Blood Mineral, Hormone, and Osteocalcin Responses of Multiparous Jersey Cows to an Oral Dose of 25-Hydroxyvitamin D₃ or Vitamin D₃ Before Parturition

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ABSTRACT

Twenty-seven multiparous Jersey cows were randomly assigned to receive an oral bolus containing corn starch (control, CON), corn starch plus 15 mg of 25-hydroxyvitamin D₃ (25-OH), or 15 mg of cholecalciferol (D₃) at 6 d before expected parturition. Cows were maintained in individual box stalls from 20 d before expected parturition and fed a common diet. Jugular blood samples were collected at -14, -13, -5, -4, -3, -2, -1 d before expected calving, at calving, and at 1, 3, 5, 7, 9, 11, 13, 28, 56, and 84 d postcalving. After calving, cows were housed in 1 pen in a free-stall barn and consumed a common diet. Colorimetric assays were used to analyze Ca, P, and Mg concentrations in serum. Serum concentrations of osteocalcin (OC), an indicator of bone formation, serum 25-hydroxyvitamin D₃, and parathyroid hormone (PTH) were determined in samples obtained from d -5 through d 13. The 9 control multiparous cows and 5 untreated primiparous cows were used to evaluate the effect of parity on the variables that were measured. There was no effect of parity on Ca, PTH, or 25-OH concentration. Compared with second-lactation cows and older cows (>2 lactations), first-lactation cows had greater serum OC (22.3, 32.0, and 48.3 ng/mL, respectively), indicating that younger animals were forming more bone. Blood Ca, P, and Mg decreased near the time of calving and then increased over time. Serum 25-hydroxyvitamin D₃ was greater for cows dosed with 25-OH (119.0 ng/mL) compared with those dosed with D₃ (77.5 ng/mL) or CON (69.3 ng/mL). Cows dosed with 25-OH tended to have lower serum PTH concentration, but treatments did not affect serum Ca, P, or Mg. Serum OC was greater in second-lactation cows compared with cows entering their third or fourth lactation but OC was unaffected by treatment. Although results indicated a 60% increase in serum 25-

hydroxyvitamin D₃ due to a single oral dose of 25-OH before calving, the amount administered in this study apparently was not sufficient for initiation of any improvement in Ca homeostasis at parturition.

Key words: calcium, cow, osteocalcin, hypocalcemia

INTRODUCTION

Hypocalcemia is a common condition near parturition for 5.2% of US dairy cows (NAHMS, 2002). Maintenance of blood Ca within the acceptable range of 8 to 10 mg/dL is a balancing act between the demand for Ca for milk production and the cow's homeostatic mechanisms to maintain blood Ca. A blood Ca concentration below 5 mg/dL typically results in parturient paresis, the condition more commonly known as milk fever. As cows age, Ca homeostatic mechanisms react more slowly to the Ca demands of lactation (Horst et al., 1994).

To prevent milk fever in cows, researchers (Hibbs and Pounden, 1951) often recommended feeding or injecting pharmacological doses of vitamin D 2 wk before calving. This practice increases intestinal absorption of Ca and helps prevent milk fever, but the recommended dose (up to 10 million units/d) of vitamin D is very close to the amount that causes irreversible metastatic calcification of soft tissue (Littledike et al., 1986).

Vitamin D is a necessary precursor for production of the Ca-regulating hormone 1,25-dihydroxyvitamin D₃ (DHVD). Vitamin D can be produced within the skin of most mammals by photochemical conversion of 7-dehydrocholesterol to vitamin D₃. The liver has a high affinity for vitamin D in circulation. In the liver, vitamin D is hydroxylated into 25-hydroxyvitamin D₃ (25-OH) by action of microsomal enzymes (Goff et al., 1991). The 25-OH then enters systemic circulation and is further converted to DHVD in the kidney.

The DHVD hormone increases active transport of Ca and P across intestinal epithelial cells and its production is tightly regulated by parathyroid hormone (PTH). Parathyroid hormone has 3 main functions in cows: to mobilize Ca from bone, to promote absorption of Ca from the digestive tract through increasing DHVD

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concentration, and to stimulate the kidneys to excrete excess P while retaining Ca for reabsorption (Goff, 2000). As blood Ca concentration decreases, PTH concentration increases. High concentrations of PTH promote the production of 1- α -hydroxylase in the kidney, the enzyme that converts 25-OH to DHVD. When blood Ca is within the normal range, PTH secretion decreases and DHVD is catabolized through a negative feedback mechanism. The 25-OH is diverted to inactive compounds rather than DHVD (Horst et al., 1994). When DHVD or PTH bind to osteoblasts (bone-forming cells), the osteoblasts secrete compounds that activate osteoclasts to resorb bone mineral and return it to the blood. Biochemical markers of bone formation such as osteocalcin (OC) can be measured in the blood to evaluate bone metabolism.

Various forms of vitamin D and their derivatives have been examined in relation to Ca mobilization and prevention of hypocalcemia (Olson et al., 1973a; Horst et al., 1983; Naito et al., 1990; Hodnett et al., 1992; Okura et al., 2004). Pharmacological doses are effective at preventing hypocalcemia but are close to the toxic dose. Lower doses may actually induce milk fever, depending on timing of administration, because high doses of 25-OH and DHVD suppress renal synthesis of DHVD and suppress release of PTH (Littledike and Horst, 1982). It is speculated that the Jersey breed is more prone to milk fever because they express fewer intestinal DHVD receptors and secrete more Ca in colostrum and milk (Goff et al., 1995).

The stimulation, regulation, and activation of the homeostatic mechanisms related to Ca metabolism represent a well-orchestrated cascade of events. One exception is the time around parturition when the animal is subject to a dramatic increase in Ca demand concomitant with a delay in the mobilization of Ca. Theoretically, exogenous manipulation of this cascade via vitamin D supplementation should be possible. Despite years of research, the most advantageous form, timing of treatment, and route of administration are still in question and new commercial products such as 25-OH have been developed to address this problem. Our hypothesis was that dosing preparturient cows with exogenous 25-OH 6 d before parturition would allow Ca homeostatic mechanisms to be active at parturition. Further, increasing blood Ca before the demand for Ca by the mammary gland at parturition could attenuate the severity of hypocalcemia and prevent parturient paresis.

MATERIALS AND METHODS

Cows and Treatments

Twenty-nine multiparous Jersey cows were randomly assigned to 1 of 3 treatments. Treatments were oral

Table 1. Ingredient and nutrient composition of prepartum diet

Item	
Ingredient, % of diet DM	
Corn silage	53.5
High-moisture corn	22.4
Chopped orchardgrass hay	13.4
Soybean meal, 44% CP	10.0
Mineral ¹	0.7
Yeast cell wall ²	0.1
Nutrient composition	
DM, %	55.6
	% of diet DM
CP	11.6
ADF	21.1
NDF	34.7
Ca	0.29
P	0.33
Mg	0.19
K	1.06
Na	0.11
NE _L , Mcal/kg ³	1.67

¹Contained 14.0% Ca; 9.0% P; 13.0% Na; 2.0% Mg; 0.2% K; 2.0% S; 24 mg/kg Co; 235 mg/kg Cu; 80 mg/kg I; 3,400 mg/kg Mn; 59 mg/kg Se; 895 mg/kg Zn; 297,000 IU/kg vitamin A; 65,250 IU/kg vitamin D₃; and 900 IU/kg vitamin E.

²MTB 100 (Alltech Inc., Lexington, KY).

³Estimated (NRC, 2001).

boluses of corn starch (**CON**), corn starch plus 15 mg of HyD (DSM, Parsippany, NJ) commercial 25-hydroxyvitamin D₃ (**25-OH**), or corn starch plus 15 mg of cholecalciferol (**D₃**) administered as 2 gel capsules 6 d before expected calving. If the cow did not calve within 6 d of bolus treatment, a second dose was administered (4 CON, 5 25-OH, and 7 D₃ cows were dosed twice). Animals were housed in individual box stalls and fed a common dry cow diet (Ca 0.29%, P 0.33%, and Mg 0.19% DM basis; Table 1) to achieve 10% refusals beginning 20 d before expected calving until parturition. After parturition, animals were relocated to a free-stall facility, group housed, and fed a common lactating cow diet. All procedures used in this experiment were approved by the Virginia Tech Animal Care and Use Committee.

A Foal Alert system (Foal Alert, Acworth, GA) was used to alert project personnel to parturition. A magnetic radio device was sewn to each side of the vulva 2 d before expected calving. When parturition began, the magnetic connection linking both sides of the device was broken and a radio signal was then sent to a receiver that was linked to a telephone line. This device allowed personnel to arrive for parturition and a blood sample to be collected within minutes of parturition.

Sample Collection

Jugular blood was collected before feeding on d -14, -13, -7, and every day until expected calving; at calving

(d 0); and 1, 3, 5, 7, 9, 11, 13, 21, and 28 d. Blood was also collected every 2 wk until 84 d of lactation. Samples were numbered after calving occurred and prepartum samples collected outside of specified times were discarded. If cows were diagnosed by veterinary staff with parturient paresis, a blood sample was collected and treatment was administered. Blood was maintained on ice until centrifugation at $2,200 \times g$ for 20 min. Serum separator tubes (Fisher Scientific, Pittsburgh, PA) were utilized to facilitate serum separation during centrifugation. Serum was harvested and stored frozen for future analysis.

Prepartum feed intake was measured daily. Samples of all feed ingredients and feed refusals were collected weekly. Milk samples were collected on 1, 3, 5, 7, 9, 11, and 13 d postpartum and stored frozen.

Sample Analysis

Feed samples and feed refusals were dried at 60°C to a constant weight and then ground through a 1-mm screen in a Wiley mill (Arthur H. Thomas, Philadelphia, PA). These samples were analyzed in duplicate for Ca, P, Mg, K, Na, and total Kjeldahl N (AOAC, 1984). Feed and refusals were analyzed sequentially for NDF and ADF according to Van Soest et al. (1991) with the addition of α -amylase in the initial wash.

Colorimetric methods were used to analyze all serum samples for Ca (Aresenazo Reagent Set, Pointe Scientific, Canton, MI), inorganic P (Inorganic Phosphorus Reagent, Pointe Scientific), and Mg (Magnesium Reagent Set, Pointe Scientific). Serum 25-OH and PTH were analyzed in samples from d -5, -4, -3, -2, -1, 0, 1, 3, 5, 7, 9, 11, and 13. A RIA was used to determine 25-OH (25-hydroxyvitamin D₃, DiaSorin, Saluggia, Italy) and PTH (N-tact PTH SP, DiaSorin) concentrations. A competitive immunoassay was used to quantify serum OC (Meta Osteocalcin, Quidel Corporation, San Diego, CA) in samples from d -5, -2, -1, 0, 1, 3, 5, 7, 13, 28, 56, and 84.

Milk samples from d 1, 3, and 7 were analyzed for 25-OH concentration by Waters HPLC (Waters, Milford, MA) according to the procedure of Chen et al. (1990). There was no detectable 25-OH found in any of the milk samples analyzed.

Five primiparous Jersey cows were added as part of a second objective within the confines of the first experiment. The primiparous animals were maintained and sampled according to the same protocol as the 29 multiparous animals. The primiparous animals received no treatment but were used to examine the effect of lactation number on Ca, P, Mg, PTH, 25-OH, and OC with the 9 control multiparous (3 second lactation

and 6 greater than second lactation) animals from the first objective.

Data for 2 multiparous cows were removed from analysis: 1 cow on the 25-OH treatment had a displaced abomasum and 1 cow on the D₃ treatment was removed because of a breach of experimental protocol, so $n = 27$ (9 cows per treatment). Data for another cow on the 25-OH treatment were removed from analysis after 13 DIM due to unexpected failure of the median suspensory ligament and a displaced abomasum (data from 28 through 84 DIM, $n = 26$; 9 cows on CON, 9 cows on D₃, and 8 cows on 25-OH). There were 3 cows on the D₃ treatment and 2 cows on the 25-OH treatment that were diagnosed and treated for parturient paresis within the first 48 h after parturition.

All cows on this study were concurrently participating in a crossbreeding study. Each animal on this study was bred with mixed Holstein-Jersey semen for the other research trial. The calves from these cows were either Jersey $\times$ Jersey or Holstein $\times$ Jersey crosses. The effect of calf weight on treatment responses was examined statistically but found to be nonsignificant.

Statistical Analysis

Serum Ca, P, Mg, and OC were analyzed using the Mixed procedure of SAS (9.1, SAS Institute, 2003) with the model

$$Y_{ijkl} = \alpha + b_1 X_{(ij)k} + T_i + L_j + (TL)_{ij} + C_{(ij)k} + D_l + (TD)_{il} + (LD)_{jl} + (TLD)_{ijl} + E_{ijkl}$$

where α = intercept; b_1 = regression of Y on X; $X_{(ij)k}$ = average pretreatment serum concentration of cow k; T_i = effect of treatment ($i = 1$ to 3); L_j = effect of lactation number ($j = 2$ to >3); $(TL)_{ij}$ = effect of interaction of treatment and lactation; $C_{(ij)k}$ = random effect of cow k within treatment and lactation; D_l = effect of day relative to calving ($l = -5$ to 84); $(TD)_{il}$ = effect of the interaction of treatment and day; $(LD)_{jl}$ = effect of the interaction of lactation number and day; $(TLD)_{ijl}$ = effect of the interaction of treatment, lactation number and day; and E_{ijkl} = random residual.

Several covariates were examined to account for the difference in breed of calf carried. This was examined because the variables in question could be influenced by differences in the calf. The current calf weight and previous calf weight were originally in the model as covariates to account for the potential effect of calf breed differences. Calf weights ranged from 21 to 43 kg but neither covariate was significant.

For all blood analyses, the pooled -14 and -13 d preliminary samples were used as a covariate for each measurement when significant. Cows were grouped by

parity into 3 groups; lactation 2, 3, or >3; the last group included both fourth- and fifth-lactation cows. Day was included as a repeated measure, using the ar(1) covariance structure. Prepartum DMI data (d -14 through calving) were analyzed with the above model without the covariate. Preplanned orthogonal contrasts were used to compare the CON treatment to the average of 25-OH and D₃ treatments, and to compare the D₃ treatment to the 25-OH treatment. Tukey's test was used for pairwise comparison of lactation number least squares means. The model was also used for PTH and 25-OH analysis until d 13 of lactation. For PTH, the slice option was used to determine significant treatment differences within each lactation number and day. Results are reported as least squares means $\pm$ SEM with differences declared significant at $P < 0.05$ and trends at $P < 0.10$.

For the evaluation of the effect of lactation number, in the primiparous and control cows, on serum Ca, P, Mg, PTH, 25-OH, and OC the model was

$$Y_{ijk} = \alpha + b_1 X_{(ij)} + L_i + C_{(ij)} + D_k + (LD)_{ik} + E_{ijk}$$

where α = intercept; b_1 = regression of Y on X; $X_{(ij)k}$ = average precalving serum concentration of cow j; L_i = effect of lactation number ($i = 1$ to >3); $C_{(ij)}$ = random effect of cow k within lactation; D_k = effect of day relative to calving ($k = -5$ to 84); $(LD)_{ik}$ = effect of the interaction of lactation number and day; and E_{ijk} = random residual. Tukey's test was used for pairwise comparison.

The pooled -14 and -13 d preliminary samples were used as a covariate for each measurement when significant. Cows were grouped by parity into 3 groups; lactation 1, 2, and >2; the last included 2 third-, 3 fourth-, and 1 fifth-lactation cows. Group size was small. However, previous literature (Shappell et al., 1986; Hodnett et al., 1992) has shown this is acceptable when examining variables such as serum Ca, P, and PTH concentrations.

RESULTS AND DISCUSSION

Ingredient and nutrient composition of the prepartum diet is reported in Table 1. Prepartum DMI (from -14 d through calving) averaged 9.6 ± 0.77 kg/d. We observed the expected significant effect of day, a ~20% decline as calving approached, but DMI was not affected by treatment, parity, or 2- and 3-way interactions of treatment, parity, and day. Based on analyzed nutrient concentration and measured DMI, the diet supplied sufficient available Ca, Mg, and P to meet the cows' requirements and supplied energy and protein in excess of requirements (NRC, 2001).

Table 2. Effect of parity on serum variables from Jersey cows beginning in the prepartum period

Variable	Parity number			SEM	P <
	1	2	>2		
Number of cows	5	3	6		
Ca, ¹ mg/dL	9.8	9.8	9.4	0.36	0.48
P, ¹ mg/dL	4.7	4.8	4.4	0.18	0.13
Mg, ¹ mg/dL	2.4 ^a	2.5	2.6 ^b	0.05	0.01
Parathyroid hormone, ² pg/mL	9.7	7.8	10.3	1.0	0.13
25-Hydroxyvitamin D ₃ , ² ng/mL	64.8	64.5	68.4	5.8	0.75
Osteocalcin, ³ ng/mL	48.3 ^a	32.0 ^b	22.3 ^c	3.3	0.0001

^{a-c}Values with different superscripts in the same row differed at $P < 0.05$.

¹Evaluated through 84 DIM.

²Evaluated through 13 DIM.

³Evaluated through 84 DIM.

Effect of Parity

Lactation number had no effect on serum Ca, P, PTH, or 25-OH concentration (Table 2). This is in contrast to other studies (Moore et al., 2000; Chan et al., 2006) that reported greater serum Ca concentrations in primiparous cows compared with multiparous cows. Moore et al. (2000) found lower serum PTH and 25-OH concentrations in primiparous cows compared with multiparous cows in a study that examined dietary cation-anion difference. In the present study first-lactation cows had lower serum Mg concentrations compared with cows with >2 lactations.

Serum OC concentration was greatest in first-lactation cows compared with all other lactations (Table 2, Figure 1), and cows in their second lactation had greater serum OC concentrations than those with >2 lactations. Liesegang et al. (2000) first reported that OC is affected by age in a study examining the effect of low and high milk yields in lactating Brown Swiss cows between the ages of 5 and 13 yr. This study did not specify OC concentration differences between the ages. A study by Kamiya et al. (2005) reported similar results to the present study with greater concentrations of OC and a marker of bone resorption in primiparous cows from -13 d prepartum to 3 d postpartum. Moore et al. (2000) observed that concentration of hydroxyproline, a marker of bone resorption, was greater in primiparous cows than in multiparous cows. The results from the present study and the Moore et al. (2000) and Kamiya et al. (2005) studies taken together would suggest that although primiparous cows resorb more bone compared with multiparous cows, they also replace that bone throughout lactation.

Keene et al. (2004) measured bone mineral content (BMC) in cadaver Holstein metacarpal and caudal vertebrae to evaluate effects of parity. Total BMC concentration (ash, % of bone DM) was not affected by parity

Figure 1. Effect of parity on serum osteocalcin (OC) concentration from -5 to 84 d relative to parturition with no treatment administered. SEM = 17.2; $P < 0.0001$ for parity; parity by day $P = 0.85$.

but Ca and P concentration of the metacarpal vertebrae increased with parity. This could indicate less resorption of these minerals in multiparous animals. However, the results of Keene et al. (2004) are likely specific to cull dairy animals and BMC may not be the most appropriate evaluation of total bone mineral reserves due to differences in bone mineral mass over time (Beigle, 1999).

Serum Ca, P, and Mg

There were no treatment (Table 3) or treatment by time interaction effects on serum Ca or serum P (Figure 2, A and B). There was an interaction of parity and time for serum Ca concentration ($P < 0.01$). The >3 lactations group had lower serum Ca concentration on d 0 and 1 compared with both the second- and third-

Table 3. Effect of treatment on serum variables from 27 Jersey cows dosed prepartum with corn starch (CON), 25-hydroxyvitamin D₃ (25-OH), or vitamin D₃ (D₃)

Variable	Treatment			SEM	$P <$	Parity			SEM	$P <$	Contrasts	
	CON	25-OH	D ₃			2	3	>3			CON vs. Avg. (25-OH, D ₃)	25-OH vs. D ₃
Number of cows	9	9 ¹	9			9 ¹	6	12				
Ca, ² mg/dL	9.6	9.9	9.5	0.2	0.33	9.8	9.4	9.3	0.3	0.26	0.70	0.15
P, mg/dL	4.5	4.5	4.6	0.1	0.84	4.7	4.5	4.4	0.2	0.20	0.62	0.75
Mg, ³ mg/dL	2.6	2.5	2.5	0.5	0.58	2.5	2.6	2.5	0.1	0.42	0.41	0.49
Parathyroid hormone, ⁴ pg/mL	10.1	9.6	11.4	0.6	0.09	9.5 ^a	12.1 ^b	9.6 ^a	0.7	0.01	0.56	0.04
25-OH, ¹ ng/mL	69.3	119.0	77.5	4.0	0.0001	89.7	88.5	87.7	4.9	0.91	0.0001	0.0001
Osteocalcin, ⁵ ng/mL	25.4	25.4	28.3	2.1	0.55	32.4 ^a	25.4 ^{ab}	21.3 ^b	2.5	0.003	0.57	0.35

^{a,b}Values for parity with different superscripts in the same row differed at $P < 0.05$.

¹Evaluated through 13 DIM; 1 cow was culled after 13 DIM, 8 cows evaluated until 84 DIM.

²Parity number $\times$ day interaction was significant ($P < 0.01$).

³Treatment $\times$ parity number interaction tended to be significant ($P < 0.09$).

⁴Evaluated through 13 DIM; treatment $\times$ parity number interaction was significant ($P < 0.02$).

⁵Parity number $\times$ day interaction was significant ($P < 0.04$).

Figure 2. Effect of time and treatment on serum A) Ca and B) P concentration in 27 Jersey cows dosed prepartum with corn starch (CON), 25-hydroxyvitamin D₃ (25-OH), or vitamin D₃ (D₃). SEM = 0.42.

lactation groups. Serum Ca and P were both different over time and were within the normal concentration range for adult ruminants (8 to 10 mg/dL and 4 to 8 mg/dL, respectively), but were unaffected by treatment. Olson et al. (1973b) similarly found that serum Ca and

P concentrations were not different in cows injected with 4.0 or 8.0 mg of 25-OH in sesame oil carrier between 72 h and 10 d before calving compared with controls. A study by Rivera et al. (2005) examined oral dosing of beef heifers with 0, 10, 100, or 1,000 mg of

25-OH in efforts to improve meat tenderness. At daily doses of 100 or 1,000 mg of 25-OH, serum Ca concentration increased in treated beef heifers compared with controls. The oral dose of 25-OH needed to increase blood Ca was much greater than used in the present study.

The DHVD analog appears to increase serum Ca and P concentrations when administered alone or in conjunction with 25-OH. Cows injected every 5 d beginning 15 d before parturition with 0.5 mg of DHVD and 4.0 mg of 25-OH had greater serum Ca and P concentrations at 2, 3, 5, and 7 d posttreatment compared with control cows (Hodnett et al., 1992). Braithwaite (1978) also found that injecting sheep with 5 µg/d of DHVD for 10 d beginning 1 wk after lambing increased serum Ca (11.6 mg/dL) and P (10.8 mg/dL) concentrations compared with control (9.2 and 8.4 mg/dL for Ca and P, respectively) treated sheep. An intravaginal dose of 1 µg of DHVD increased plasma Ca concentration from 12 to 72 h after treatment compared with the 0-h sample (Okura et al., 2004). Taken with the present data it appears that both the timing of administration of the vitamin D analog and the form are critical factors. In the present study, both timing of administration as well as the dose and form of vitamin D administered could be responsible for the failure to increase serum Ca and P concentrations.

Serum Mg concentration was not affected by treatment. The interaction of treatment and parity number tended to be significant ($P < 0.09$) for serum Mg concentration. The treatment by parity interaction can be explained by the third-lactation cows behaving differently on the 25-OH treatment. The third-lactation cows treated with 25-OH had lower serum Mg concentrations compared with the other treatments. A biological explanation for this response is not obvious.

Serum Hormones

As expected, concentration of 25-OH was greater in serum from cows dosed with 25-OH compared with cows dosed with CON and D₃ (Table 3). There was no effect of time by treatment interaction (Figure 3) or lactation number on serum 25-OH concentration. Parathyroid hormone concentration was lower in 25-OH-dosed cows when compared with the D₃-dosed cows (Table 3). There was a treatment by parity interaction for PTH concentration whereby cows in the >3 lactations group dosed with 25-OH had lower serum PTH compared with other >3 lactation cows (Figure 4).

Similarly, Rivera et al. (2005) observed that the blood concentration of 25-OH increased when heifers were treated with exogenous 25-OH. However, in the present study the increase in serum 25-OH in the 25-OH treated

Figure 3. Serum 25-hydroxyvitamin D₃ (25-OH) concentration from -5 d prepartum until d 13 of lactation in 27 Jersey cows dosed prepartum with corn starch (CON), 25-hydroxyvitamin D₃ (25-OH), or vitamin D₃ (D₃). SEM = 10.1.

group did not result in an increase in serum Ca concentration. The lack of response in serum Ca suggests that these cows did not sufficiently convert 25-OH into the active compound DHVD, but rather catabolized the hormone. This theory is corroborated by serum PTH concentrations tending to be lower in the 25-OH-treated cows compared with CON and D₃ cows. High circulating PTH concentrations depress catabolic enzymes in the kidney that metabolize 25-OH to inactive metabolites (Goff et al., 1991). In the present study where PTH concentration was low, 25-OH concentration was high, and there was no effect of 25-OH dosing on Ca concentration, the authors speculate that the catabolic enzymes were active and degraded the 25-OH.

Figure 4. Effect of parity and treatment on serum parathyroid hormone (PTH) concentration in 27 Jersey cows dosed prepartum with corn starch (CON), 25-hydroxyvitamin D₃ (25-OH), or vitamin D₃ (D₃). Interaction of treatment × parity, $P < 0.02$.

Blood Marker of Bone Metabolism

In the present study there was no effect of treatment (Table 3) on serum OC concentration. In contrast, others have observed an increase in OC concentration when dosing with DHVD in humans and sheep (Markowitz et al., 1987; Fortune et al., 1989). The response of the bovine may differ from these species as Naito et al. (1990) observed no correlation between blood OC and DHVD concentration in preparturient and postparturient cows. The cows in the study of Naito et al. (1990) were not administered exogenous vitamin D in any form. In the present study, the authors suggest that although serum 25-OH concentration increased in cows treated with 25-OH, the 25-OH was not converted to DHVD sufficiently to stimulate bone formation.

Second-lactation cows had greater serum concentrations of OC compared with cows in the 3 or >3 lactation groups (Table 3). As OC is a marker of osteoblast activity resulting in bone formation (Farrugia et al., 1989), the results from the present study were expected because osteoblast numbers decrease with age (Liao et al., 1990). Also, osteoblasts are the only bone cells to contain DHVD receptors (Liao et al., 1990), and Horst et al. (1990) demonstrated that bone from older rats contains fewer DHVD receptors than bone from young rats.

CONCLUSIONS

It appears that within the control treatment the first-lactation animals were more active in bone formation regardless of serum Ca concentration compared with multiparous cows. The increase in serum 25-OH in the group treated with 25-OH did not result in an increase in serum Ca concentration. The lack of response in serum Ca suggests that conversion of 25-OH into the active compound DHVD was insufficient, perhaps due to catabolism of this compound. This theory is corroborated by serum PTH concentrations tending to be lower in the 25-OH-treated cows compared with CON and D₃ cows. Although a 60% increase in serum 25-OH was observed due to a single oral dose of 25-OH before calving, the amount administered in this study was apparently not sufficient for improvement in Ca homeostasis at parturition. Oral dosing with 15 mg of 25-OH at 6 d before expected calving is not justified.

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