Animal Health: Joint Animal Health/Reproduction Symposium: Transition Cow Calcium Homeostasis—Health Effects of Hypocalcemia and Strategies for Prevention

274 Calcium transport mechanisms in different epithelia of ruminants. M. Wilkens*, Institute of Physiology and Cell Biology, University of Veterinary Medicine, Hannover, Foundation, Hanover, Germany.

If luminal Ca concentrations are high, Ca transport across epithelia occurs mainly via passive, paracellular mechanisms driven by an electrochemical gradient or solvent drag. Restricted supply as well as an increased demand induce an endocrine response, mainly mediated by calcitriol, resulting in a relatively greater contribution of a more efficient, active, transcellular Ca transport. In intestinal and renal epithelia, this is a 3-step process involving apical uptake via Ca channels (TRPV5, TRPV6), protein-bound diffusion through the cell (CaBPD28K, CaBPD9K) and active extrusion at the basolateral membrane (NCX1, PMCA1b). To further improve our strategies to prevent hypocalcemia, applied studies should be combined with fundamental research on the complex regulation of these transport processes, especially because ruminants show some particularities in comparison to monogastric animals. Although the small intestine expresses the same vitamin D-dependent Ca transport proteins (TRPV6, CaBPD9K, PMCA1b), flux rates determined using mucosal preparations from sheep and goats were demonstrated to be much smaller than those detected in samples from pigs or horses. Nevertheless, the expression of the above mentioned transport proteins is regulated and altered by dietary Ca, N restriction and lactation. The rumen has also been shown to actively absorb Ca in many in vitro and in vivo experiments. But the absence of any relevant amounts of TRPV6 or CaBPD9K, the unresponsiveness to dietary Ca restriction or calcitriol treatment and the pivotal role of luminal SCFA indicate an alternative, so far unknown mechanism. Interestingly, lactation and a diet negative in DCAD increased ruminal flux rates. Renal Ca excretion is generally low in ruminants and cannot be significantly diminished to compensate for challenges of Ca homeostasis. But when the animals are kept on a ration negative in DCAD renal Ca resorption is inhibited. Preliminary experiments demonstrated that the expression of TRPV5, CaBPD28K and NCX1 is not significantly altered under these conditions. This might explain why renal resorption is immediately restored when the ration is changed p.p. An adaptation on the functional level occurs faster than the stimulation via the genomic pathway.

Key Words: Ca absorption, vitamin D, dietary cation-anion difference (DCAD)


Attempts have been made to utilize vitamin D for prevention and treatment of hypocalcemia in postpartum dairy cows since the discovery that vitamin D was required for calcium homeostasis. A few initial experiments established that feeding 10,000 to 20,000 IU of vitamin D3 was adequate for maintaining blood Ca concentrations in lactating dairy cows. Hypocalcemia, however, is not necessarily a vitamin D nutrition problem but, rather, the inability of Ca homeostatic mechanisms to account for irreversible mammary loss with the onset of lactation. The failure to maintain Ca homeostasis, in part, is due to inadequate synthesis of 1,25-dihydroxyvitamin D3 from 25-hydroxyvitamin D3 in response to parathyroid hormone and decreased sensitivity of tissues to 1,25-dihydroxyvitamin D3. Feeding acidic diets prepartum to induce a compensated metabolic acidosis is a proven strategy to minimize postpartum hypocalcemia. A diet with negative DCAD increases concentrations of 1,25-dihydroxyvitamin D3 in serum in response to parathyroid hormone and, perhaps more important, it increases Ca flux from intake and skeletal stores to urine which can be rapidly diverted to the mammary gland at the onset of lactation. Increasing supplemental vitamin D3 above current practices (30,000 to 50,000 IU/d) does little to augment a prepartum diet with negative DCAD because cows seem to have a limited capacity to convert vitamin D3 to 25-hydroxyvitamin D3. However, dose titration experiments with supplemental vitamin D3 in combination with a negative DCAD are needed. In contrast, feeding 25-hydroxyvitamin D3 in combination with a diet with negative DCAD is a promising approach to improving Ca homeostasis and performance of transition cows on the basis of outcomes from recent experiments. Parental administration of 1,25-dihydroxyvitamin D3 at, or soon after, parturition also results in a sustained increase in serum Ca. In summary, vitamin D is required for Ca homeostasis, but vitamin D nutrition is not the sole solution to hypocalcemia. A prepartum diet with negative DCAD is effective at reducing the risk of hypocalcemia and may benefit from nutritional or therapeutic use of vitamin D metabolites.

Key Words: vitamin D, calcium, transition cow

276 Novel role for serotonin in calcium homeostasis and effects on transition health. L. Hernandez*, J. Laporta2, S. Weaver3, and M. Connelly1, 1University of Wisconsin-Madison, Madison, WI, 2University of Florida, Gainesville, FL, 3Mayo Clinic-Rochester, Rochester, MN.

Seroserogenic regulation of calcium (Ca) metabolism during the peripartal period has only recently been elucidated. The discovery of mammary gland-derived serotonin and its subsequent interaction with peripartal Ca is a relatively new concept, particularly in the bovine model. Much progress has been made understanding serotonin’s role in regulating Ca status by utilizing the precursor to serotonin synthesis, 5-hydroxy-L-tryptophan (5HTP). A study performed in late-lactation dairy cows demonstrated that treatment with 5HTP decreased circulating total Ca concentrations and urine Ca concentrations, but increased milk Ca concentrations. This suggested that serotonin was potentially coordinating Ca flux between kidney, bone, gut, and milk. When peripartal multiparous cows were treated with 5HTP prepartum, total Ca concentrations increased postpartum compared with controls, and further improved when 5HTP was given in combination with a negative DCAD diet. Interestingly, cows treated with 5HTP had decreased circulating parathyroid hormone concentrations compared with controls and increased concentrations of urinary deoxypyridinoline, a bone resorption marker. Previous data in mice suggested serotonin induced transcriptional and translational changes in Ca transporters and pumps in the mammary gland. We confirmed these findings in the dairy cow, demonstrating that transcription of several pumps and transporters, along with parathyroid hormone related-protein were increased on d 8 of lactation in mammary glands of cows treated with 5HTP prepartum. In an attempt to determine if serotonin and Ca are working in a feedback loop to
maintain blood Ca concentrations, we measured circulating serotonin in response to chelation of circulating Ca, in non-pregnant, nonlactating cows. We determined circulating serotonin concentrations differentially responded to the challenge, based on dietary Ca fed. Our data to this point indicates that serotonin and Ca are working in a feedback loop to regulate Ca homeostasis in the peripartal cow. We are currently working on dissecting pathways involved in the serotonin-Ca feedback loop and the contribution of the mammary gland to the regulation of this process.

**Key Words:** serotonin, calcium

277 **Use of oral calcium for treatment of hypocalcemia and effects on health and production.** J. A. A. McArt*, Cornell University, Ithaca, NY.

Given the technological constraints of accurately measuring Ca and the negative consequences of hypocalcemia on cow health and farm economics, many dairy cows are supplemented with Ca immediately after calving. Administration of oral Ca, generally in bolus form containing 40 to 50 g of Ca, is a common supplementation strategy both for prevention and treatment of subclinical hypocalcemia, and several manufacturers have introduced oral Ca boluses containing differing combinations of rapidly and slowly absorbed Ca salts. The benefit of rapidly absorbed salts, such as Ca chloride, is that it is both highly bioavailable and acidifying (supporting mobilization of the cow’s own Ca stores); however, it is irritating to oral mucous membranes and must be administered quickly. Slowly absorbed Ca salts (such as Ca propionate, Ca sulfate, and Ca carbonate) have either an equivalent efficacy and longer duration of action than quickly-absorbed Ca salts or are ineffective as an immediate Ca source due to their poor bioavailability. Depending on the product, label instructions require administration of 1 to 3 boluses at calving, with some products requiring a second bolus administered 12 h later. Although studies agree that oral Ca increases blood Ca concentration, the length of increase varies from 1 to 24 h, likely due to the dose and frequency of administration and the production capacity of the cows under study. It is interesting that this short-term change in blood Ca concentration can have effects on cow health and production. However, these effects are not always beneficial, and most studies do not recommend their use as a blanket treatment, especially in primiparous cows. Conversely, there is good evidence that oral Ca supplementation to older cows and those with a greater production potential is valuable. It is thus important to take the formulation of oral Ca boluses, the timing and frequency with which they are administered, and cow-level variables into account when using oral Ca for treatment or prevention of hypocalcemia in dairy cows. It is important that these supplements complement the progression of, but do not interfere with, Ca homeostasis.

**Key Words:** calcium, subclinical hypocalcemia, oral calcium