaluation in cannulated beef heifers (Table 2, n = 4) using the assumptions of linearity, independent calcidol dosing response, and rate of absorption, and the average systemic clearance are consistent for each calcidol dosing interval (Figure 3A, 3B, and 3C), but these results should be confirmed *in vivo* in animals prior to implementation.

Implications

Calcidol can effectively elevate circulating 25(OH)D_3 concentrations in the serum of beef cattle. Greater circulating levels of 25(OH)D_3 would allow the calves to have a better chance at activating the vitamin D receptor in the body that would allow for a response in performance, immune function, and potentials in total carcass weight.

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Table 1. Composition of experimental diets for experiment one

	Treatment[1]			
Item	**CON**	**D3**	**HyD Low**	**HyD High**
Ingredient, % dry matter				
Dry rolled corn	39.5	39.5	39.5	39.5
Supplement[2]	---	7.5	---	---
Supplement[3]	7.5	---	7.5	7.5
Wet corn gluten feed[4]	40.0	40.0	40.0	40.0
Prairie hay	13.0	13.0	13.0	13.0

[1] CON = no supplemental vitamin D_3 or calcidol (n = 24); D_3 = 3,000 IU supplemental vitamin D_3/head/day (n = 24); HyD Low = 0.5 mg calcidol/head/day (n = 24); HyD High = 1.0 mg calcidol/head/day (n = 24).
[2] Supplement pellet formulated to contain (dry matter basis) 7.5% calcium, 4.7% salt, 5,992,800 IU vitamin D_3/ton and 10.8 oz/ton monensin (Rumensin 90; Elanco, Greenfield, IN).
[3] Supplement pellet formulated to contain (dry matter basis) 7.5% calcium, 4.7% salt, and 10.8 oz/ton monensin (Rumensin 90; Elanco, Greenfield, IN).
[4] Sweet Bran, Cargill Corn Milling, Blair, NE.

Table 2. Mean (range) of nutrikinetic parameters from non-compartmental analysis for change in serum 25-hydroxyvitamin D_3 concentrations in experiment two.

	Dietary 25-hydroxyvitamin D_3 supplementation	
	3 mg	5 mg
Parameters	**Mean (range)[1]**	**Mean (range)**
Dose[2], mg	3.83 (3.37-4.39)	5.52 (3.9-6.40)
$C_{baseline}$ [3]	52.4 (45.1-67.3)	56.6 (47.1-63.7)
C_{max} [4]	31.6 (28.5-36.8)	40.3 (33.8-49.6)
Dose-normalized C_{max} [b,5]	2.87 (2.59-3.35)	2.19 (1.8-2.7)
T_{max} [a,6], hour	60 (24-120)	48 (48-72)
$t_{½}$ [7], hour	177 (108-497)	164.3 (74.6-247)
$AUC_{0\text{-last}}$ [8]	10,224 (8,876-12,181)	13,028 (8,786-19,037)
Dose-normalized $AUC_{0\text{-last}}$ [b,9]	856 (581-1,107)	709 (479-1,036)

[1] Mean = geometric mean.
[2] Dose = oral dose of 25(OH)D_3 in mg administered to achieve target dose.
[3] $C_{baseline}$ = baseline serum concentration of 25-hydroxyvitamin D_3 prior to dosing.
[4] C_{max} = maximum observed change in serum concentration from baseline reached.
[5] Dose-normalized C_{max} = C_{max} normalized to a dose of 1 mcg/kg.
[6] T_{max} [a] = time to reach maximum observed change in serum concentration.
[7] $t_{½}$ = terminal half-life.
[8] $AUC_{0\text{-last}}$ = area under change in concentration-time curve from time 0 to the last time point that measured above baseline concentration, post dose.
[9] Dose-normalized $AUC_{0\text{-last}}$ = $AUC_{0\text{-last}}$ normalized to a dose of 1 mcg/kg.
[a] Tmax is expressed as median with minimum and maximum.
[b] *P* values were > 0.05 proving linearity between two treatments; (Dose-normalized C_{max} = 0.06) (Dose-normalized $AUC_{0\text{-last}}$ = 0.49).