Dietary Manipulations and Interventions to Improve Calcium Metabolism

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Introduction

Hypocalcemia is a common and important problem in dairy cows. It is usually defined as subclinical and clinical according to blood concentrations of total (**tCa**) or ionized (**iCa**) calcium (**Ca**) and the diagnosis of clinical signs. Cows with clinical hypocalcemia present muscle weakness and fasciculation, inability to control body temperature, anorexia, and or inability to stand which eventually leads to recumbency, coma, and death if untreated. Although the clinical form of hypocalcemia (**CH**) can result in death, it usually is easily controlled affecting only 3 to 5% of the postpartum dairy cows, primarily older cows. On the other hand, the subclinical form is much more prevalent and can have detrimental impacts to subsequent health. Depending upon how it is defined and the frequency of blood sampling for diagnosis, subclinical hypocalcemia (**SCH**) can affect 25 to 40% of primiparous and 45 to 80% of the multiparous cows. Cows with SCH have reduced dry matter (**DM**) intake, suppressed measures of innate and acquired immune function, compromised energy metabolism and increased incidence of other periparturient diseases. The reason why cows develop hypocalcemia is the combination of colostrum synthesis associated with the inability to quickly restore the blood pool of Ca either from bone remodeling, gut absorption, or renal reabsorption. Removing the mammary gland greatly diminishes the decline in blood Ca around parturition. Improper diets are a major risk factor for hypocalcemia. Dietary manipulations are opportunities to improve early lactation Ca homeostasis. Altering the mineral composition of the prepartum diet to result in a negative dietary cation-anion difference (**DCAD**) to induce a compensated metabolic acidosis has been shown to reduce the risk of CH and SCH. Furthermore, adjusting the concentrations of Ca, P, and Mg also are important for success of a negative DCAD diet. Other alternatives to control hypocalcemia include feeding very low concentrations of dietary Ca prepartum (<0.30%), intestinal sequestration of Ca by feeding synthetic zeolite, or administration of Ca salts immediately after calving. This manuscript reviews recent research on methods to control and reduce the impact of hypocalcemia in dairy cows.

Hypocalcemia

Dairy cows develop hypocalcemia because of the inability to restore blood concentrations of Ca with the onset of colostrogenesis and lactation. In general, blood

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concentrations of Ca start to decline on the last day or two of gestation (Goff et al., 2002; Kimura et al., 2006) because of sequestration in the mammary gland for colostrum synthesis. Mastectomized Jersey cows did not experience any drop in concentrations of tCa in plasma with parturition, thereby reinforcing the concept that changes in Ca around calving are the result of mammary secretion into colostrum and milk, and not related to the endocrine changes with calving (Goff et al., 2002).

In general, the dairy cow in late gestation and early lactation has very dynamic and responsive Ca homeostatic mechanisms to assure that the degree of hypocalcemia is controlled and does not lead to death. Nevertheless, whenever these homeostatic and homeorhetic mechanisms fail at the onset of lactation, then CH might occur. Therefore, milk fever or CH is caused by the inability of the cow to rapidly adapt to the increased needs of Ca and not because of a dietary deficit. It is known that CH is a problem that affects primarily older cows and prepartum nulliparous cows are almost never diagnosed with milk fever. It is thought that the greater colostrum synthesis associated with a less dynamic and active Ca resorption mechanism favors the occurrence of CH in older than younger cows. It has been estimated that the risk of CH increases 9% for every lactation in the life of a cow (DeGaris and Lean, 2008). Figure 1 illustrates the changes in colostrum yield and concentration of Ca in colostrum according to parity and prepartum DCAD fed (Martinez et al., 2014). It is clear that multiparous cows secrete larger quantities of Ca in the first milking (52% more or 9 g), and this difference is almost 3 times the entire plasma pool of a dairy cow. If one assumes that the plasma volume in adult Holstein cows is similar to those estimated for beef cattle and Guernsey cows, approximately 40 mL/kg of live weight (Reynolds, 1953; Springel, 1968), then typical postpartum cows would have approximately 27 L of plasma containing approximately 90 mg of Ca/L or a total of 2.43 g. It is not surprising that an additional 9 g of Ca secreted during the first milking would impose a greater challenge for multiparous cow to adjust their blood Ca concentration compared with the challenge faced by primiparous cows.

Although CH can be tragic, the most common presentation of this disorder is the subclinical form, in which blood Ca concentrations are below those considered normal, but the cow presents no visible clinical signs. In general, SCH is defined as tCa ≤ 2.0 m*M* or < 8 mg/dL by most authors (Goff et al, 2014; Reinhardt et al., 2011), although the rationale for such a cut-off has not been clearly defined. Recently, we reported that cows with serum tCa of < 2.15 m*M* (< 8.59 mg/dL) had a marked increase in the risks of metritis, puerperal metritis and other diseases in the first month postpartum (Martinez et al., 2012). More striking was the fact that the risk of uterine diseases greatly increased with a decrease in serum tCa concentrations in the first 3 DIM (**Figure 2**). Inducing SCH by intravenous infusion of a Ca-specific chelating agent in dry cows depressed DM intake almost 5 kg/d compared with saline, depressed rumen contractility, impaired insulin release and increased lipid mobilization (Martinez et al., 2014). Induction of SCH reduced iCa in immune cells, which impaired their ability to phagocytize and kill bacteria in vitro. It seems that SCH can have a range of detrimental effects on dairy cows. Therefore, managing blood Ca in dairy cows involves not only reducing the risk of CH but also preventing SCH.

Dietary Methods to Reduce Hypocalcemia

Three dietary strategies have been evaluated to reduce the risk of CH and SCH in dairy cows immediately after calving. Those strategies involve altering the mineral composition of the prepartum diet or adding sequestering agents that bind Ca in the gut and prevent its absorption.

Limiting Dietary Ca Intake

One of the oldest approaches to controling hypocalcemia in dairy cows is to limit the amount of Ca consumed and absorbed in the gut to induce a state of negative Ca balance in the last weeks of gestation. Work at Iowa State University in the early 1970's demonstrated that feeding prepartum diets with low Ca content effectively reduced the incidence of CH in cows considered to be highly susceptible to this metabolic disorder (Goings et al., 1974). When cows are fed diets that induce a negative Ca balance, they have increased concentrations of parathyroid hormone (**PTH**) which is critical to stimulate bone resorption, intestinal absorption, and renal reabsorption.

Yarrington et al. (1974) compared dairy cows fed a diet that supplied < 10 g of Ca and approximately 25 g of P per day (low Ca diet) with cows fed 25 g of Ca and 25 g of P per day prepartum (control diet). The authors challenged the cows at approximately 10 d prepartum with intravenous EDTA for 4 h, a salt that chelates iCa in blood and increases renal excretion inducing a period of SCH. They observed that cows fed the low Ca diet had a faster return of blood Ca to the normal concentrations after EDTA challenge than cows fed the control diet. Cows fed the low Ca diet had increased markers of bone remodeling suggesting greater Ca resorption activity. In fact, hydroxyproline concentrations in urine increased to a greater extent in cows fed the low Ca than the control diet. Hydroxyproline is an amino acid that is a major component of the protein collagen and increased concentrations in urine are an indication of bone resorption. One of the interesting findings was that the Chief cells in the parathyroid glands of cows receiving the low Ca diet were characterized as being in an active synthesizing phase with alterations of the organelles indicating increased secretory activity of PTH. It seems that feeding diets that induce a negative Ca balance promotes increased mobilization of Ca from bone in order to maintain normal concentrations in blood when intestinal absorption is inadequate. Upregulating these mechanisms before calving likely explain the reduced susceptibility of dairy cows to CH when fed low Ca diets.

The challenge with low Ca diets is that they have to induce a negative Ca balance. In late gestation, dairy cows require approximately 20 g of absorbable Ca to meet the needs for endogenous losses in feces (~ 10 g/d), uterine and fetal accretion (~ 9.5 g/d) and urinary loss (~ 0.5 g/d). Most feeds and Ca sources have bioavailability estimated at 50 to 70%; therefore, to induce a negative Ca balance in prepartum cows with typical intake of 10 to 12 kg of DM per day in the last two weeks of gestation, a diet would have to contain no more than 0.25% Ca to assure that intestinal absorption would

be less than the 20 g needed. Obviously, this is not simple to achieve because most forages, grains, and by products fed to dairy cows have at least 0.25% Ca.

Feeding Zeolite to Sequester Ca in the Gut

Feeding low Ca diets prepartum reduces the risk of hypocalcemia in dairy cows, but achieving diets that induce a negative Ca balance is challenging. One approach to reduce Ca availability is to feed supplements that sequester Ca in the gut, therefore, preventing its absorption. One such strategy that has been investigated is the addition of Zeolite to prepartum diets. Zeolites are complex structural compounds consisting of interlocking molecules of SiO_4 and AlO_4 in the form of a honey-comb. The aluminum silicate formed carries negative charges that attract positively charged ions such as Ca^{2+} and Mg^{2+} in the gut.

Thilsing et al. (2006) investigated the binding capacity of zeolite to Ca, P, and Mg in vitro using a system to mimic the conditions of the rumen of cattle. The addition of zeolite to the incubation containing rumen fluid reduced supernatant Ca and Mg, but had no effect on P. When the pH of the rumen fluid was reduced by addition of HCl then Zeolite was capable of binding P. The authors suggested that the ability of Zeolite to bind Ca when the pH of the suspension is similar to that of the rumen, or P under more acidic pH would be desirable to prevent hypocalcemia in cattle. A reduction in the intestinal absorption of Ca and P prepartum would improve the ability of the cow to mobilize Ca at the onset of lactation. However, Zeolite also bound Mg, which would be unfavorable to prevent CH and SCH, and could potentially induce hypomagnesemia in cows fed diets low in Mg.

The concept of feeding Zeolite has been evaluated in dairy cattle in a few experiments and the results are promising. In general, cows are fed 0.7 to 1.0 kg of Zeolite which represents 6 to 10% of the total DM intake of a prepartum cow in the last 2 weeks of gestation. Feeding Zeolite during the last 2 weeks of gestation increased plasma tCa concentration on the day of calving and the first few days postpartum (Thilsing et al., 2002). Cows fed Zeolite had increased concentration of $1,25(OH)_2$ Vitamin D_3 in serum prepartum, the active form of Vitamin D_3. However, feeding Zeolite depressed DM intake, a common finding with feeding large quantities of minerals to cattle, and reduced concentrations of Mg and P in serum. Although sequestering Ca prepartum seems effective at improving Ca metabolism at the onset of lactation, it poses issues with DM intake and blood Mg concentrations.

Altering the Dietary Cation-Anion Difference

In the US, the most widely implemented method to reduce the risk of hypocalcemia in dairy cows is to alter the mineral composition of the prepartum diet to induce a compensated metabolic acidosis in the last weeks of gestation. This concept is based on the fact that cows under metabolic acidosis have increased sensitivity to PTH (Goff et al., 2014) and induction of metabolic acidosis with acidogenic salts increases the expression of PTH receptor in the kidney of cattle (Aris et al., 2016). In general, the

maximal PTH response to Ca chelation occurs during metabolic acidosis compared with normal blood pH (Lopez et al., 2002).

When salts containing strong anions are fed, the premise is that the rate and extent of absorption of the anion is greater than that of the cation in the salt. In some cases, the cation in the salt can be utilized by the rumen microbes such as in the case of NH_4Cl. The most common strong anions fed are Cl^- and S^{2-} in the form of SO_4^{2-}. It is thought that Cl^- is more bioavailable than S^{2-} so it has greater acidifying power. When salts of Cl and SO4 are fed, for instance $CaCl_2$, more equivalents of the anion (Cl^-) from the molecule is absorbed than the cation (Ca^{2+}). This causes an imbalance in charges in the epithelial cell of the intestine (increase in negative charges), which forces secretion of HCO_3^- into the intestinal lumen or retention of H^+ ions. The end result is a loss of HCO_3^- and an increase in H^+ concentration which ultimately results in a state of metabolic acidosis. If compensated, then minor changes in blood pH occur, with changes in blood HCO_3^- and the partial pressure of CO_2 caused by changes in respiration rate. A common finding is aciduria because of the increased H^+ excretion in urine as part of the compensatory mechanism.

One of the problems with metabolic acidosis is that, if uncompensated, it can impair insulin signaling and exacerbate the status of insulin resistance that occurs in late gestation and early lactation. Excessive feeding of strong anions or errors during diet formulation because of inaccurate mineral composition or mixing of ingredients can potentially result in excessive intake of Cl and SO_4, which can depress blood pH and influence energy metabolism in dairy cows. Cows fed large quantities of acidogenic salts had impaired glucose utilization after a glucose tolerance test suggesting interference with insulin action on peripheral tissues (Bigner et al., 1996). Therefore, it is critical that prepartum diet formulation using negative DCAD be based on continuous monitoring of the chemical composition of the ingredients, and not on tabular values for mineral content.

Formulating diets to achieve a negative DCAD follows some logical concepts. The first is to limit the intake of strong cations. Ingredients should be selected such that low K and Na intakes are prioritized. It makes little sense to feed diets that are high in K and Na and then try to counter act their effects by feeding large quantities of strong anions. Acidogenic salts are known to depress DM intake either because of palatability issues or because of the metabolic acidosis they induce (Charbonneau et al., 2006).

When proper feed selection is made, then most diets should require fewer than 2 equivalents (**Eq**) of strong anions fed to achieve a desirable negative DCAD. An Eq is a unit of electrical charge and refers to the atomic mass of a given mineral divided by its valence. In the case of Cl-, the atomic mass is 35.5 and the valence is 1, so 1 Eq of Cl^- is the same as 35.5 g. One Eq of anion supplies enough charges capable of neutralizing 1 Eq of cation. For instance, let's suppose that the target DCAD of the diet fed to prepartum cows is -100 mEq/kg. The negative value indicates that the diet provides more Eq of anions (negatively charged ions) than cations (positively charged ions). In other words, for this diet, each kg of diet DM contains an excess of 100 mEq (or 0.1 Eq)

of anions relative to cations. Now, let's assume that the expected DM intake for the prepartum cows will be 12 kg. Therefore, each cow will consume an excess of 1.2 Eq of anions relative to cations (12 kg x 0.1 Eq = 1.2 Eq anions). In order for 2 Eq of anions to reduce the dietary DCAD to -100 mEq/kg, then the basal diet cannot have a DCAD > +100 mEq/kg. This is why it is critical to select ingredients with low concentrations of K and Na or with relatively low DCAD. This will assure that inclusion of acidogenic salts will be minimal which, in turn, should reduce the risk of suppression of DM intake and increase efficacy of the program to prevent hypocalcemia. Remember, it is not the relative DCAD of the diet that is critical, but the total Eq of strong anions relative to strong cations consumed by the cow. If a diet contains a DCAD of -100 mEq/kg, but the cow only eats 6 kg/day, the acidifying ability will be limited because the relative excess intake of anions will be only 0.6 Eq. On the other hand, a diet with DCAD of -80 mEq/kg fed to cows consuming 13 kg of DM will induce a more exacerbated metabolic acidosis because the relative excess intake of anions will be 1.04 Eq.

It is important to mention that the ideal DCAD to prevent hypocalcemia is unknown. Most suggestions range from -50 to -150 mEq/kg, a range that would result in a differential of 1.2 Eq of anions consumed per day. Reducing the DCAD improves blood Ca concentrations (Charbonneau et al., 2006) and this effect can be seen in Holstein cows fed diets containing +130, -80, -130, and -180 mEq/kg. However, the association between DCAD and blood Ca is nonexistent if we look only at the data from cows fed the negative DCAD (-80 to -180 mEq/kg) suggesting equal ability to prevent hypocalcemia within that range (**Figure 3**).

Manipulating DCAD only is not enough. Prepartum diets should have limited concentration of P. Increasing dietary intake of P to amounts above 50 g/day during the prepartum period can increase the risk of CH (Lean et al., 2006). Increase in blood P concentrations, induced by release of Ca and P from bone resorption, is controlled initially through PTH by increased filtration and urinary P excretion. In addition, fibroblast growth factor (**FGF**) 23 produced by osteocytes and osteoblasts regulates blood P concentration (Bergwitz and Jüppner, 2010). Under high blood P concentrations, FGF23 expression is up-regulated, which helps increase urinary P loss to maintain blood P under a tight range. However, FGF23 suppresses the activity of 1-α hydroxylase in the kidneys, the key enzyme responsible for synthesis of active vitamin D3. Therefore, if blood phosphate increases because of overfeeding P, then circulating concentrations of $1,25(OH)_2$ vitamin D_3 decreases, which may result in hypocalcemia (Bergwitz and Jüppner, 2010). Therefore, it is recommended that diets for prepartum cows should contain no supplemental P and concentration of 0.30% P in the dietary DM is more than enough to meet the P needs of the pregnant cow.

Another aspect is the concentration of Mg in the diet. It is clear that NRC (2001) recommendations for Mg in diets of prepartum cows are inadequate. Magnesium is important not only to prevent hypomagnesemia, but also to enhance the ability of the cow to mobilize Ca from bone when stimulated by PTH. Magnesium is involved in the second messenger system of PTH and low blood Mg impairs Ca resorption (Robson et al., 2004). It is unclear what the ideal Mg content in the diet should be, but most

recommendations are around 0.40 to 0.45% of the DM. This is based on the idea that intakes of 40 to 50 g of Mg/d will provide sufficient soluble Mg to increase ruminal concentrations that will favor passive diffusion. This high concentration of Mg might be more important when the main source fed is in the oxide form. It is known that MgO is poorly soluble and bioavailability usually is less than 50%.

Finally, debate exists about the ideal concentration of Ca in the diet when cows are fed rations containing a negative DCAD. Lean et al (2006) conducted a meta-analysis to critically and systematically review the literature on hypocalcemia in dairy cattle. They demonstrated that the risk of CH is low when dietary Ca < 0.6%, then the risk increases with increasing dietary Ca up to 1.5%, after which it decreases again. The lowest risks of CH were detected when dietary Ca was either < 0.6% of > 2.0%. Because diets that induce metabolic acidosis rely on increased Ca resorption from bones, it is poorly justifiable to overfeed Ca. The reduced risk of CH when diets contain > 2.0% Ca are likely the result of transcellular transport because of diffusion from the lumen of the rumen and intestine to the vascular space through cellular junctions because of the large differential concentration between the lumen and the interstitial space. However, it is important to remember that Ca is a cation and large increases in Ca feeding with intestinal absorption will attenuate the acidifying effect of the acidogenic salts fed.

Duration of Feeding Acidogenic Salts Prepartum and Urinary pH

To our knowledge, only two one experiments have evaluated the impact of duration of feeding of acidogenic salts for prepartum cows (Weich et al., 2013; Wu et al., 2014). Sixty cows were fed one of 3 treatments starting at 42 d relative to the expected calving date. Treatments were a control diet (+120 mEq/kg), a positive DCAD in the first 21 d followed by a negative DCAD diet in the final 21 d of gestation (+120 mEq/kg followed by -160 mEq/kg), or 42-d of feeding a negative DCAD diet (-160 mEq/kg). The authors found feeding acidogenic salts for the last 21 d of gestation improved Ca homeostasis and milk yield (5.6 kg/d). They also found that extending the feeding of acidogenic salts from 21 to 42 d had no statistically significant effect on the subsequent lactation, although cows fed the diet for the extended period produced 2.3 kg less milk (44.8 vs. 42.5 kg/d). Wu et al. (2014) showed no differences in postpartum performance when prepartum cows were fed a diet with a DCAD of -210 mEq/kg for the last 3, 4 or 6 weeks of gestation. These data suggest that flexibility exists on how long acidogenic salts can be fed to prepartum cows.

Because cows fed acidogenic salts excrete acidic urine, measuring urine pH has become a common method to monitor the effectiveness of feeding such diets. Cows should be on the diet for at least 48 h for urine pH to drop and become somewhat stable. Recommendations for urininary pH vary, and most are based on personal observation to prevent CH (6.2 to 6.8; Jardon, 1995). Charbonneau et al. (2006) clearly showed that as the dietary DCAD decreases, so does urinary pH. Very likely, when urinary pH drops below 5.00, the cow responds by reducing DM intake which prevents further increments in the acidotic state. We have found little or no association between

average urinary pH measured twice weekly in the last 2 weeks of gestation and blood iCa concentration in the first 2 DIM (**Figure 3**). It seems that urinary pH is a good monitor to evaluate the degree of metabolic acidosis, but once it is below 7.0 it is not necessarily associated with improvements in blood Ca in early lactation. It important to mention that within a given diet, substantial variability exists in mean urinary pH in the last 2 weeks of gestation, particularly for cows fed diets of very low DCAD (**Figure 4**). Therefore, one should be cautious of making dietary changes based on small changes in urinary pH or over-interpret the variations in urinary pH among cows fed a given diet.

Supplementing Ca after Calving

One method commonly used to prevent CH is the administration of injectable or oral Ca salts immediately after calving. In many cases, those injectable solutions (Ca borogluconate) or oral gels or bolus (primarily Ca chloride or combinations with other salts) are administered repeatedly in the first day or two after calving. The premise is that the oral Ca will increase blood concentrations of Ca that will prevent cows from developing CM. However, in recent years, the use of oral Ca products have become an alternative to minimize the risk of SCH in postpartum dairy cows.

Oetzel and Miller (2012) administered 43 g of Ca as an oral bolus containing $CaCl_2$ and $CaSO_4$ to dairy cows in the first hours after calving and repeated the application 8 to 35 h after calving. The authors observed no change in blood concentration of iCa, likely because sampling time was too late relative to treatment. In general, 43 g of oral Ca as salts of Cl and SO4 increase blood iCa for only 2 h. Therefore, if samples are not collected within that time frame, no differences will be observed. Administration of oral Ca benefited subpopulations of cows, those that were lame at calving and cows of greater potential for milk yield based on the previous lactation mature equivalent (**ME**) for milk yield. Lame cows that received oral Ca had reduced incidence of health events in the first month of lactation. Cows with a previous lactation 305-d ME of at least 5% above the mean value for the herd produced more milk in the first month postpartum if treated with Ca at calving.

We have recently completed 2 experiments 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, incidence of diseases, and reproductive and productive performance (Martinez et al, 2016). 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 at 0.5, 1, 2, 4, 8, 12, and 24 h after treatments to characterize acid-base status and mineral concentrations. Concentrations of 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 (**Figure 5**). The changes in iCa concentrations, from pre-treatment to 0.5 h after 86 g of Ca supplementated on d 0 were of 0.11 ± 0.03 m*M* in multiparous and 0.25 ± 0.03 mM in primiparous cows.

In experiment 2, 450 Holstein cows considered of low (LRM; normal calving) or high risk (HRM; dystocia, twins, stillbirth, retained placenta and/or vulvo-vaginal

laceration) of metritis on the day of calving were blocked by parity as primiparous or multiparous 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 on d 7 and 10 for determination of concentrations of minerals and metabolites and blood acid-base responses. Disease was evaluated for the first 30 DIM. Milk yield was measured daily for the first 5 months of lactation. Reproduction and cow survival were evaluated for the first 210 DIM. On the day of calving and before any treatment, 48, 49 and 36% of the control, CaS1 and CaS4 cows had SCH (tCa < 2.125 m*M*). Oral Ca reduced the incidence of SCH (control = 69.3%; CaS1 = 57.5%; CaS4 = 34.2%). Calcium supplementation decreased the prevalence of SCH on d 0 and 1 posptarutm 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. To our surprise, oral Ca tended to increase the incidence of metritis (control = 22.7%; CaS1 = 35.9%; CaS4 = 31.2%), primarily because of an increment 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 impact on multiparous cows (control = 38.2%; CaS1 = 35.1%; CaS4 = 30.1%). On the other hand, oral Ca reduced the incidence of certain diseases (mastitis + lameness + digestive problems) in multiparous cows (control = 16.3%; CaS1 = 6.2%; CaS4 = 5.3%). The body condition did not differ among treatments, and cows lost on average 0.44 units of body condition in the first month of lactation. Calcium supplementation did not affect milk yield in the first 5 months postpartum. However, as reported by Oetzel and Miller (2012) for multiparous cows, Ca supplementation was beneficial to milk yield in the first 30 DIM for cows of greater production potential (above the mean 305-d ME milk yield of the previous lactation; 14,003 kg), but detrimental to multiparous cows below average production potential. Calcium supplementation to primiparous cows reduced pregnancy per artificial insemination (**P/AI**) at the first AI (control = 55.8, CaS1 = 31.5, CaS4 = 37.0%) and at all AI (control = 48.5, CaS1 = 34.6, CaS4 = 38.5%); however, Ca supplementation to multiparous cows improved P/AI at the first AI (control = 32.1, CaS1 = 38.6, CaS4 = 41.3%) and at all AI (control = 28.1, CaS1 = 35.3, CaS4 = 40.5%). These responses of P/AI to Ca supplementation resulted in extended median days to pregnancy (control = 75, CaS1 = 100, CaS4 = 94 d) and a smaller proportion of pregnant cows (control = 89.3, CaS1 = 83.9, CaS4 = 83.9%) in primiparous cows, but fewer days to pregnancy (control = 115, CaS1 = 94, CaS4 = 94 d) and increased proportion of pregnant cows in multiparous cows (control = 67.0, CaS1 = 77.2, CaS4 = 74.3%).

Collectively, these results indicate that responses to oral Ca supplementation are conditional on parity and production potential of cows. Oral Ca supplementation in the first days of lactation might be beneficial to health, production and reproduction in multiparous cows, particularly those of greater production potential that might be at a greater risk for SCH. On the other hand, the work by Martinez et al. (2016a,b) suggests that dosing primiparous cows with oral Ca for 2 to 5 consecutive days should be discouraged. It increased the risk of diseases, depressed reproduction, and had no benefit on production.

Conclusions

Hypocalcemia is a prevalent metabolic disorder in dairy cows in early lactation. It is not related to inadequate intake of Ca but caused by the inability of the cow to mobilize Ca from bones quickly at the onset of colostrogenesis and lactation. Hypocalcemia increases the risks of numerous other health problems resulting in economic losses to dairy producers. Dietary manipulation remains the method of choice to minimize the incidence of hypocalcemia. It involves limiting the intake of Na, K and P, and then manipulating the remainder of the macrominerals to achieve a negative dietary DCAD. Alternative methods such as the use of Ca sequestering agents are available, but they also present challenges as does feeding of acidogenic salts prepartum. In some cases, supplementing Ca in an oral bolus can benefit multiparous cows but the practice is discouraged in primiparous cows. Alternative dietary and pharmacological methods are currently under investigation. Manipulating the source of vitamin D3 fed prepartum or administering to dairy cows immediately after calving show some promise.

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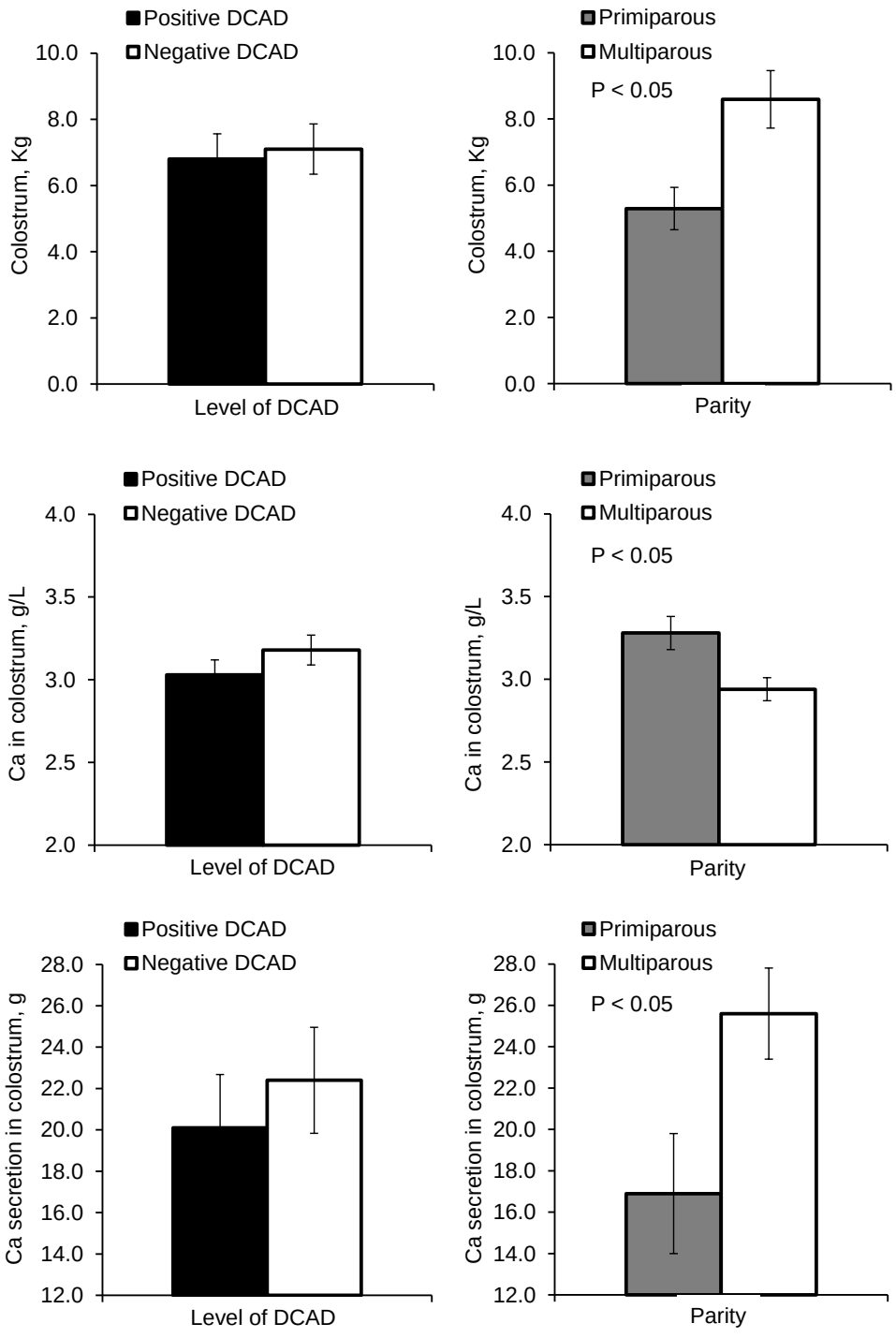

Figure 1. Colostrum yield (kg), concentration of Ca in colostrum and Ca secretion in colostrum of primiparous and multiparous cows fed a diet prepartum containing either +130 mEq/kg (positive DCAD) or -130 mEq/kg (negative DCAD). Adapted from Martinez et al. (2014).

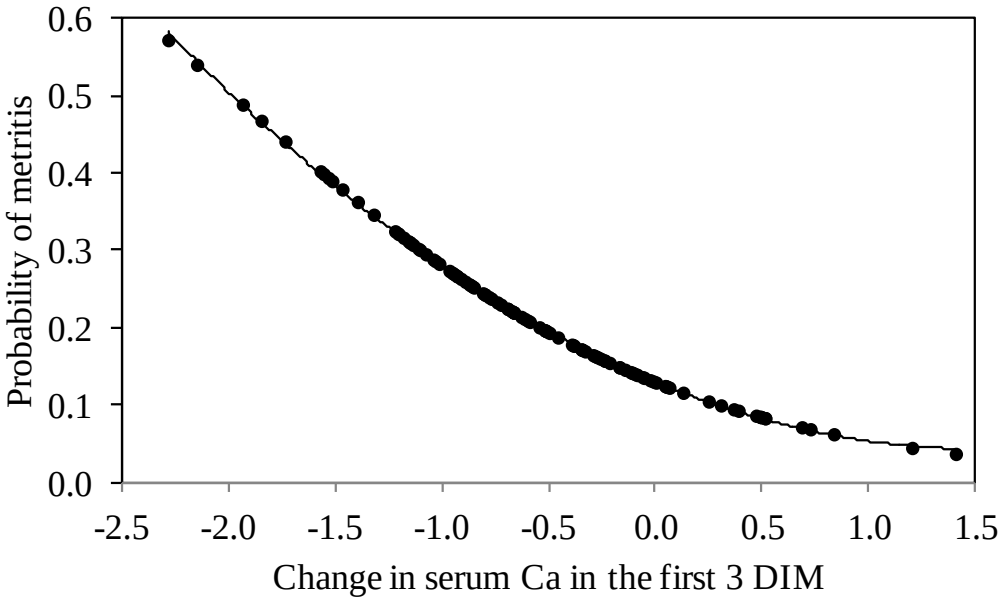

Figure 2. Probability of metritis relative to the change in serum tCa concentrations between the d of calving and the lowest value within the first 3 DIM. As serum tCa decreased, the risk of metritis increased ($P < 0.05$). Adapted from Martinez et al. (2012).

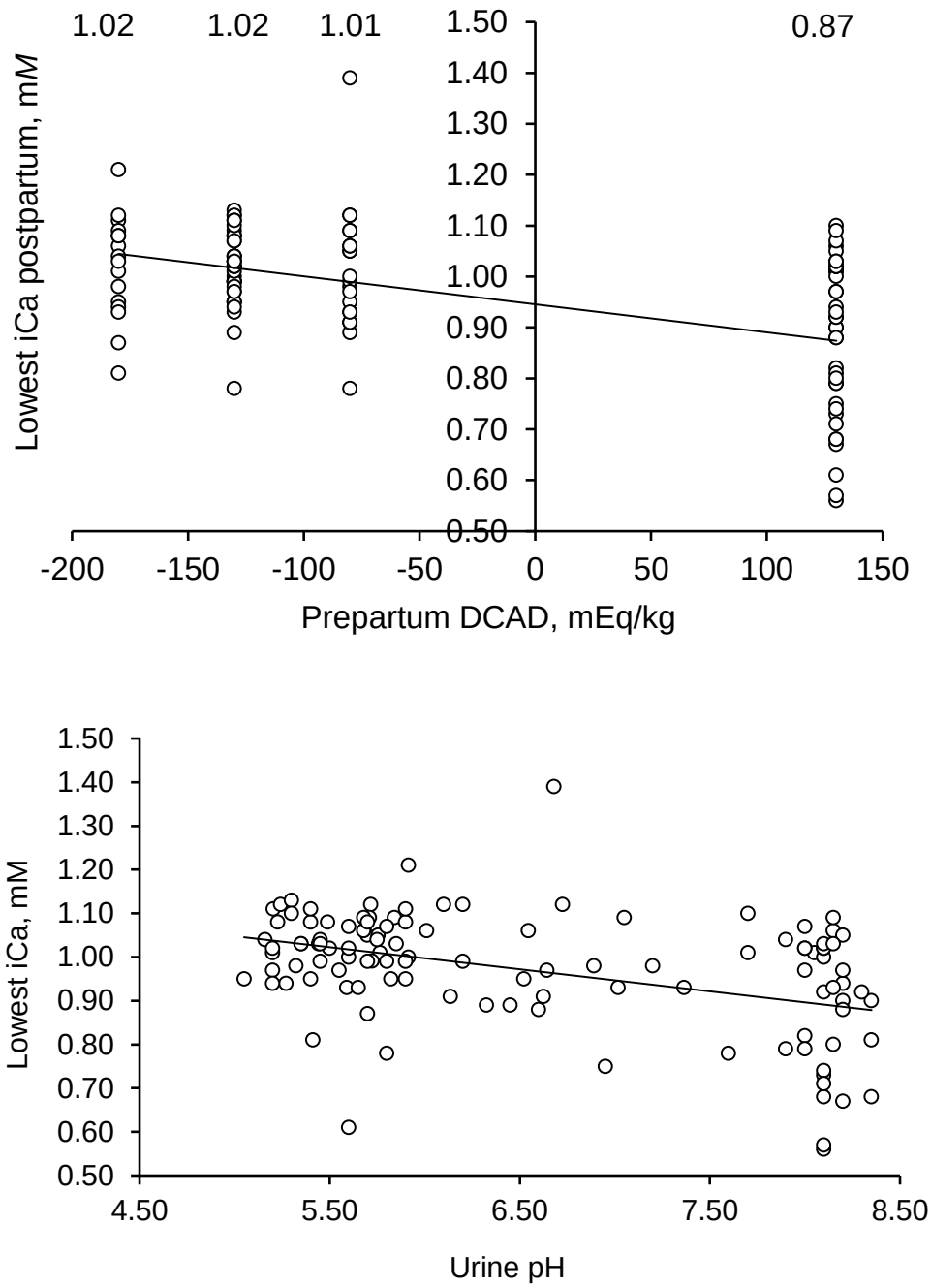

Figure 3. Lowest blood iCa concentration in the first 2 DIM (0, 1, and 2 DIM) of Holstein cows fed diets that differed in DCAD (+130, -80, -130, -180 mEq/kg) and according to the average urine pH in the last 2 weeks of gestation. Average values for iCa are depicted for each dietary DCAD. Santos et al. unpublished results.

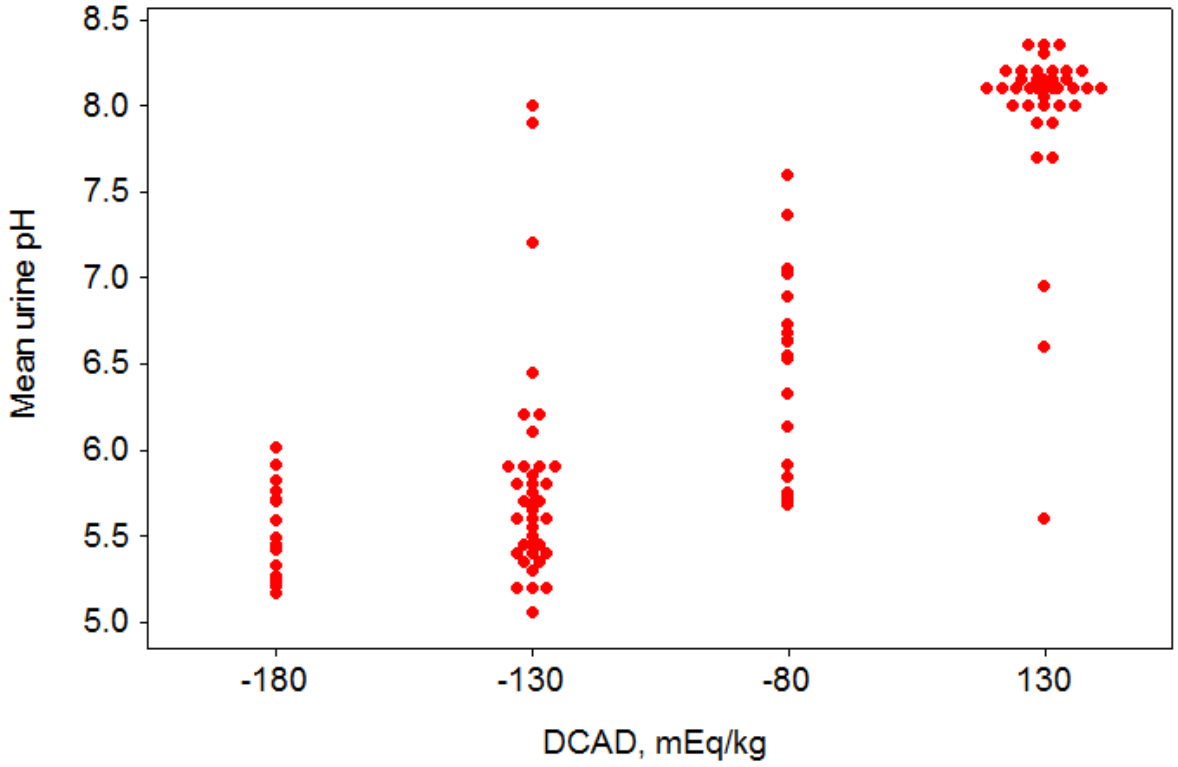

Figure 4. Distribution of mean urine pH in Holstein cows in the last 2 weeks of gestation (mean of 4 measurements per cow) according to the DCAD of the diet offered.

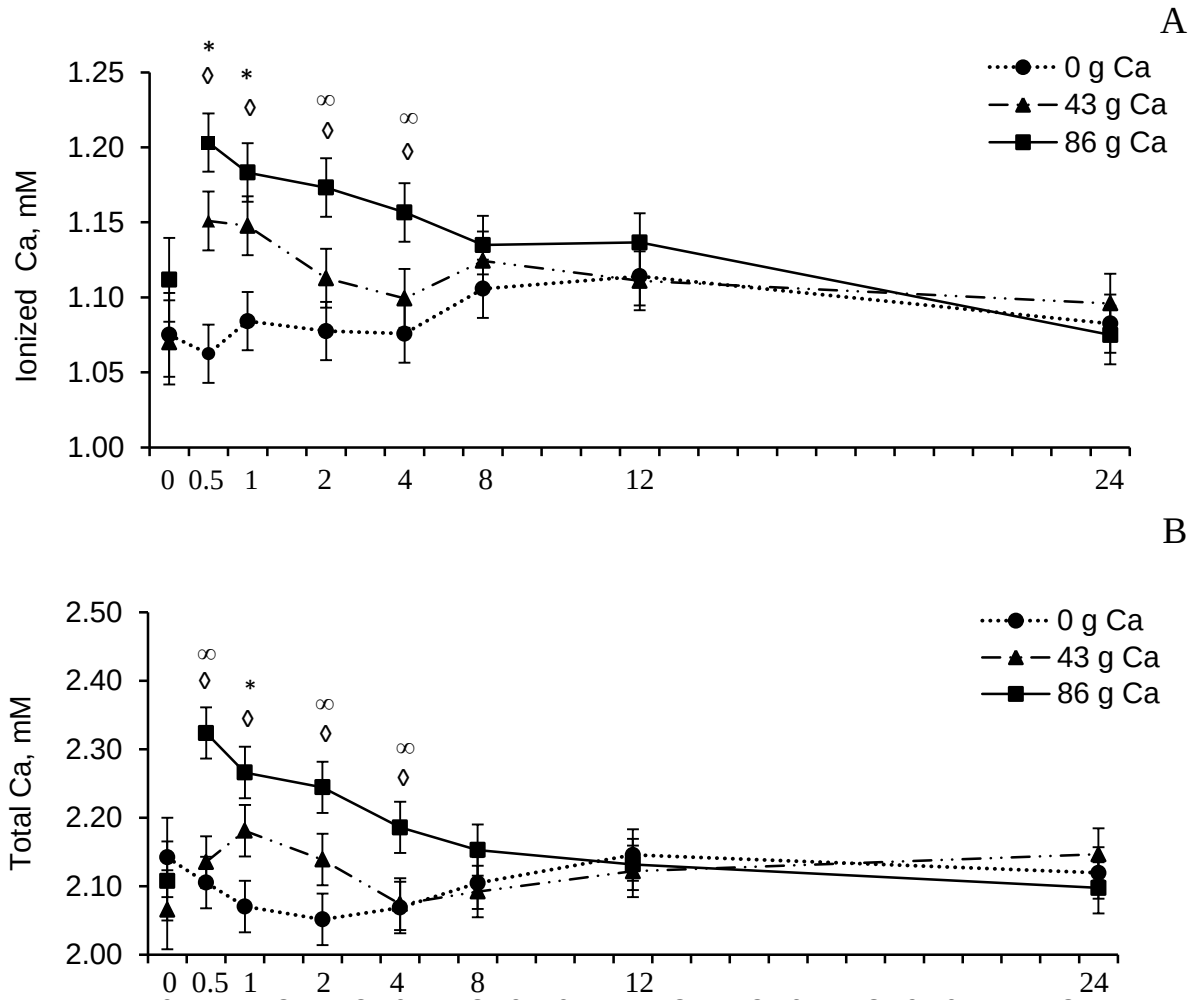

Figure 5. Characterization of blood ionized Ca (iCa; A) and serum total Ca (tCa; B) concentrations after oral supplementation with 0, 43, or 86 g of oral Ca in Holstein cows. Administration of oral Ca increased ($P < 0.01$) blood iCa and tCa, and the increments were dose-dependent. A dose of 43 g of oral Ca increase blood iCa and serum tCa for 2 h, whereas 86 g of oral Ca increased iCa and tCa for 4 to 8 h (Adapted from Martinez et al., 2016).

SESSION NOTES