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Effect of oral calcium bolus supplementation on early-lactation health and milk yield in commercial dairy herds

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ABSTRACT

The objective of this study was to evaluate the effect of supplementation with oral Ca boluses after calving on early-lactation health and milk yield. Cows in their second lactation or greater (n = 927) from 2 large dairies in Wisconsin were enrolled during the summer of 2010. Both herds were fed supplemental anions during the prefresh period and less than 1% of fresh cows were treated for clinical milk fever. Cows were scored before calving for lameness and body condition, and then randomly assigned to either a control group or an oral Ca bolus-supplemented group. Control cows received no oral Ca boluses around calving. Cows in the oral Ca bolus group received 2 oral Ca boluses (Bovikalc, Boehringer Ingelheim, St. Joseph, MO), one bolus 0 to 2 h after calving and the second 8 to 35 h after calving. The oral Ca bolus administration schedule allowed fresh cows to be restrained in headlocks only once daily. Whole-blood samples were collected immediately before the second oral Ca bolus was given and were analyzed for ionized Ca (Ca^{2+}) concentration. Early-lactation health events were recorded and summed for each cow. Only 6 cases (0.6% of calvings) of clinical milk fever occurred during the trial, and only 14% of cows tested were hypocalcemic (Ca^{2+} less than 1.0 mmol/L) at 8 to 35 h after calving. Mean Ca^{2+} concentrations were not different between the control and oral Ca bolus-supplemented groups. Blood samples from the cows given oral Ca boluses were collected an average of 20.6 h after administration of the first bolus. Subpopulations of cows with significant responses to oral Ca bolus supplementation were identified based on significant interactions between oral Ca bolus supplementation and covariates in mixed multiple regression models. Lame cows supplemented with oral Ca boluses averaged 0.34 fewer health events in the first 30 d in milk compared with lame cows that were not supplemented with oral Ca boluses. Cows with a higher previous lactation mature-equivalent milk production (greater than 105% of herd rank) and supplemented with oral Ca boluses produced 2.9 kg more milk at their first test after calving compared with cows with higher previous lactation milk yields that were not supplemented. Results of this study indicate that lame cows and higher producing cows responded favorably to supplementation with oral Ca boluses. Supplementing targeted subpopulations of cows with oral Ca boluses was beneficial even for dairies with a very low incidence of hypocalcemia.
Key words: oral calcium chloride, oral calcium bolus, hypocalcemia, dairy cow

INTRODUCTION

Milk fever (parturient hypocalcemia) is an important metabolic disorder of dairy cattle around the time of calving. The mean incidence of clinical milk fever in published field studies was about 3.5% for North American and Australasian studies and about 6.2% for European studies (DeGaris and Lean, 2008). About 50% of cows in their second lactation and greater have blood Ca concentrations that fall below the threshold for subclinical hypocalcemia after calving (Reinhardt et al., 2011). Hypocalcemia may lead to reduced feed intake, poor rumen and intestine motility, increased risk of displaced abomasum, reduced milk yield, increased susceptibility to infectious diseases, and increased risk of early-lactation removal from the herd (Curtis et al., 1983; Goff, 2008; Seifi et al., 2011). Mechanisms that may explain the detrimental effects of hypocalcemia include impaired energy balance, which is reflected in higher serum NEFA concentrations (Reinhardt et al., 2011), and direct impairment of immune cell responses to an activating stimulus (Kimura et al., 2006).

Identification of cows with subclinical hypocalcemia is impractical because these cows, by definition, do not display overt clinical signs. Thus, prevention is the only option for managing subclinical hypocalcemia. One prevention strategy is to supplement anions before calving. Charbonneau et al. (2006) conducted a large meta-analysis of previously published studies and determined that feeding a typical dose of anions before calving results in a 5-fold reduction in the risk of clini-

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cal milk fever. Fewer studies have evaluated the effect of anion supplementation on subclinical hypocalcemia. Beede et al. (1992) reported that feeding anionic salts before calving in a large field study (n = 510 cows, all parities) reduced the subclinical hypocalcemia (defined as Ca^{2+} ≤1.00 mmol/L on the day of calving) from 50% in the control cows to 19% in the cows receiving the anionic salts. Other, smaller studies have shown similar reductions in subclinical hypocalcemia when anions were supplemented (Oetzel et al., 1988) or have shown smaller numerical reductions in the incidence of subclinical hypocalcemia that were not statistically significant (Goff and Horst, 1997; Ramos-Nieves et al., 2009).

Another approach to prevention of subclinical hypocalcemia is oral Ca supplementation around calving. Calcium chloride may be particularly beneficial as an oral supplement because it provides highly available oral Ca (Goff and Horst, 1993, 1994) and because it is a more potent acidifier than other anion sources (Goff et al., 2004; Gelfert et al., 2010). Systemic acidification has been associated with beneficial effects on Ca metabolism beyond the expected contribution of Ca absorbed from the gastrointestinal tract. The underlying mechanism for the benefits of systemic acidification is the correction of metabolic alkalosis, which blunts the response of the cow to parathyroid hormone (Goff et al., 1991; Phillippo and Reid, 1994; Goff, 2008).

Thilsing-Hansen et al. (2002) summarized oral Ca supplementation trials and found oral Ca from a variety of formulations to be consistently beneficial. Using oral $CaCl_2$ as the source of oral Ca has been shown to increase blood Ca concentrations, reduce the risk of clinical and subclinical hypocalcemia, and reduce the risk of displaced abomasum (Oetzel, 1996; Dhiman and Sasidharan, 1999). However, $CaCl_2$ may be caustic to the oral mucosa, and large, repeated doses could induce uncompensated metabolic acidosis, especially if the cow is already being fed an acidogenic diet (Goff and Horst, 1993).

The effect of oral Ca supplementation in cows that have received an acidogenic diet before calving has been minimally studied. Melendez et al. (2002) evaluated oral $CaCl_2$ in a herd fed anionic salts and found no effect of oral Ca supplementation on Ca^{2+} at 24 h postcalving. The authors concluded that oral Ca supplementation around calving may not be necessary when negative DCAD diets are fed. However, relatively few cows were enrolled in this study (30 control cows and 30 cows supplemented with oral $CaCl_2$), and it was not possible to identify subpopulations of cows that may have responded well to the oral $CaCl_2$ supplementation. Neither milk yield nor cow health was evaluated in this study.

Calcium chloride, in combination with $CaSO_4$, has been formulated into a solid bolus coated with fat (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO). One bolus provides 43 g of Ca (71% from $CaCl_2$ and 29% from $CaSO_4$). Compared with oral Ca gel formulations, the bolus has the advantages of protecting the cow from the sharp taste of the $CaCl_2$ and eliminating the risk of aspiration pneumonia (Pehrson and Jonsson, 1991). In a 2-part field study, Pehrson and Jonsson (1991) gave 4 total oral Ca boluses (1 before calving, 1 at calving, and 2 after calving) and reported that the boluses reduced the risk of clinical milk fever 4-fold compared with that of cows administered a placebo bolus. They concluded that the oral Ca boluses were at least as effective as a $CaCl_2$ gel in preventing clinical milk fever and that the more sustained release of Ca from the bolus formulation could be responsible for its beneficial effects.

Sampson et al. (2009) supplemented multiparous cows (n = 20) with 2 oral Ca boluses after calving. They reported significantly increased Ca^{2+} concentrations 1 h after administration of the first oral Ca bolus (which was given at calving) and 1 h after administration of the second bolus (which was given 12 h after calving). Urinary pH was significantly reduced from about 8.0 to 6.8 in cows given the oral Ca boluses; the authors concluded that acidification likely contributed to the ability of the boluses to support blood Ca^{2+} concentrations after calving. No larger scale studies have been conducted with oral Ca boluses, and no studies have evaluated milk production or cow health outcomes.

The objectives of this study were to conduct a large field study in commercial dairy herds with effective anionic salt feeding programs already in place 1) to evaluate the effects of supplementation with an oral Ca bolus containing $CaCl_2$ and $CaSO_4$ on detailed measures of early-lactation health and milk yield and 2) to determine whether groups of cows could be identified within these herds that have significantly different responses to oral Ca bolus supplementation.

MATERIALS AND METHODS

Study Population

The study was conducted on 2 large commercial dairy farms in Wisconsin during the summer of 2010. To be selected for the study, the herds had to meet the following criteria: milk at least 1,500 cows, have headlocks in the prefresh and postfresh cow pens, use Dairy Comp 305 (Valley Agricultural Software, Tulare, CA) records for on-farm management, be willing to administer the boluses according to the project protocol, and be willing to collect and properly handle whole-blood samples

after calving. A description of the study herds has been published previously (McArt et al., 2011). Herd A in the current study corresponds to herd C in the previous description, and herd B in the current study corresponds to herd D. A more detailed description of typical diets fed to the herds during the trial is presented in Table 1. Herd A contributed 327 cows (40% of total cows) to the study, and herd B contributed 555 cows (60% of total cows). Both cooperating dairies signed a consent form agreeing to the project protocol and were given a document containing information on disease definitions used in the trial. The study protocol was reviewed and approved by the University of Wisconsin–Madison School of Veterinary Medicine Animal Care and Use Committee (No. V01479-0-05-10).

Cows were randomly assigned to either the control or oral Ca bolus group before calving. A random number generator was used to determine the treatment assignment for the first cow enrolled; remaining treatment assignments were made sequentially (every other cow). Treatment assignments were indicated by color-coded neck chain tags placed on the cows.

At the same time the cows were assigned to treatment, they were also evaluated for locomotion score and BCS. Locomotion score was determined using the 1- to 4-point scoring system described by Nordlund et al. (2004), in which cows were categorized as nonlame (score 1), slightly lame, moderately lame, or severely lame (score 4). Prefresh BCS was determined using a 1- to 5-point scoring system with 0.25-unit increments as described by Ferguson et al. (1994), in which a higher score represents a greater body condition. Two trained evaluators assigned all the prefresh scores, with 1 evaluator assigning each locomotion score and 1 evaluator assigning each BCS. Scores were taken an average of 15.6 d (±0.3 SEM) before calving.

Cows were enrolled in the study immediately after calving; prefresh data were collected from some cows that did not meet the final criteria for enrollment. Cows in the control group received no oral Ca boluses after calving, and cows in the oral Ca bolus group received 2 boluses. The first bolus was administered within 2 h after calving. The second bolus was given when the cow was next locked up in the postfresh pen after calving

Table 1. Summary of formulated feed ingredient amounts and formulated nutrient composition of example diets fed on 2 commercial dairies to the pre- and postfresh cows during the study

	Herd A		Herd B	
Feed ingredient or nutrient	Prefresh	Postfresh	Prefresh	Postfresh
Ingredient, % of DM				
Alfalfa hay	13.0	9.8	—	—
Alfalfa silage	—	17.4	7.1	24.5
Corn silage	29.8	36.5	16.3	41.6
Grass hay	14.0	—	10.7	—
Wheat straw	14.0	2.2	22.7	—
Ground corn	—	8.7	13.3	1.9
Whey permeate	—	2.2	—	—
Corn gluten feed (dry)	—	8.5	10.7	6.5
Corn distillers grains (dry)	—	—	9.2	8.8
Corn distillers grains (wet)	—	—	—	2.3
Brewers grains (wet)	—	—	7.1	6.5
Prefresh concentrate mix	29.2	—	2.9	—
Postfresh concentrate mix	—	14.8	—	7.9
DM, %, as fed	45.2	43.0	59.0	41.5
Nutrient composition (DM basis)				
CP, %	13.7	17.2	15.0	17.5
Ether extract, %	3.5	4.7	4.3	4.9
NDF, %	44.3	30.3	43.1	33.5
Starch, %	14.8	19.8	19.6	21.8
NFC,[1] %	30.5	39.3	29.4	36.0
Ash, %	8.04	8.50	8.23	8.10
Ca, %	0.93	0.92	0.88	0.79
P, %	0.34	0.43	0.41	0.44
Mg, %	0.39	0.37	0.34	0.37
Na, %	0.09	0.48	0.14	0.46
K, %	1.08	1.54	1.27	1.44
Cl, %	0.73	0.58	0.88	0.45
S, %	0.35	0.25	0.25	0.25
DCAD,[2] mEq/kg	−109	283	−18	285

[1]Calculated as 100 − CP − ether extract − NDF − ash.

[2]Calculated as mEq [(Na + K) − (Cl + S)].

and had to be administered between 8 to 35 h after calving. If the cow reached the postfresh pen before 8 h postcalving, she was given her second bolus the next day. The bolus administration schedule was chosen to fit within the normal management activities of large dairies, and it required cows to be restrained in headlocks only once daily. The schedule was also chosen to include the time period cows are expected to be experiencing the most profound hypocalcemia, which is about 12 to 24 h postcalving (Goff, 2008; Ramos-Nieves et al., 2009). The mean time between calving and administration of the second bolus was 20.6 h (±0.2 SEM).

In total, 1,780 calvings occurred during the study period; 1,127 of these involved cows in their second lactation or greater. To be eligible for the trial, multiparous cows needed valid on-farm record information, could not start the lactation with an abortion (defined as gestation length <260 d), could not have a calving ease score of 5 (indicative of a C-section or fetotomy), had to remain in the herd until at least 2 DIM, had to have been randomly assigned to treatment before calving, and (for cows assigned to the oral Ca bolus group) had to receive both of the boluses within the specified time periods. Of the 1,127 possible cows, 927 were entered into the trial and 200 were excluded. Table 2 presents a summary description of cows excluded from the study.

Of the 927 cows enrolled, 431 were in the oral Ca bolus group and 496 were in the control group. The slight imbalance occurred because more of the cows initially assigned to the oral Ca bolus group were excluded from the study. More criteria had to be met for a cow to fulfill the requirements for being in the oral Ca bolus group (i.e., correct bolus administration both times) compared with the very minimal requirements for inclusion in the control group.

Study Outcomes

Whole-blood samples were collected for Ca^{2+} analysis at 8 to 35 h after calving. Between 1 and 3 mL of whole blood was collected from the coccygeal vein or artery into syringes containing dry Li heparin (Portex Pro-Vent Plus; Smith's Medical, New York, NY). After collection, air was excluded from the syringes using the filter tip provided, and the syringes were refrigerated within 30 m. A portable blood analyzer (VetStat Electrolyte and Blood Gas Analyzer; Idexx Laboratories, Westbrook, ME) was used to measure Ca^{2+}. Whole blood from the syringes was analyzed for Ca^{2+} concentration within 72 h of collection (average time from collection to analysis was 28.1 ± 0.6 h (SEM). This storage and sampling protocol was validated by collecting a blood sample from 16 parturient cows into dry Li heparin syringes and measuring the Ca^{2+} concentration from this syringe at 0, 24, 48, and 72 h after collection. The mean concentration of Ca^{2+} changed minimally (0.01 mmol/L) after 72 h of storage.

The Ca^{2+} results from the portable analyzer were validated by comparing them with in-house laboratory results. Ionized Ca result samples collected from 20 parturient cows were analyzed on both the portable analyzer and on an in-house blood gas plus Ca^{2+} analyzer (Nova Stat Profile pHOx Plus; Nova Biomedical Corp., Waltham, MA). Results were compared by linear regression, and agreement between the 2 different analyzers was excellent ($R^2 = 0.92$). The difference between intercepts for the 2 different analyzers was corrected by adding 0.09 mmol/L to each Ca^{2+} result from the portable analyzer.

Whole-blood BHBA concentration was determined 6 times for each cow between 3 and 16 DIM on Mondays, Wednesdays, and Fridays using a handheld meter (Precision Xtra; Abbott Diabetes Care, Alameda, CA). Iwersen et al. (2009) reported that this meter has excellent agreement with laboratory analysis of serum for BHBA ($R^2 = 0.90$). Ketosis was defined as BHBA ≥1.2 mmol/L on any BHBA test (McArt et al., 2011). Cows were required to have 5 or 6 negative BHBA tests before they were classified as negative for ketosis.

First-test daily milk weights came either from DHI test weights (herd A) or from daily milk weights collected by the parlor meters (herd B). About 8% of the parlor milking weights were missing for herd B. To minimize the number of missing first-test-day milk weights that would result from a cow missing any one of her 3 milking weights on test day, missing milk weights were imputed using a method based on hot-deck imputation. A randomly selected milking weight from 1 of the 5 milking weights before or after the missing weight was used to fill in the missing value. A milking weight was not imputed (i.e., it was left as a missing value) if the 10 milking weights around it were all missing as well.

Early-lactation health outcomes recorded were metritis, ketosis, displaced abomasum, mastitis, pneumonia, herd removal, or death. Clinical milk fever, hypocalcemia (defined as blood Ca^{2+} ≤1.00 mmol/L at 8 to 35 h

Table 2. Reasons for excluding cows from the trial[1]

Reason	Cows, n
Invalid record information	4
Aborted (<260-d gestation length)	31
Calving ease score of 5 (C-section or fetotomy)	1
Removed before 2 DIM	9
Calved without random treatment assignment (no tag)	69
Received the first oral Ca bolus but not the second	85
Received the second oral Ca bolus but not the first	1

[1]Experimental cows were selected from multiparous cows that calved during a 3-mo time period on 2 commercial dairies.

after calving), and retained placenta were summarized but not evaluated statistically because they could be diagnosed before both oral Ca boluses were administered. Health events were considered only if they occurred in the first 30 DIM. Health outcomes were recorded by the cooperating dairy producers. Early-lactation cow health was analyzed as individual events and as a single, continuous variable that represented the sum of individual health events during the first 30 DIM. Up to 6 events per cow were possible; the actual range was 0 to 4 events per cow.

Other study outcomes included postfresh locomotion score, postfresh BCS, and reproduction outcomes [first-service conception, pregnancy by 150 DIM, days open for cows pregnant by 150 DIM, and days from the voluntary waiting period (**VWP**) to conception by 305 DIM]. Postfresh locomotion and BCS were determined between 40 and 60 DIM by using the same methods as described before, with the addition of a third trained evaluator who assigned about 65% of the postfresh scores.

Study Covariates

Covariates for early-lactation outcomes were factors that could be known about the cow at the time of calving. These included parity, prefresh locomotion score, prefresh BCS, twin calves or a single birth, a stillborn or live calf, previous gestation length (i.e., length of the gestation preceding enrollment in the study), previous lactation length, previous dry period length, and calving ease score (1 to 5 scale, with 1 representing no calving assistance and 5 representing extreme assistance). The time interval between calving and blood sample collection was included as an additional covariate for the Ca^{2+} analysis, DIM at the first DHI test was included as an additional covariate for the first test milk yield analysis, and DIM at scoring was included as an additional covariate for postfresh locomotion score and BCS analyses. Additional covariates included in the analyses for first-service conception, pregnancy by 150 DIM, and days open for cows pregnant by 150 DIM included DIM at the first breeding, AI synchronization status (synchronized = 1; not synchronized = 0), and first breeding month. Categorical covariates were compressed into combined categories as needed to avoid missing combinations of covariates and to make the standard errors as equivalent as possible across group means. Continuous covariates were plotted against study outcomes, and the resulting plots were inspected for evidence of breakpoints in the relationship along the spectrum of values for the continuous covariates. No logical breakpoints were apparent, so no continuous covariates were compressed into categorical variables for the initial evaluations.

Statistical Analysis

Descriptive statistics were generated with the MEANS and FREQ procedures of SAS 9.3 (SAS Institute Inc., Cary, NC). Continuous study outcomes (Ca^{2+} 8 to 35 h after calving, first-test milk yield, sum of health events in the first 30 DIM, postfresh locomotion score, postfresh BCS, and days open for cows pregnant by 150 DIM) were analyzed using multivariate linear regression with the MIXED procedure of SAS. Study outcomes with a binary response (metritis, ketosis, displaced abomasum, mastitis, pneumonia, herd removal, death, first-service conception, and pregnant by 150 DIM) were analyzed using a mixed-effects multivariate Poisson regression with the GENMOD procedure of SAS (Frome and Checkoway, 1985; Spiegelman and Hertzmark, 2005). Poisson regression has the advantage of directly estimating disease rates and relative risk, which is the most intuitive approach to modeling and presenting these data (Ospina et al., 2012).

Large models for the analysis of pregnancy status through 305 DIM were conducted using a semiparametric proportional hazards model (Cox, 1972) in the PHREG procedure of SAS. The time series variable for the model was the number of days from the end of the VWP (65 d for herd A and 78 d for herd B) until conception or censoring. Cows were dropped from the survival analysis (uninformative censoring) when they were removed from the herd (either sold or died) or declared ineligible for additional breedings ("do not breed" designation in the herd records). A small number of cows (n = 23) were still open and eligible for additional breedings by 305 DIM.

The effect of blanket supplementation with 2 oral Ca boluses for all study cows was evaluated using a 2-step statistical method. The method was the same whether the outcome was continuous or categorical (using multivariate linear regression), binary (using multivariate Poisson regression), or pregnancy status by 305 DIM (using survival analyses). First, a large model for each study outcome was fitted using every potential covariate applicable to that outcome, plus the interactions of each covariate with oral Ca bolus supplementation and with herd. The specific terms available to the large models were herd (as a fixed effect), oral Ca bolus supplementation, lactation group (second, third, or fourth and greater), prefresh lameness status (0 if a locomotion score 1 or 2, 1 if a locomotion score 3 or 4), prefresh BCS ($\leq$2.75, 3.00, 3.25, 3.50, 3.75, or $\geq$4.00), twin (0 if single birth, 1 if twin birth), stillbirth (0 if live calf or calves, 1 if 1 or 2 calves born dead), calving

ease score category (1 if ease score of 1, 2 if ease score of 2, 3 if ease score of 3 or 4), calving month (June, July, or August), previous lactation mature-equivalent milk production (expressed as percentage rank within herd—the values for all cows in each herd were ranked from lowest to highest and then assigned a percentage rank, with a value of 100% representing the average mature-equivalent milk production in the herd at that time), previous lactation length (days), previous lactation days dry, and previous lactation gestation length (days). Days in milk at first breeding, AI synchronization status (synchronized = 1; not synchronized = 0), and first breeding month (instead of calving month) were included in the analyses for first-service conception, pregnancy by 150 DIM, and days open for cows pregnant by 150 DIM. The interactions between all variables and herd, plus all interactions between these variables and oral Ca bolus supplementation were also eligible for inclusion in the large models. Terms were removed from the models in a stepwise, backward fashion until all were $P < 0.05$ in the model. Single variables were removed from the model only after no interaction terms were including that variable remaining in the model.

Survival analysis of pregnancy status by 305 DIM required the additional step of testing the reduced large model to determine if the assumption of proportional hazards was valid. This was done by including time-dependent covariates (log-transformed days since VWP) in the large model (Allison, 1995). Because the time-dependent covariates were significant, time-dependent covariates for every variable (plus their interactions) were made available and the model with the extra terms was reduced again by stepwise, backward elimination.

The purpose of the large models was to establish whether an effect of oral Ca bolus supplementation existed after all possible covariates (and interactions) had been considered. However, the large models were not useful for determining effect sizes. Almost all the large models contained continuous covariates after the backward elimination procedure, and least squares means calculated from such models are specific to a discrete value for each continuous covariate in the model. Many of the models contained 3 or 4 continuous covariates, which rendered it impractical to estimate the oral Ca bolus effect at every possible combination of these covariates. Therefore, a second analysis was conducted for each study outcome by using small models that consisted of herd (as a fixed effect), oral Ca bolus supplementation, and the interaction of herd and oral Ca bolus supplementation. The interaction term was removed if $P < 0.05$. Because the small models contained no continuous covariates, they were used to determine the estimates of effect sizes.

The effect of the oral Ca boluses was considered significant for an outcome only if oral Ca bolus supplementation was $P < 0.05$ in both the large and small models for that outcome. Because no continuous covariates were present in the small models, overall least squares means could be calculated for control versus oral Ca bolus-supplemented cows. Least squares means and *P*-values from the small models were then reported for each outcome.

For the pregnancy status by 305 DIM survival analysis, the small model consisted of a Kaplan-Meier analysis (Kaplan and Meier, 1958) using the LIFETEST procedure of SAS. The model included oral Ca bolus supplementation and days from the end of VWP. From this procedure, the effect size of oral Ca supplementation was evaluated by calculating mean days from the end of the VWP until conception for both groups. Days open could be estimated by adding the average VWP to the mean value for days from the end of the VWP until conception.

After all the large and small models were completed and the effects of blanket supplementation for all cows were evaluated, the large models were examined to find interactions ($P < 0.05$) between oral Ca bolus supplementation and any covariate. These interactions were the starting point for determining whether subpopulations of cows responded differently to oral Ca bolus supplementation. When such interactions were found for a continuous covariate, a cut point was derived after visual inspection of a plot of the covariate versus the outcome, and the covariate was dichotomized based on this cut point. The dichotomized covariate was then reevaluated in a large model as a binary outcome. If the interaction of oral Ca bolus supplementation with the dichotomized covariate remained $P < 0.05$ (or if the interaction with any binary covariate was $P < 0.05$), then the interaction was evaluated in a small model that contained only oral Ca bolus supplementation, herd, the covariate of interest, the interaction of this covariate with oral Ca bolus supplementation, the interaction of this covariate with herd, and the interaction of herd with oral Ca bolus supplementation. Interaction terms with herd were removed from the model if $P > 0.05$. Least squares means were computed for the oral Ca bolus-supplemented versus control cows.

Two interactions with oral Ca bolus supplementation were significant at every evaluation point in the analyses described above. Specifically, they were 1) the interaction between prefresh lameness and oral Ca bolus supplementation for the sum of health events before 30 DIM and 2) previous lactation mature-equivalent milk production and oral Ca bolus supplementation for milk production at the first DHI test. Because some cows would be represented in both subpopulations and

Table 3. Summary of continuous and categorical study outcomes and covariates by herd; data are from 927 cows in their second lactation and greater in 2 commercial dairies

	Herd A		Herd B	
Item	n	Mean ± SEM	n	Mean ± SEM
Continuous or categorical outcome				
Ca^{2+} at 8 to 35 h postcalving, mmol/L	318	1.13 ± 0.01	525	1.16 ± 0.01
First-test milk yield, kg	364	44.4 ± 0.6	527	37.2 ± 0.5
Sum of health events[1] ≤30 DIM	372	0.59 ± 0.04	555	1.01 ± 0.04
Postfresh locomotion score, 1 to 4 scale	324	1.79 ± 0.04	466	1.71 ± 0.03
Postfresh BCS, 1 to 5 scale	325	2.51 ± 0.02	466	2.56 ± 0.02
Days open for cows pregnant by 150 DIM	207	90.4 ± 1.7	298	99.5 ± 1.2
Continuous or categorical covariate				
Lactation number	372	2.79 ± 0.05	555	3.05 ± 0.04
Previous lactation length, d	371	361.0 ± 4.1	554	353.1 ± 3.1
Previous gestation length, d	372	277.6 ± 0.3	555	277.4 ± 0.2
Previous lactation 305-d mature-equivalent milk yield, % rank within herd	371	100.6 ± 0.8	554	99.7 ± 0.7
Previous days dry	372	48.6 ± 0.8	555	58.8 ± 1.0
Prefresh locomotion score, 1 to 4 scale	366	1.60 ± 0.04	532	1.63 ± 0.03
Prefresh BCS, 1 to 5 scale	364	3.18 ± 0.02	529	3.26 ± 0.02
Calving ease score, 1 to 5 scale	372	1.19 ± 0.03	555	1.28 ± 0.03
DIM at first test	364	19.4 ± 0.5	527	19.4 ± 0.4
DIM at first breeding	332	73.5 ± 0.3	409	84.3 ± 0.2

[1]Health events included were metritis, ketosis, displaced abomasum, mastitis, pneumonia, herd removal, or death (only for events in the first 30 DIM).

because the most practical application of these results would be to target both subpopulations together for oral Ca bolus supplementation, the 2 covariates were combined into a single covariate. The analyses described above (large models followed by small models) were then repeated using the new, combined covariate as though it were a single covariate. Results were interpreted by evaluating the interaction between the combined covariate and oral Ca bolus supplementation. Least squares means were then reported for the combined subpopulation of cows that would be targeted for oral Ca bolus supplementation.

Residual versus predicted value plots from analysis of the continuous outcomes were visually evaluated as a test for the assumption of normal distribution of the data. Heteroscedasticity or atypical distribution did not appear. Significance was claimed at $P < 0.05$ unless otherwise stated.

RESULTS AND DISCUSSION

Table 3 presents continuous outcomes and covariates by herd, and Table 4 presents binary outcomes and covariates by herd. Only 6 cows (0.6%) were treated for clinical milk fever during the study, and only 14.2% of cows had hypocalcemia (blood Ca^{2+} ≤1.00 mmol/L) when evaluated at 8 to 35 h postcalving. These results are extremely low compared with previously published data (DeGaris and Lean, 2008; Reinhardt et al., 2011) and indicate excellent overall effectiveness of the anionic salt feeding program that was in place for both herds.

The study was conducted only in the summer months; however, it is unlikely that the low observed incidence of hypocalcemia was a seasonal effect. Østergaard et al. (2003) attempted to find published evidence for seasonality of clinical milk fever but was unsuccessful. An evaluation of calvings and cases of clinical milk fever from 6 yr of data in the Dairy Comp 305 archives for both study herds (80 cases of milk fever and 18,887 fresh events for cows in their second lactation and greater) revealed no difference between the risk of milk fever for cows calving in the summer months compared with cows that calved any other time of the year (relative risk of milk fever with summer calvings was 0.63, with a 95% confidence interval of 0.36 to 1.13).

Oral Ca bolus supplementation did not affect ($P > 0.05$) any study outcomes when all study cows were considered together. This result was expected, given the very low incidence of hypocalcemia during the study period. Melendez et al. (2002) also gave oral Ca supplements to multiparous cows fed a low DCAD diet and found no effect of these supplements on plasma concentrations of total Ca, P, Mg, NEFA, BHBA, or glucose.

No effect of oral Ca bolus supplementation was observed on days from the end of the VWP to conception in the large survival model (data not shown) or in the small survival models. Kaplan-Meier curves from the small models are presented in Figure 1 (data from all cows) and Figure 2 (data from cows in the subpopulation targeted for oral Ca bolus supplementation). Hernandez et al. (1999) also reported no effect of oral Ca supplementation on first-service conception;

Table 4. Summary of binary study outcomes and covariates by herd; data are from 927 cows in their second lactation and greater in 2 commercial dairies

	Herd A			Herd B		
Item	1[1]	0[2]	Cows, %	1	0	Cows, %
Binary outcome						
Clinical milk fever	0	372	0.0	6	549	1.1
Hypocalcemia[3]	55	263	17.3	65	460	12.4
Retained placenta	30	342	8.1	63	492	11.4
Metritis ≤14 DIM	52	320	14.0	103	452	18.6
Ketosis[4] ≤16 DIM	98	84	53.8	284	158	64.3
Displaced abomasum ≤30 DIM	12	360	3.2	31	524	5.6
Mastitis ≤30 DIM	38	334	10.2	76	479	13.7
Pneumonia ≤30 DIM	5	367	1.3	22	533	4.0
Herd removal ≤30 DIM	14	358	3.8	44	511	7.9
Died ≤30 DIM	5	367	1.3	18	537	3.2
First-service conception	129	203	38.9	172	237	42.1
Pregnant by 150 DIM	207	104	66.6	298	118	71.6
Binary covariate						
Twin calves	26	346	7.0	46	509	8.3
Stillborn (1 or more calves dead)	11	361	3.0	24	531	4.3
Prefresh lameness[5]	41	325	11.2	63	469	11.8

[1]1 = count of cows with the condition.

[2]0 = count of cows without the condition.

[3]Hypocalcemia was defined as blood Ca^{2+} ≤1.00 mmol/L at 8 to 35 h after calving.

[4]Ketosis was defined as 1 or more blood BHBA tests ≥1.2 mmol/L. Cows were tested 6 times between 3 and 16 DIM and were classified if they had ≥5 total BHBA tests or ≥1 positive test.

[5]Lame cows had a prefresh locomotion score of 3 or 4, using a 1- to 4-point scale.

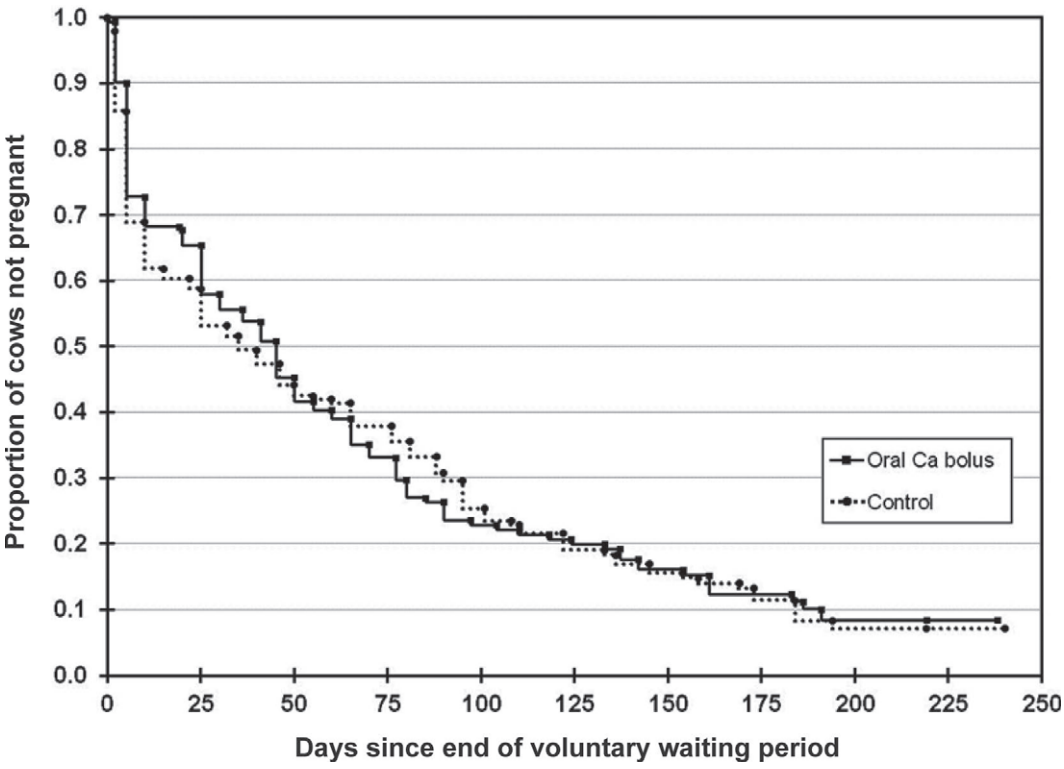

Figure 1. Kaplan-Meier plot for the effect of oral Ca bolus supplementation on pregnancy to 305 DIM. Oral Ca bolus-supplemented cows received 2 boluses (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) after calving. Control cows were not supplemented with oral Ca boluses. Data are from 638 cows in their second lactation and greater in 2 commercial dairies that were eligible to be bred at the end of the voluntary waiting period.

however, this was a small study that enrolled cows only with retained fetal membranes. Chapinal et al. (2012) reported that cows with low serum Ca either the week before or the week after calving had reduced odds for conceiving at first service. The authors did not evaluate reproductive performance beyond the first service.

Two variables had significant interactions with oral Ca bolus supplementation that were present throughout the process of evaluating the large and small models. The first was the interaction between oral Ca bolus supplementation and prefresh lameness (locomotion score 3 or 4) for the sum of health events by 30 DIM (Table 5; $P = 0.005$). The other variable to have a significant interaction with oral Ca bolus supplementation was previous lactation mature-equivalent milk production rank with first-test milk yield (Table 6; $P = 0.015$). Prefresh lameness had a significant interaction with first-test milk yield in the large model; however, this interaction was not significant in the small model.

Using the small models, we calculated least squares means for oral Ca bolus-supplemented and control cows for first-test milk yield across a range of values for previous lactation milk yield. These least squares means were then plotted (Figure 3). Based on an evaluation of this plot, cut points between 100 and 115 previous lactation milk yield percentage rank were considered. These cut points were evaluated for their effect on both first test milk yield and the sum of health events in early lactation. The cut point was kept as low as possible to maximize the number of cows that could benefit from oral Ca bolus supplementation, still preserve a significant increase in milk yield, and not increase the number of health events before 30 DIM. A cut point of >105% of herd rank was the lowest cut point at which oral Ca bolus supplementation significantly increased milk yield without impairing health.

A new analysis was then conducted, starting with a new stepwise, backward elimination in the large model, to determine how the new dichotomous variable (previous lactation mature-equivalent milk yield >105% or ≤105% of herd rank) affected oral Ca bolus response. Cows above the cut point had significantly ($P = 0.024$) increased milk yield when supplemented with the oral Ca bolus compared with cows above the cut point that were not supplemented. This dichotomized variable was then included in a final, small model. The response to oral Ca bolus supplementation in cows with a high previous lactation milk yield was +2.9 kg of milk at the

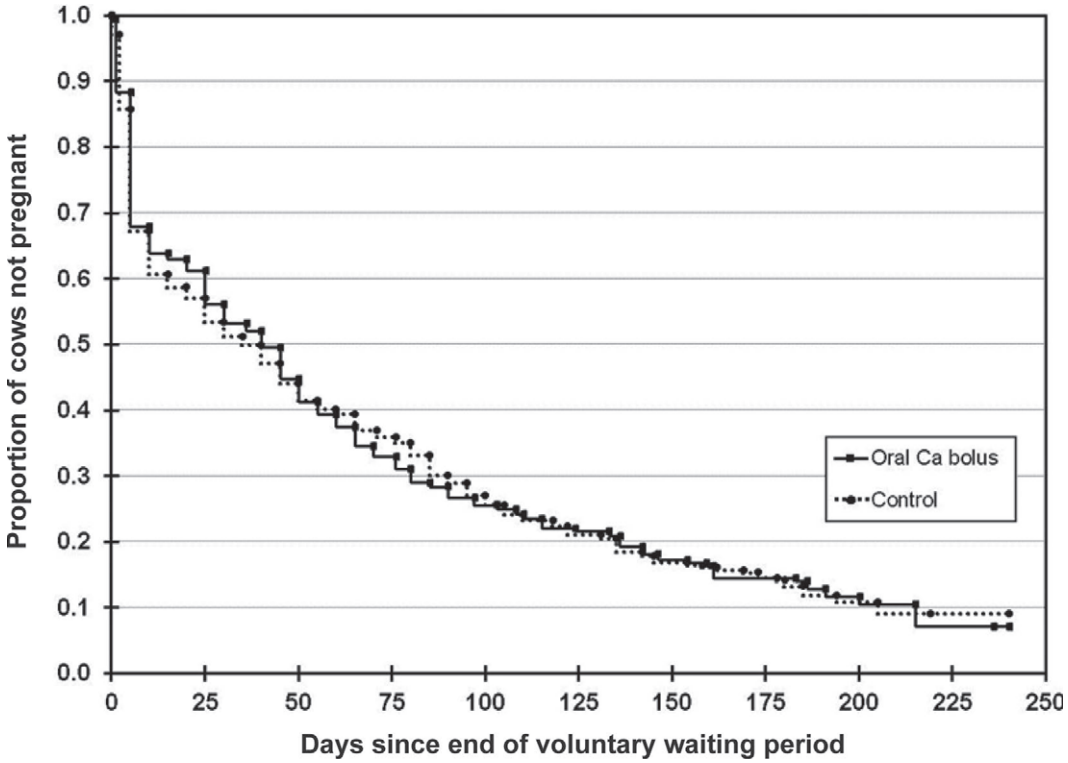

Figure 2. Kaplan-Meier plot for the effect of oral Ca bolus supplementation on pregnancy to 305 DIM. Oral Ca bolus-supplemented cows received 2 boluses (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) after calving. Control cows were not supplemented with oral Ca boluses. Data are from 313 cows in their second lactation and greater in 2 commercial dairies that were eligible to be bred at the end of the voluntary waiting period and were in the subpopulation targeted for oral Ca bolus supplementation (previous lactation mature-equivalent milk production >105% of herd average at calving or prefresh lameness, or both).

Table 5. Estimates and type 3 tests of fixed effects from a reduced mixed regression model for the sum of health events[1] in the first 30 DIM[2]

Effect and effect level	Estimate	SE	Numerator df	Denominator df	*P*-value[3]
Intercept	1.292	0.289	—	—	<0.001
Oral Ca bolus supplementation			1	867	0.120
Control (no oral Ca boluses)	0.368	0.159			
Supplemented (2 oral Ca boluses given)	—[4]	—[4]			
Herd			1	867	0.002
Herd A	−0.406	0.322			
Herd B	—[4]	—[4]			
Lactation group			2	867	0.032
Lactation = 2	−0.170	0.068			
Lactation = 3	−0.051	0.073			
Lactation ≥4	—[4]	—[4]			
Prefresh lameness			1	867	0.046
Not lame (locomotion score 1 or 2)	0.064	0.121			
Lame (locomotion score 3 or 4)	—[4]	—[4]			
Prefresh BCS			4	867	0.382
≤2.75 BCS	0.006	0.149			
3.00 BCS	0.163	0.133			
3.25 BCS	0.033	0.121			
3.50 BCS	0.167	0.128			
≥3.75 BCS	—[4]	—[4]			
Calving month			2	867	<0.001
June	—[4]	—[4]			
July	0.037	0.070			
August	−0.276	0.072			
Previous lactation milk yield,[5] % rank within herd	−0.005	0.002	1	867	0.003
Previous lactation length, d	0.0003	0.0005	1	867	0.005
Previous dry period length, d	0.004	0.001	1	867	0.009
Herd × previous lactation length			1	867	0.049
Herd A and previous lactation length	0.0014	0.0007			
Herd B and previous lactation length	—[4]	—[4]			
Herd × prefresh BCS			4	867	0.021
Herd A and ≤2.75 BCS	−0.464	0.230			
Herd A and 3.00 BCS	−0.689	0.212			
Herd A and 3.25 BCS	−0.416	0.203			
Herd A and 3.50 BCS	−0.573	0.218			
All other combinations	—[4]	—[4]			
Oral Ca bolus × prefresh lameness			1	867	0.005
No oral Ca boluses and not lame	−0.474	0.169			
All other combinations	—[4]	—[4]			

[1]Health events included were metritis, ketosis, displaced abomasum, mastitis, pneumonia, herd removal, or death (only for events in the first 30 DIM).

[2]All possible covariates plus interactions with herd and oral Ca bolus supplementation (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) were considered and removed by backward elimination until $P < 0.05$ in the model. Cows in the oral Ca bolus group received 2 oral Ca boluses (1 bolus at calving and 1 bolus 8 to 35 h after calving). Data are from 927 cows in their second lactation and greater in 2 commercial dairies.

[3]Except for the intercept, *P*-values reported are the type 3 test of fixed effects for the entire variable.

[4]Reference group.

[5]The 305-d mature-equivalent milk production; 100% represented the average cow in the herd at the time the cow calved.

first DHI test after calving ($P = 0.009$; Table 7). This increase in milk yield (7.2%) was of greater magnitude than the 3.6% increase in milk yield reported for cows supplemented with anionic salts (Beede et al., 1992). The inclusion of first-lactation animals in the analysis of Beede et al. (1992) could explain a portion of the lower overall milk production response. Smaller scale studies have shown no effect of oral Ca supplementation on subsequent milk yield (Goff et al., 1996; Dhiman and Sasidharan, 1999; Melendez et al., 2002); these studies did not attempt to identify subpopulations of cows that might have a different response to oral Ca supplementation.

Although a significant interaction was observed between oral Ca bolus supplementation and lameness for the sum of early-lactation health events, no significant effect of oral Ca bolus supplementation was observed for any of the individual disease or reproductive outcomes (Table 8). Oetzel (1996) reported a decreased incidence of displaced abomasum after oral Ca administration around calving; however, the underlying incidence of hypocalcemia (53%) was much greater in this study

compared with 14% in the current one. Melendez et al. (2002) and Dhiman and Sasidharan (1999) reported no effect of oral Ca supplementation around calving on later concentrations of BHBA, and Goff et al. (1996) reported no effect of oral Ca supplementation on rates of primary ketosis. These findings are in agreement with the current study, which demonstrated no effect of oral Ca supplementation on the incidence of cows with blood BHBA ≥1.2 mmol/L.

No other variables had a significant interaction with oral Ca bolus supplementation. Thus, the final target group for oral Ca bolus supplementation was cows that were lame in the prefresh period and cows with higher previous lactation mature-equivalent milk production (>105% of herd rank). Lame cows and cows with higher previous milk production were combined and designated with a single new binary variable in the data set. This subpopulation represented 444 cows, or

Table 6. Type 3 tests of fixed effects from a reduced mixed regression model for first-test milk yield (kg/cow per day)[1]

Effect and effect level	Estimate	SE	Numerator df	Denominator df	*P*-value[2]
Intercept	−2.00	22.52	—	—	0.929
Oral Ca bolus supplementation			1	831	0.057
Control (no oral Ca boluses)	5.42	4.14			
Supplemented (2 oral Ca boluses given)	—[3]	—[3]			
Herd			1	831	0.045
Herd A	−73.39	34.54			
Herd B	—[3]	—[3]			
Prefresh lameness			1	831	0.478
Not lame (locomotion score 1 or 2)	−1.30	1.40			
Lame (locomotion score 3 or 4)	—[3]	—[3]			
Prefresh BCS			4	831	0.337
≤2.75 BCS	−3.41	1.70			
3.00 BCS	−3.84	1.48			
3.25 BCS	−2.42	1.37			
3.50 BCS	−2.54	1.47			
≥3.75 BCS	—[3]	—[3]			
Calving month			2	831	0.271
June	—[3]	—[3]			
July	1.42	1.06			
August	0.24	1.06			
Previous lactation milk yield,[4] % rank within herd	0.260	0.029	1	831	<0.001
Previous lactation length, d	−0.0095	0.0041	1	831	0.023
Previous gestation length, d	0.040	0.081	1	831	0.005
DIM at first test	0.449	0.033	1	831	<0.001
Herd × previous gestation length			1	831	0.028
Herd A and previous gestation length	0.275	0.125			
Herd B and previous gestation length	—[3]	—[3]			
Herd × calving month			2	831	0.003
Herd A and July calving month	−3.77	1.67			
Herd A and August calving month	0.94	1.64			
All other combinations	—[3]	—[3]			
Herd × prefresh BCS			4	831	0.028
Herd A and ≤2.75 BCS	5.01	2.63			
Herd A and 3.00 BCS	7.17	2.41			
Herd A and 3.25 BCS	6.80	2.30			
Herd A and 3.50 BCS	4.50	2.48			
All other combinations	—[3]	—[3]			
Oral Ca bolus × previous lactation milk yield			1	831	0.015
No oral Ca boluses and previous milk yield	−0.092	0.038			
Oral Ca boluses and previous milk yield	—[3]	—[3]			
Oral Ca bolus × prefresh lameness			1	831	0.042
No oral Ca bolus and not lame	4.00	1.97			
All other combinations	—[3]	—[3]			

[1]All possible covariates plus interactions with herd and oral Ca bolus (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) supplementation were considered and removed by backward elimination until $P < 0.05$ in the model. Cows in the oral Ca bolus group received 2 oral Ca boluses (1 bolus at calving and 1 bolus 8 to 35 h after calving). Data are from 927 cows in their second lactation and greater in 2 commercial dairies. Health events included were metritis, ketosis, displaced abomasum, mastitis, pneumonia, herd removal, or death (only for events in the first 30 DIM).

[2]Except for the intercept, *P*-values reported are the type 3 test of fixed effects for the entire variable.

[3]Reference group.

[4]The 305-d mature-equivalent milk production; 100% represented the average cow in the herd at the time the cow calved.

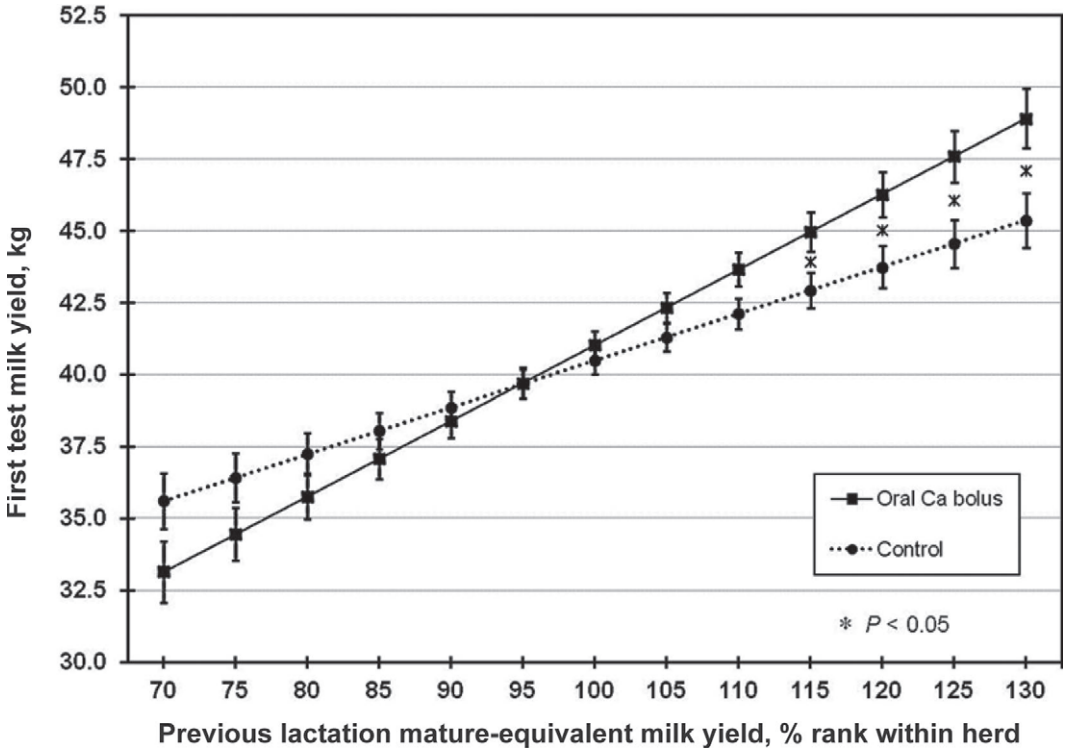

Figure 3. Interaction between oral Ca bolus supplementation and previous lactation mature-equivalent milk yield (expressed as percentage rank within herd) for first-test milk yield after calving. Oral Ca bolus-supplemented cows received 2 boluses (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO) after calving. Control cows were not supplemented with oral Ca boluses. Data are from 927 cows in their second lactation and greater in 2 commercial dairies.

about 48% of the eligible cows. After combining the 2 targeted groups, the same analyses using the smaller models were done for all outcomes, this time looking at the interaction between oral Ca bolus and the new variable that represented the combined subpopulations. These results are reported in Tables 7 and 8. The combined lame cows and cows with high previous lactation milk production gave 3.1 kg more milk ($P = 0.002$) compared with the control cows. This same group of cows had 0.04 fewer health events in the first 30 DIM. This difference was not significant ($P = 0.628$), although it is noteworthy that cows supplemented with oral Ca boluses gave more milk without a concomitant increase in health events. The size of the milk yield increase after oral Ca bolus supplementation to the targeted subpopulation of cows in the current study was very similar to the early-lactation milk yield losses of 3.2 kg/d for cows with serum Ca $\leq$2.1 mmol/L during wk -1 relative to calving and 4.8 kg/d for cows with serum Ca $\leq$2.1 mmol/L during wk $+1$ relative to calving reported by Chapinal et al. (2012).

Oral Ca bolus supplementation did not improve Ca^{2+} concentrations in the sample collected at 8 to 35 h after calving ($P = 0.271$). The timing of the collection of the Ca^{2+} sample (20.6 h after administration of the first bolus, and immediately before the administration of the second bolus) was such that an effect of oral Ca supplementation was not expected. Sampson et al. (2009) reported that oral Ca boluses increased blood Ca^{2+} concentrations at only 2 time points—1 h after administration of both the first oral Ca bolus (given at calving) and 1 h after administration of the second bolus (given 12 h after calving). Sampson et al. (2009) also reported a significant decrease in urinary pH at 24 h after calving, which could explain more prolonged benefits to oral Ca bolus administration beyond the short time period of increased blood Ca^{2+}.

It was not feasible in the current study to document blood Ca^{2+} changes soon after the second bolus was administered because the cows could be restrained in headlocks only once daily and were restrained for the shortest time possible at each lockup. Ramos-Nieves et al. (2009) reported that cows had the highest proportion of subclinical hypocalcemia about 16 h after calving, which is close to the mean time (20.6 h postcalving) that the second bolus was administered in the current study.

The mechanism for the beneficial effect of oral Ca bolus supplementation cannot be determined from the results of this study. Lame cows could be prone

to injury after calving, especially if they are weakened by hypocalcemia. Transient correction of hypocalcemia could prevent injury and decrease the total number of health events in lame cows. Stimulation of additional DMI after correction of transient hypocalcemia is a plausible explanation for the increased milk yield. This explanation is consistent with the observation that feeding low DCAD diets before calving was associated with higher DMI in early lactation (Eppard et al., 1996; Joyce et al., 1997). However, DMI in individual cows was not measured in the current study.

Heuer et al. (1999) reported that overconditioned cows are at increased risk of hypocalcemia. However, prefresh BCS did not have a significant interaction with oral Ca bolus supplementation in the current study. The number of overly conditioned animals (BCS $\geq$4.00) was only about 4% for the 2 study herds.

Increasing lactation number has been associated with increased risk of hypocalcemia (Reinhardt et al., 2011). However, parity did not have a significant interaction with oral Ca bolus supplementation in the current study. This finding suggests that oral Ca supplementation should not be restricted to very old (e.g., lactation 3 or greater) cows only.

Results of this study did not reveal any detrimental effects of providing additional anions (in this case, chloride and sulfate anions from the oral Ca boluses) to cows that had received a low DCAD diet before calving. This was not surprising, considering that cows have lowered feed intake on the day of calving and are typically switched from the low DCAD diet soon after calving. Cows in the current study were all consuming a higher DCAD (lactating) diet when they received their second oral Ca bolus. It appeared that the benefits of the additional acidification from oral Ca bolus administration (Sampson et al., 2009) caused more benefits via improved Ca metabolism than potentially detrimental effects from systemic acidification. Supporting higher

Table 7. Least squares means for cows supplemented with an oral Ca bolus[1] or control cows (no oral Ca bolus supplementation) for continuous or categorical study outcomes from 927 cows in their second lactation and greater in 2 commercial dairies[2]

	Oral Ca bolus		Control			
Outcome	n	Least squares mean ± SE	n	Least squares mean ± SE	Difference[3]	*P*-value[4]
Ionized Ca, 8 to 35 h postcalving, mmol/L						
All cows	418	1.15 ± 0.01	425	1.14 ± 0.01	0.01	0.271
Lame[5] or previous milk >105%[6]	199	1.15 ± 0.01	209	1.12 ± 0.01	0.02	0.123
First-test milk yield, kg						
All cows	412	41.1 ± 0.5	497	40.5 ± 0.5	0.6	0.404
Previous milk >105%	168	46.1 ± 0.8	244	43.3 ± 0.7	2.9	0.009
Lame or previous milk >105%	198	45.2 ± 0.7	233	42.2 ± 0.7	3.1	0.002
Sum of health events ≤30 DIM						
All cows	431	0.84 ± 0.04	496	0.76 ± 0.04	0.07	0.182
Lame	52	0.89 ± 0.12	51	1.23 ± 0.12	−0.34	0.040
Lame or previous milk >105%	204	0.72 ± 0.06	238	0.76 ± 0.05	−0.04	0.628
Postfresh locomotion score						
All cows	381	1.74 ± 0.04	409	1.82 ± 0.05	−0.06	0.256
Lame or previous milk >105%	187	1.78 ± 0.06	202	1.82 ± 0.05	−0.04	0.776
Postfresh BCS						
All cows	381	2.49 ± 0.02	410	2.57 ± 0.02	−0.08	0.089[7]
Lame or previous milk >105%	187	2.46 ± 0.03	202	2.48 ± 0.03	−0.01	0.756
Days open for cows pregnant by 150 DIM						
All cows	239	96.6 ± 1.5	266	93.5 ± 3.1	2.0	0.124
Lame or previous milk >105%	119	99.8 ± 2.1	124	93.0 ± 2.0	6.8	0.053
Days from VWP to conception for cows to 305 DIM[8]						
All cows	295	70.9 ± 4.2	343	68.8 ± 3.7	2.1	0.930
Lame or previous milk >105%	146	69.0 ± 5.4	167	68.0 ± 5.1	0.9	0.796

[1]Cows in the supplemented group received 2 oral Ca boluses (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO; 1 bolus at calving and 1 bolus 8 to 35 h after calving).

[2]Results are from small models that included oral Ca bolus supplementation, herd, and their interaction (if $P < 0.05$ for the interaction term).

[3]Difference in least squares means, oral Ca bolus − control.

[4]For interaction terms, *P* is the higher of the specific comparison or the interaction term.

[5]Lame cows had a prefresh locomotion score of 3 or 4, using a 1- to 4-point scale.

[6]Previous lactation mature-equivalent milk yield, % of herd rank.

[7]The *P*-value for postfresh BCS is from the large model, which was $P > 0.05$ and was greater than the *P*-value from the small model.

[8]Estimate of mean days from the end of the voluntary waiting period (VWP) to pregnancy using Kaplan-Meier analysis. The mean voluntary waiting period was 72.5 d for all cows and 72.7 d for cows in the subpopulation targeted for oral Ca bolus supplementation.

Table 8. Least squares means for cows supplemented with an oral Ca bolus[1] or control cows with no oral Ca bolus supplementation for binary outcomes (health events ≤30 DIM and reproductive outcomes) from 927 cows in their second lactation and greater in 2 commercial dairies[2]

	Oral Ca bolus[1]		Control		Oral Ca versus control		
Outcome	n	Risk, %	n	Risk, %	Risk ratio	95% CI	*P*-value[3]
Metritis, %							
All cows	431	17.2	496	15.2	1.13	0.85 to 1.51	0.394
Lame[4] or previous milk >105%[5]	206	14.0	238	14.9	0.94	0.61 to 1.47	0.794
Ketosis,[6] %							
All cows	290	60.5	334	57.4	1.40	0.93 to 1.19	0.422
Lame or previous milk >105%	129	55.7	165	54.2	1.03	0.85 to 1.25	0.834
Displaced abomasum, %							
All cows	431	4.4	496	4.1	1.09	0.61 to 1.96	0.764
Lame or previous milk >105%	206	4.0	238	5.0	0.81	0.35 to 1.87	0.619
Mastitis, %							
All cows	431	12.9	496	10.6	1.22	0.84 to 1.77	0.297
Lame or previous milk >105%	206	13.7	238	9.8	1.39	0.83 to 2.34	0.512
Pneumonia, %							
All cows	431	2.2	496	2.4	0.91	0.43 to 1.93	0.813
Lame or previous milk >105%	206	1.2	238	3.6	0.32	0.09 to 1.11	0.073
Removal from the herd %							
All cows	431	6.5	496	4.6	1.41	0.85 to 2.33	0.182
Lame or previous milk >105%	206	5.1	238	4.3	1.17	0.54 to 2.55	0.686
Died, %							
All cows	431	2.7	496	1.5	1.78	0.79 to 4.02	0.167
Lame or previous milk >105%	206	2.5	238	1.4	1.76	0.52 to 6.04	0.877
First-service conception, %							
All cows	343	38.6	398	42.0	0.92	0.77 to 1.10	0.347
Lame or previous milk >105%	168	33.8	193	39.6	0.85	0.65 to 1.11	0.434
Pregnancy by 150 DIM, %							
All cows	337	70.5	390	67.8	1.04	0.95 to 1.15	0.416
Lame or previous milk >105%	164	72.1	186	66.1	1.09	0.95 to 1.26	0.391

[1]Cows in the supplemented group received 2 oral Ca boluses (Bovikalc, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO; 1 bolus at calving and 1 bolus 8 to 35 h after calving).

[2]Results are from small models that included oral Ca bolus supplementation, herd, and their interaction (if $P < 0.05$ for the interaction term).

[3]For interaction terms, *P* is the higher of the specific comparison or the interaction term.

[4]Lame cows had a prefresh locomotion score of 3 or 4, using a 1- to 4-point scale.

[5]Previous lactation mature-equivalent milk production, % of herd rank.

[6]Ketosis was defined as 1 or more blood BHBA tests ≥1.2 mmol/L. Cows were tested 6 times between 3 and 16 DIM and were classified if they had ≥5 total BHBA tests or ≥1 positive test.

blood Ca concentrations during the critical first 2 d after calving may be of primary importance to multiparous cows.

CONCLUSIONS

Supplementing all cows in their second lactation and greater with 2 oral Ca boluses in herds with very effective programs of feeding anionic salts neither harmed nor benefited early-lactation health or milk yield. Cows that were lame before calving and were supplemented with oral Ca boluses had improved early-lactation health compared with lame cows that were not supplemented. Cows that had high previous lactation mature-equivalent milk production and were supplemented with oral Ca boluses had increased early-lactation milk yield compared with high-producing cows that were not supplemented. This subpopulation of lame and higher producing cows represented 48% of the multiparous cows in the 2 study herds. Supplementation of the combined subpopulation of cows with oral Ca boluses resulted in increased milk yield without affecting early-lactation health. These results indicate that dairy herds already experiencing a very low incidence of hypocalcemia can target a subpopulation of cows that will respond favorably to supplementation with oral Ca boluses.

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