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# Effects of oral calcium supplementation on mineral and acid-base status, energy metabolites, and health of postpartum dairy cows

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## ABSTRACT

Two experiments were conducted to characterize blood concentrations of minerals and acid-base status after oral dosing of Ca salts and to determine the effects of oral Ca on mineral and metabolic status and incidence diseases. The hypotheses were that administration of oral Ca as $CaCl_2$ and $CaSO_4$ maintains blood total Ca (tCa) concentrations ≥2.125 m*M* and reduces the incidence of diseases in early lactation. In experiment 1, 18 Holstein cows on the day of calving were assigned to receive a single dose of 0, 43, or 86 g of Ca as an oral bolus. Blood was sampled before and after treatments to characterize acid-base status and concentrations of minerals. In experiment 2, 450 Holstein cows considered of low (LRM; normal calving) or high risk (HRM; dystocia, twins, stillbirth, retained placenta, vulvo-vaginal laceration, or a combination of these) of metritis (primiparous-LRM = 84; primiparous-HRM = 84; multiparous-LRM = 138; multiparous-HRM = 138) on the day of calving were blocked by parity and then randomly assigned to control, no Ca supplementation; 86 g of Ca on d 0 and 1 postpartum (CaS1); or 86 g of Ca on d 0 and 1 postpartum followed by 43 g/d on d 2 to 4 postpartum (CaS4). Blood was sampled before and 30 min after treatment on d 0, and 30 min after treatments on d 1 to 4, and d 7 and 10 for determination of concentrations of minerals and metabolites and blood acid-base responses. Disease incidence was evaluated for the first 30 DIM. Concentrations of ionized Ca (iCa) increased for 2 h in cows supplemented with 43 g of Ca and fewer than 8 h in cows supplemented with 86 g of Ca. The changes in iCa concentrations from pretreatment to 30 min after 86 g of Ca supplemented on d 0 were 0.11 ± 0.03 m*M* in multiparous cows and 0.25 ± 0.03 m*M* in primiparous cows. Oral Ca reduced the incidence of subclinical hypocalcemia (SCH; tCa <2.125 m*M*) in the first 4 d in the experiment (control = 69.3%; CaS1 = 57.5%; CaS4 = 34.2%). Calcium supplementation decreased the prevalence of SCH on d 0 and 1 postpartum in all cows. Stopping oral Ca in CaS1 on d 1 postpartum, however, caused a rebound in SCH on d 2 to 4 postpartum in primiparous cows. Oral Ca increased the incidence of metritis (control = 22.7%; CaS1 = 34.8%; CaS4 = 32.8%), primarily because of an increase in LRM primiparous cows (control = 17.9%; CaS1 = 35.7%; CaS4 = 42.9%). Oral Ca increased morbidity in primiparous cows (control = 38.1%; CaS1 = 61.8%; CaS4 = 60.3%) but had no effect on multiparous cows (control = 38.2%; CaS1 = 35.1%; CaS4 = 30.1%). Large doses of oral Ca as salts of chloride and sulfate in the first days postpartum should be avoided in primiparous cows and used only in cows at risk of clinical hypocalcemia.

**Key words:** calcium supplementation, dairy cow, metritis, subclinical hypocalcemia

## INTRODUCTION

Subclinical hypocalcemia (**SCH**) affects approximately 47% of the multiparous cows and 25% of the primiparous cows in dairy farms in the United States (Reinhardt et al., 2011). Recent studies demonstrated that SCH increased concentrations of nonesterified fatty acids in plasma and impaired innate immune function (Martinez et al., 2014). In addition, SCH was associated with increased incidence of uterine and other diseases (Seifi et al., 2011; Martinez et al., 2012), increased risk of culling, and reduced productive and reproductive performance (Chapinal et al., 2012). The increased incidence of uterine diseases observed in cows with SCH was attributed to a compromised innate immune system (Martinez et al., 2012). Induction of SCH in nonpregnant nonlactating cows reduced rumen contractions and DMI, and impaired insulin release

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based on decreased concentrations of insulin concurrent with increased concentrations of glucose and fatty acids (Martinez et al., 2014). Also, parathyroid hormone, which is in high concentrations during hypocalcemia, is known to suppress insulin signaling in adipocytes and exacerbate insulin resistance (Chang et al., 2009). Furthermore, cows induced to have SCH had neutrophils with less cytosolic ionized Ca (**iCa**), which affected phagocytosis and oxidative burst activities (Martinez et al., 2014). Collectively, it is clear that SCH can have many detrimental effects on health of dairy cows and it plausible to suggest that maintaining adequate circulating iCa concentrations during the first days postpartum might improve energetic status and innate immunity, and reduce the incidence of uterine diseases (Martinez et al., 2012).

Implementation of prepartum acidogenic diets, limited Ca intake prepartum, and supplementation with vitamin D have reduced the incidence of clinical hypocalcemia to 3 to 7%; nevertheless, the prevalence of SCH remains high (Reinhardt et al., 2011). Therefore, alternative strategies that complement the use of prepartum feeding of acidogenic salts or other methods of prevention are needed to further minimize the issues associated with early lactation SCH. Supplementation with oral Ca around calving was implemented originally to prevent clinical hypocalcemia (Thilsing-Hansen et al., 2002). Providing a highly soluble source of oral Ca induces high concentrations of iCa in the lumen of the gastrointestinal tract, likely much greater than that typically detected in the vascular compartment (Höller et al., 1988). Thus, the high concentrations of iCa in the rumen lumen induce a chemical gradient that passively transports iCa from the mucosa through the tight junctions toward the extracellular space in the serosal side, increasing concentrations of iCa in blood (Bronner, 1987). Multiple studies evaluating administration of oral Ca concluded that $CaCl_2$ provided a rapid increase in blood iCa for prevention of clinical hypocalcemia (Jorgensen, 1974; Goff and Horst, 1993, 1994). In spite of those findings, studies evaluating the effect of oral administration of different Ca salts have observed contrasting results on blood concentrations of Ca and incidence of peripartum diseases (Oetzel, 1996; Melendez et al., 2003; Oetzel and Miller, 2012).

We hypothesized that oral Ca supplementation during the early postpartum period maintains blood total Ca (**tCa**) concentrations $\geq$2.125 m*M* and reduces the incidence of SCH and metritis early postpartum, particularly when supplementation is extended for the first 4 d postpartum. It was also anticipated that the benefits of oral Ca would be observed in cows regardless of risk of developing metritis. Therefore, the objectives were to characterize the concentrations of Ca in blood after oral administration of Ca as $CaCl_2$ and $CaSO_4$, and to evaluate the effect of Ca supplementation and duration of supplementation on the incidence of uterine and other diseases during the early postpartum period in dairy cows considered to be of low or high risk of developing metritis.

## MATERIALS AND METHODS

All procedures involving cows in the experiment were approved by the University of Florida Institute of Food and Agricultural Sciences Animal Research Committee protocol ARC-002-14ANS. The experiments were conducted from September 2013 to February 2014 in a commercial dairy farm in California milking 5,226 cows during the experimental period and with a rolling herd average of 13,635 kg of 3.5% FCM.

### *Experiment 1: Blood Ca Concentrations and Acid-Base Status After Oral Ca Administration*

The experiment was a completely randomized design. Nine primiparous and 9 multiparous Holstein cows without complications at calving (no assistance, singleton live calf, and shed the placenta within 12 h) were used in this experiment to characterize blood concentrations of Ca and Mg as well as acid-base status with or without supplemental oral Ca administration. On the day of calving, after colostrum milking, treatments were randomly assigned to cows such that 3 primiparous and 3 multiparous cows each received one dose of 0, 43, or 86 g of supplemental Ca as an oral bolus containing a combination of $CaCl_2$, $CaSO_4 \cdot 0.5H_2O$, and $CaSO_4 \cdot 2H_2O$ (Bovikalc; Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO). Jugular venous blood was collected into 3-mL lithium heparin evacuated tubes (Vacutainer, Becton Dickinson, Franklin Lakes, NJ) immediately before and at 0.5, 1, 2, 4, 8, 12, and 24 h after treatment. Samples were analyzed within 5 min of collection for pH, partial pressure of $CO_2$ (**$PCO_2$**), base excess, and concentrations of iCa, $HCO_3$, Na, and K using a handheld biochemical analyzer (VetScan i-STAT, Abaxis, Union City, CA). In addition, at each sampling point, blood was also sampled into evacuated tubes without anticoagulant, allowed to clot, and placed in ice until processing. Within 4 h of collection, samples were centrifuged, and serum was harvested and frozen at −20°C until analyses. Serum samples were analyzed for concentrations of tCa and Mg using an atomic absorption spectrophotometer (AAnalyst 200, Perkin-Elmer Inc., Waltham, MA) and according to a procedure previously described (Martinez et al., 2012).