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Case Study: Evaluation of Calcium Propionate and Propylene Glycol Administered into the Esophagus of Dairy Cattle at Calving[1]

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Abstract

A field study was conducted to evaluate the effects of oral drenching with additional energy or energy plus calcium on blood parameters and performance of fresh cows. Treatments were 9.5 L water (control), 9.5 L water plus 300 mL (310 g) propylene glycol (PG), or 9.5 L water plus 0.68 kg calcium propionate (CP). Cows received the assigned drench within 4 h of calving and again 24 h post-calving. Animals were bled prior to each drench and on d 4 and 10 of lactation. Animals were fed and managed by parity (primiparous vs multiparous) in a commercial setting. Health events were recorded during calving and for the first 15 d in milk (DIM). Milk records were evaluated from monthly test weights the first 4 mo in lactation. The addition of PG or CP did not affect either plasma calcium or glucose ($P>0.05$). Plasma nonesterified fatty acid levels were lower in animals receiving the PG drench as compared with animals receiving either the control or CP treatment ($P<0.05$). Plasma ß-hydroxybutyrate was lowest at calving but was not affected by treatment. Health disorders (retained placenta, ketosis, hypocalcemia, displaced abomasum, metritis) were low across all treatment groups. Cattle receiving either PG or CP at calving had a significantly lower incidence of metritis compared with control animals ($P<0.05$). Averaged across all trial periods, animals receiving PG had 3.1 kg/d greater milk production than those receiving the control drench ($P<0.05$).

(Key Words: Calcium, Oral Drenching, Energy, Transition, Periparturient Problems.)

Introduction

At the onset of lactation, the dairy cow must cope with a tremendous increase in both calcium and energy demand by the mammary gland. Cows failing to meet these demands can develop milk fever or ketosis. Though the severe hypocalcemia of milk fever is rather easily treated by intravenous injection of calcium salt solutions, cows that have recovered from milk fever are less productive and more susceptible to other metabolic and infectious diseases (6, 7, 23). Cows that develop clinical ketosis are also at increased risk of developing left displaced abomasum and retained placenta (5). Bertics et al. (1) demonstrated that the lack of DMI observed in most cows at calving and the ensuing energy deficiency were particularly detrimental to the cow in that it stimulated lipolysis and greatly accelerated deposition of fat in the liver on the day of calving. Although dietary manipulations can reduce the incidence of milk fever and ketosis (2, 9, 15, 19), they are not always practical, and their effectiveness is compromised if feed intake declines.

Oral administration of large amounts of calcium salts to force calcium into the blood by passive diffusion can be used to increase blood calcium concentration during the periparturient period. Calcium

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TABLE 1. Ingredients and composition of diets.

	Cow diets			Heifer diets		
Ingredients	Close-up dry	Fresh (1–15 DIM)[a]	Lactation (>15 DIM)	Close-up dry	Fresh (1–15 DIM)	Lactation (>15 DIM)
	(kg fed per day, DM basis)					
Corn silage	4.1	5.4	8.4	2.5	3.4	2.5
Alfalfa hay	4.9	6.2	6.7	4.5	4.0	10.7
Corn	2.0	4.5	8.1	1.8	2.7	6.9
Whole cottonseed	0.5	1.4	2.7	0.5	0.9	2.1
Cottonseed hulls	1.3	0.0	0.0	0.9	0.0	0.0
Protein + fat supplement	0.3	3.4	4.1	0.6	2.3	3.6
Close-up dry cow anionic premix	1.8	0.0	0.0	0.0	0.0	0.0
Composition[b]	(DM basis)					
Crude protein, %	14.0	18.5	18.0	14.5	18.5	17.5
Net energy (lactation), mcal/kg	1.50	1.68	1.71	1.45	1.68	1.72
NDF, %	35	27	28	41	27	28
NFC[c], %	41	41	42	32	42	42
Calcium, %	1.1	1.0	0.8	0.7	1.0	0.8
Phosphorus, %	0.35	0.35	0.42	0.31	0.57	0.43
Magnesium, %	0.36	0.28	0.26	0.30	0.28	0.27
Sulfur, %	0.44	0.24	0.20	0.23	0.21	0.20
Potassium, %	1.4	1.4	1.4	1.5	1.4	1.3
Sodium[d], %	0.19	0.21	0.18	0.15	0.21	0.18
Chlorine[d], %	0.80	0.26	0.25	0.18	0.25	0.24
Vitamin A, kIU supplemented/d	172	215	154	182	118	154
Vitamin D, kIU supplemented/d	43	63	53	54	40	53
Vitamin E, IU supplemented/d	1,861	742	617	3,000	467	617
DCAD[e], meq/100 g dietary DM	–6	23	24	26	25	22

[a]DIM = days in milk.

[b]Diet composition calculated from actual forage chemical analyses. Concentrate and mineral values are those found in NRC tables.

[c]NFC = nonfiber carbohydrates.

[d]Lactating cattle were offered additional free-choice salt.

[e]Dietary cation-anion difference (DCAD) values were calculated with the following equation: [(% Na/0.023) + (% K/0.039)] – [(% Cl/0.0355) + (% S/0.016)].

chloride will rapidly acidify the cow's blood and urine; however, it also can cause metabolic acidosis in high or repeated doses, which limits the amount of calcium that can be administered. Additionally, calcium chloride is rather irritating to the cow's mouth and has been implicated as a cause of ulcers in the mouth, esophagus, rumen, and abomasum in some cows (26).

Several compounds, if administered orally, can serve as glucose precursors in ruminants. Propylene glycol has gained commercial use based on the concept that it has an advantage over common dietary glucose precursors, such as lactate and propionate, in that it is generally not degraded in the rumen and passes into the blood intact (10). However, it now appears that a portion of the PG given to the cow is metabolized within the rumen to propionate (16). Grummer et al. (16) reported increased glucose and insulin levels, with decreased nonessential fatty acids (NEFA) and ß-hydroxybutyrate, in response to PG dosage during feed intake restriction. Results from that study suggest that a dose of 296 mL was almost as effective as a dose of 887 mL in reducing lipid mobilization. However, some authors have reported higher intakes (>500 mL) of PG to be toxic, with symptoms ranging from poor rumen function to incoordination and depression of consciousness (4, 17, 22).

Recently, CP has been incorporated into drenches because it provides gluconeogenic propionate in addition to calcium to the cow (13). Though its effects on blood calcium are not as rapid as with calcium chloride, CP may have a more sustained action. Oral delivery of 50 to100 g calcium as CP will increase plasma calcium concentrations for several hours in dry cows, which

TABLE 2. Metabolic disorder occurrences.

Disorder	Treatment[a]	Occurrence, total number	Average DIM[b] at occurrence	Occurrence in heifers, number	Occurrence in cows, number
Retained placenta	Control	0			
	PG	3	1	1	2
	CP	0			
Ketosis	Control	1	7	0	1
	PG	0			
	CP	2	15	1	1
Hypocalcemia	Control	1	0	0	1
	PG	0			
	CP	0			
Displaced abomasum	Control	1	4	0	1
	PG	0			
	CP	3	61	1	2
Metritis	Control	6	8	3	3
	PG	1	8	0	1
	CP	0			

[a]CP = calcium proprionate; PG = propylene glycol.
[b]DIM = days in milk.

suggests it could prove a useful aid in amelioration of the acute hypocalcemia associated with the onset of lactation in dairy cows. The objectives of this study were to determine the effects of supplying supplemental energy (PG) or calcium plus energy (CP) as an oral drench at calving on blood measurements, health events, and milk production in a commercial dairy.

Materials and Methods

Holstein cattle were sorted by parity (heifers = first lactation or cows = second or greater lactation) and assigned to treatment. Cows and heifers were managed in similar fashion but were housed in separate pens from the dry period through mid lactation. Animals were moved from the close-up dry pen into a maternity barn ca. 10 d prior to their projected calving date (or by physical signs of an early calving). Rations were delivered as a complete total mixed ration (Table 1). Cows were fed a negative dietary cation-anion difference (DCAD) diet formulated to achieve a urine pH of 6.5. Urine was measured weekly, and the DCAD supplement was adjusted according to pH. Heifers were fed a traditional close-up ration.

Animals received the assigned drench within 4 h of calving and again 24 h post-calving. Treatments were 9.5 L water (control), 9.5 L water plus 300 mL (310 g) PG; or 9.5 L water plus 0.68 kg CP (NutroCal®, Kemin Industries, Inc., Des Moines, IA). All drenches were delivered into the esophagus via an esophageal feeder tube connected to a bilge pump (Springer-McGrath Esophageal Feeder System, McCook, NE). Each PG

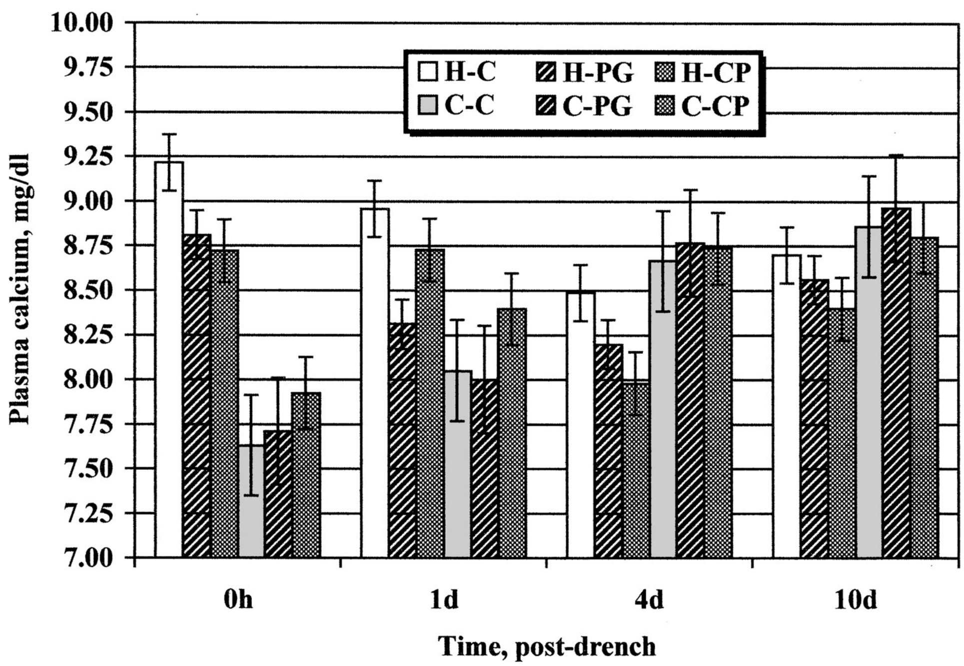

Figure 1. Effects of experimental oral drench on plasma calcium levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control (C) = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken a 0 and 24 h were obtained before drenches were administered.

TABLE 3. Plasma levels of calcium, magnesium, glucose, and nonesterified fatty acids (NEFA).

	Heifers		Cows		Drench[a]				*P*	
Item	Average	SEM	Average	SEM	Control	PG	CP	SEM	Age	Drench
Calcium, mg/dL	8.59	0.0775	8.38	0.0562	8.57	8.41	8.46	0.0788	0.0279	0.3698
Magnesium, mg/dL	1.96	0.0342	2.08	0.0248	2.06	2.00	2.00	0.0348	0.0001	0.0433[b]
Glucose, mg/dL	74.25	1.5932	70.14	1.1560	72.08	72.00	72.55	1.6206	0.0391	0.9696
NEFA, meq/L	0.5144	0.0200	0.5126	0.0144	0.5333[c]	0.4649[d]	0.5424[e]	0.0202	0.9409	0.0216
β-hydroxybutyrate, mg/dL	6.04	0.2754	6.38	0.2015	6.19	5.91	6.53	0.2828	0.3176	0.3677

[a]Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken at 0 and 24 h were obtained before drenches were administered; averages listed are across all samples.

[b]Although there was a statistically significant drench effect (*P*=0.05), the post-hoc test could not separate differences.

[c,d,e]Drench means within the same row with different superscripts are significantly different by respective *P* level listed.

drench delivered 4.08-mol glucose precursor per drench (total treatment = 8.16 mol glucose precursor). Each CP drench delivered 146 g calcium and 7.3 mol of glucose precursor (total treatment = 292 g calcium and 14.6 mol glucose precursor). The amount of CP administered was chosen based on previous experiments by Goff and Horst (13).

After calving, animals were moved into their respective fresh pen and observed daily for the first 15 DIM. Cattle were monitored for visual and behavioral signs of stress (appearance, activity, etc.), and rectal temperatures were recorded daily for early identification of animals requiring further veterinary attention and diagnosis. Cattle were palpated rectally, and uterine secretions were scored for the presence of metritis between 8 and 15 DIM. Health events in the fresh period were diagnosed by the herdsman or herd veterinarian and recorded for each animal. If cattle had good health and normal temperatures at 15 DIM, they were moved into the appropriate lactation pen. Milk weights were collected at monthly intervals.

Blood samples were collected prior to each drench (calving and 24 h later) and again on d 4 and 10. Samples were collected by jugular or coccygeal venipuncture, refrigerated until transport back to lab (average of 12 h; always <23 h), centrifuged. Serum was harvested and frozen (–20°C) until subsequent analyses. Serum determinations included calcium, magnesium, glucose, and NEFA. Serum calcium and magnesium concentrations were determined by atomic absorption spectrophotometry (21). Serum ß-hydroxybutyrate (27), glucose (25), and NEFA (18) were determined colorimetrically.

Statistics. Statistical analyses of data (for blood and milk) were performed by ANOVA using the GLM procedures of SAS (24) with animals blocked by parity (heifers = first lactation and cows = second or greater lactation). Experimental model included age, drench, and age × drench interaction. Monthly milk weights were grouped into periods for statistical purposes, according to calving schedule. Period 1 included milk weights obtained during the first test in lactation; Period 2 included milk weights obtained from the second test in lactation, etc. The model for blood analyses included age, drench, time, and any interactions. Means of independent variables found to be significant in the

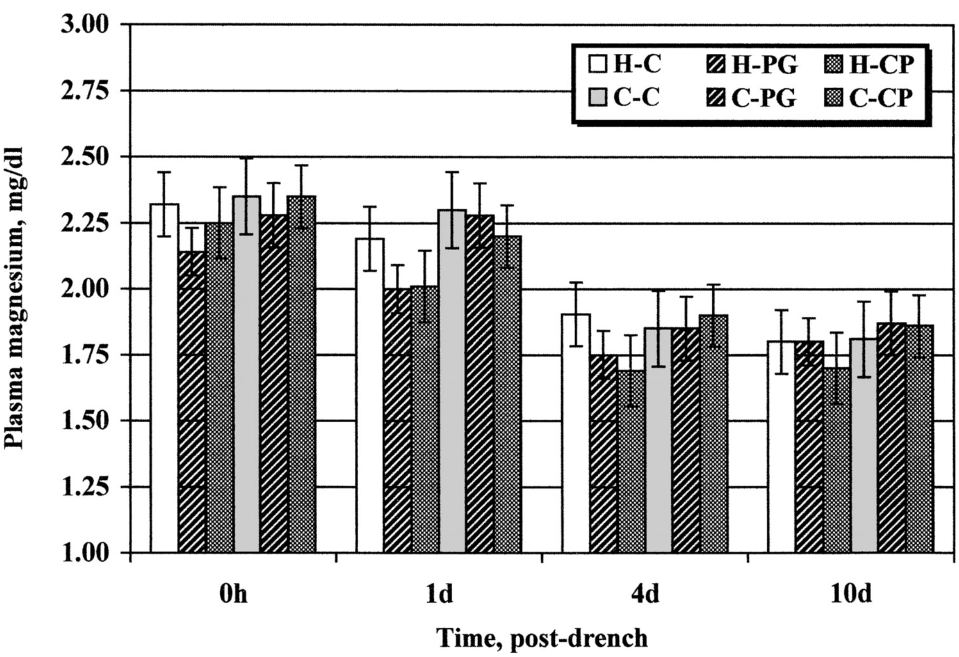

Figure 2. Effects of experimental oral drench on plasma magnesium levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control (C) = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken at 0 and 24 h were obtained before drenches were administered.

TABLE 4. Milk production response to oral drenching.

	Heifers		Cows		Drench[a]				P	
Item	Average	SEM	Average	SEM	Control	PG	CP	SEM	Age	Drench
Period 1	32.3	0.9854	47.4	0.7096	38.2	41.2	40.3	0.9975	0.0001	0.1118
Period 2	34.2	0.9854	48.7	0.7153	41.1	40.7	42.6	1.0025	0.0001	0.4528
Period 3	36.0	1.0546	47.9	0.7889	40.8	43.2	41.8	1.0727	0.0001	0.3246
Period 4	36.3	0.9403	43.9	0.6518	39.9	40.8	39.6	0.9280	0.0001	0.6801
Average kg/d, all periods	35.4	0.8436	47.0	0.5754	39.7[b]	42.8[c]	41.1[bc]	0.8234	0.0001	0.0495

[a]Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate.

[b,c]Drench means within the same row with different superscripts are significantly different by respective *P* level listed.

experimental model were separated by use of a Duncan's post-hoc test. Chi-square analysis was used to assess the effect of treatment on the incidence of retained placenta, clinical ketosis, clinical milk fever, displaced abomasum, and metritis and to determine significance of group differences.

Results and Discussion

Animals (n = 169) utilized in this trial were arranged in the following groups. The control group consisted of 22 heifers and 39 cows; the PG treatment group consisted of 21 heifers and 37 cows; and the CP group consisted of 16 heifers and 34 cows. All animals calved within a 53-d window (March 13, 2000 through May 5, 2000). Health events were recorded at calving and continued throughout the trial. Overall incidences were 1.8% retained placentas; 1.8% ketosis, 0.6% milk fever, 2.4% displaced abomasums, and 4.1% metritis. Clinical milk fever developed in 1 of the 39 cows receiving the control (water) drench; no incidences of clinical milk fever occurred in cows receiving either PG or CP. Treatments had no significant effect on the incidences of retained placenta, ketosis, milk fever, or displaced abomasum (Table 2); however, it would be difficult to discern treatment effects when the incidence of these disorders were very low. One case of ketosis was diagnosed in the control group, and two cases were diagnosed in the animals receiving the CP; no animals receiving the PG drench were diagnosed with ketosis.

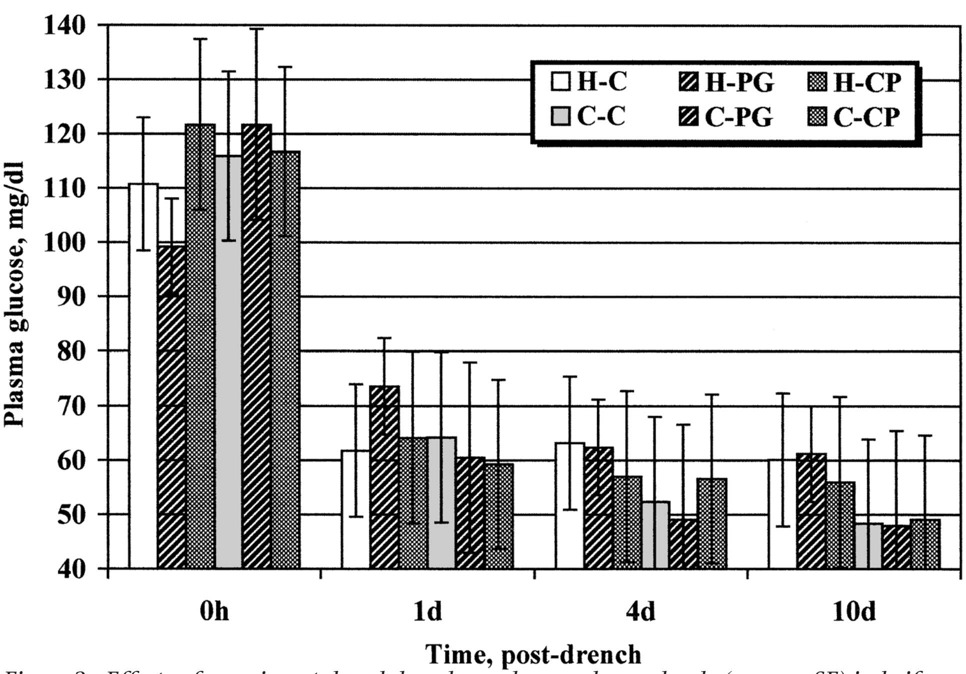

Figure 3. Effects of experimental oral drench on plasma glucose levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control (C) = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken at 0 and 24 h were obtained before drenches were administered.

The majority of metritis occurred in the control group (6 diagnosed cases out of 61 animals in the control group), with one case in the PG group, and no cases diagnosed in the cattle receiving CP. Chi-square analysis of these data indicated the control group had a significantly greater incidence ($P<0.05$) of metritis than cattle receiving either the CP or PG drench. The average DIM at which metritis was diagnosed was d 8; thus, the addition of calcium or energy at calving might have improved smooth muscle contraction and assisted in quicker uterine involution.

Hypocalcemia has been suggested as a causative factor for displacement of the abomasum (8), and the work of Oetzel (20) demonstrated that oral calcium chloride treatment to reduce hypocalcemia also reduced displacement of the abomasum. A concern with CP treatment is that the propionate might actually induce displacement of the abomasum. There is

TABLE 5. Average and range of days in milk by period for milk production.

		Drench[a]									
		Heifers				Cows				P	
Period	Overall average[b]	Control	PG	CP	SEM	Control	PG	CP	SEM	Age	Drench
1	21.8	22.4	25.7	24.8	1.1072	19.8	21.1	20.9	0.7325	0.0039	0.2698
2	50.0	50.6	54.9	53.2	1.0689	47.9	48.7	48.9	0.7758	0.0011	0.2401
3	81.5	82.7	86.9	86.0	1.1305	78.3	80.5	80.2	0.8205	0.0001	0.1238
4	112.1	113.0	114.6	114.9	1.0198	109.8	111.8	111.8	0.7071	0.0178	0.3307

[a]Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate.
[b]Overall average includes both cows and heifers across all treatments.

some evidence that propionate within the abomasum inhibits contractility of the abomasum, thus increasing the risk of distension and displacement (3). In this trial, the incidence of displaced abomasum did not increase as a result of CP treatment. Perhaps any possible deleterious effects of propionate in the abomasum were offset by the beneficial effects of calcium entering the blood to maintain abomasal motility.

Previous work reported CP, delivered as a concentrated drench, raised blood calcium concentration for 4 to 6 h after treatment (13). We did not observe any significant increases in blood calcium level resulting from treatment. Drenching animals with either PG or CP had no significant effect (P>0.10) on calcium or glucose status of the animals when determined in blood samples taken more than 24 h after treatment (Table 3). There were expected differences in blood constituent concentrations between parity (cows typically have lower blood calcium than heifers at calving). In general, the herd had a low incidence of metabolic disorders, and most animals calved within normal parameters of blood calcium, magnesium, or glucose concentrations.

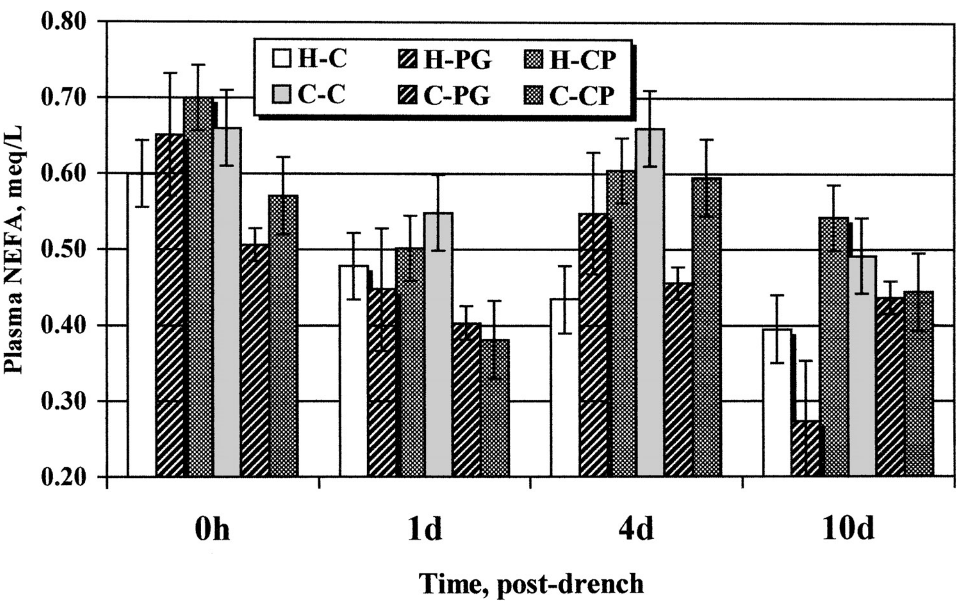

Figure 4. Effects of experimental oral drench on plasma nonessential fatty acid (NEFA) levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control (C) = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken at 0 and 24 h were obtained before drenches were administered.

The average plasma calcium concentration increased over time, and the increase was similar in both control and treated animals (Figure 1). Plasma calcium concentrations at calving (prior to treatment) were 7.6, 7.7, and 7.9 for control, PG-, and CP-treated cows, respectively. Plasma calcium concentrations were 8.1, 8.0, and 8.4 mg/dL 24 h later for control, PG-, and CP-treated cows, respectively. After calving (10 d), plasma calcium concentrations were 8.9, 9.0, and 8.8 mg/dL in control, PG-, and CP-treated cows, respectively. Incidence of subclinical hypocalcemia, defined as <7.5 mg/dL plasma calcium (14, 20), averaged 39%. All plasma calcium concentrations were higher than those reported in previous work (14), which may reflect the attention given to maintaining an effective DCAD in this herd.

Similar to calcium, plasma magnesium (Table 3) was affected by age (average plasma magnesium was 1.96 and 2.08 mg/dL for cows and heifers, respectively). There was a significant drench effect (P=0.04); however, the biological importance between drench averages may be unimportant. The post-hoc test could not separate differences. The plasma responses in magnesium level by age and drench over time are illustrated

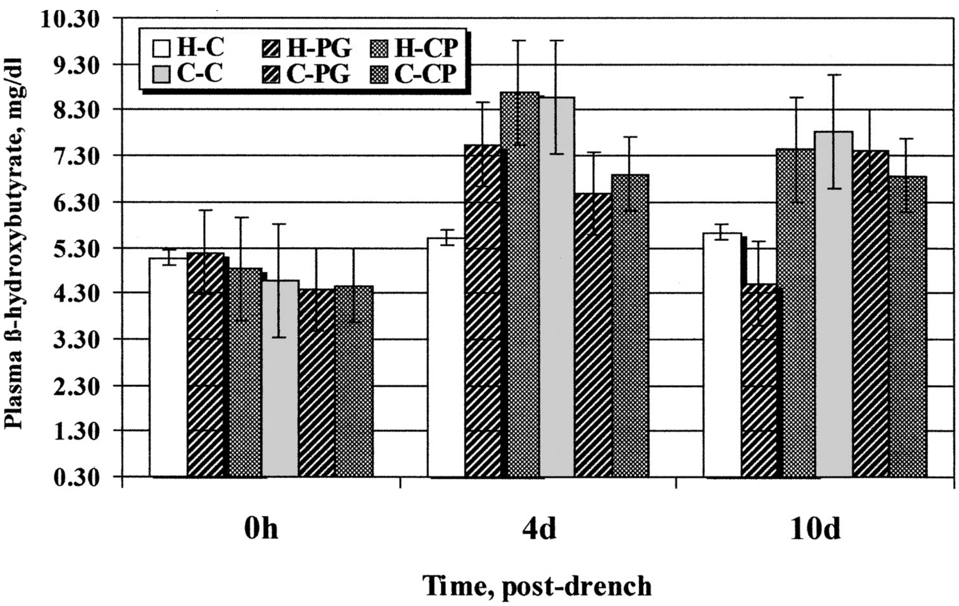

Figure 5. Effects of experimental oral drench on plasma ß-hydroxybutyrate levels (mean ± SE) in heifers (H) and cows (C). Drench treatments: Control (C) = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Blood samples taken at 0 and 24 h were obtained before drenches were administered.

in Figure 2. Blood magnesium concentrations were marginal (<2 mg/dL) in both cows and heifers on d 4 and 10 post-drench, suggesting inadequate dietary magnesium intake in the lactating cow ration or interference with magnesium absorption (11).

Drenching with additional energy, as either PG or CP, had no effect on blood glucose. As seen in other studies, cattle calved with elevated plasma glucose concentrations (Figure 3; Table 3). These higher blood glucose concentrations at calving may be a result of the combination of glucocorticoid release at calving and failure to secrete insulin when blood calcium is reduced (12). As lactation began, plasma glucose levels declined but remained within normal limits for plasma glucose.

Plasma NEFA responded to oral drench (P=0.02; Figure 4; Table 3); animals receiving PG had lower NEFA levels than those receiving either the control or CP treatment (0.533, 0.465, and 0.542 meq/L for the control, PG, and CP treatments, respectively). Plasma ß-hydroxybutyrate was not affected by oral drench (P>0.05; Figure 5; Table 3); as expected, levels were lowest at calving (averaging 4.74, 7.28, and 6.61 mg/dL for the calving, 4-d, and 10-d bleed, respectively). Incidence of subclinical ketosis, defined as >10 mg/dL plasma ß-hydroxybutyrate, appeared to be higher in control cows than in cows receiving PG or CP (15/39, 8/37, and 10/34 subclinical/total cows for control, PG, and CP treatments, respectively). Within these cases, the control group had a greater incidence (P<0.05) of repeat high plasma ß-hydroxybutyrate levels (>10 mg/dL) than cows receiving either the PG or CP drench (8/15, 2/8, and 2/10 repeat/subclinical ketotic cows for control, PG, and CP treatments, respectively).

Milk production, averaged across all periods, was 3.1 kg/d greater (P=0.0495) for cattle receiving PG as compared with those receiving the water drench (Table 4). Although not statistically significant, milk production (averaged across periods) was 1.4 kg/d greater for cattle receiving CP as compared with those receiving the water drench. It appeared that heifers received no advantage in milk production from additional calcium, but may have benefited from additional energy in the form of propylene glycol (Figure 6A). Goff et al. (14) observed no significant increase in milk production in a commercial Holstein herd (multiparous cows only) receiving a lower dose (352 g per drench) of CP as a paste delivered at calving and again at 24 h post-calving. In this trial, cows receiving a larger dose of CP (680 g per drench) averaged 1.8 kg more milk per day than cows receiving the water control (Figure 6B). Despite the higher dose of CP, this difference in milk production was not statistically different (P>0.05). Period average DIM for both heifers and cows is listed in Table 5. Differences in DIM between drench treatments were evaluated for potential effects on milk production. Differences were significant for age (heifers *vs* cows; P<0.05), but there were no differences (P>0.05) across treatments.

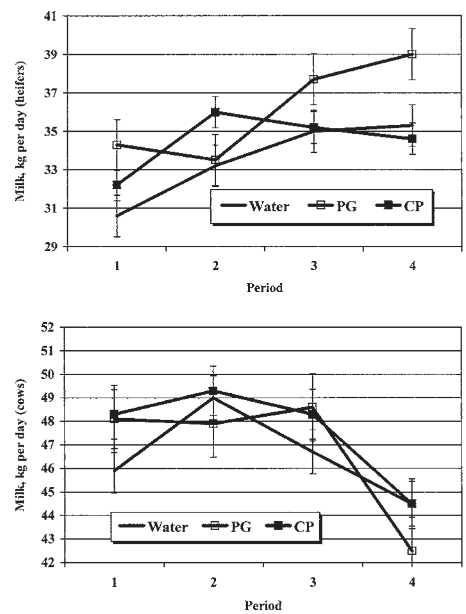

Figure 6. Top panel: Effects of experimental oral drench on milk production (mean ± SE) in heifers. Milk production was averaged by period (1 through 4). Period designates monthly test weight; average days in milk (DIM) for heifers in each period were 24, 52, 85, and 114 for Periods 1, 2, 3, and 4, respectively. Drench treatments: Control = 9.5 L water; PG = 9.5 L water + 300 mL propylene glycol; CP = 9.5 L water + 0.68 kg calcium propionate. Bottom panel: Effects of experimental oral drench on milk production (mean ± SE) in cows. Milk production is averaged by period (1 through 4). Period designates monthly test weight; average DIM for cows in each period were 21, 49, 80, and 111 for Periods 1, 2, 3, and 4, respectively.

Implications

Supplying both additional calcium and energy during the metabolic and feed intake challenge imposed at calving may be of benefit to the cow. Hypocalcemia results in the loss of muscle tone in the gut, uterus, and teat sphincter. This loss of muscle tone, combined with the immunosuppression of excess cortisol at calving, predisposes these animals to displaced abomasum, retained placenta, uterine prolapse, and mastitis. Additionally, the reduced feed intake often noted with hypocalcemic conditions further aggravates the negative energy balance commonly observed in early lactation. Even if clinical milk fever or ketosis is not prevalent in the older cows, as was the case in this herd, the cost of the preventative oral treatment may be justified by potentially higher milk yields and reduced health complications.

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