Calcium and phosphorus homeostasis in reproducing sows – a focus on mineral efficiencies

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Take-home message

Based on results from a recent experiment, pelvic organ prolapses (**POP**) in sows are not likely due to a failure in Ca homeostasis. Instead of over-supplementing diets with Ca or other nutrients to prevent POP, swine nutritionists should apply principles of the intrinsic pathways which control homeostatic regulation of nutrients. Practical applications of these pathways will reduce complications associated with nutrient imbalances and help promote a sustainable industry. The sow herd offers ample opportunities for improvements in nutrient efficiency, especially in mineral and vitamin fortification of diets. The sow is resilient to nutrient inputs and adapts to marginal nutrient inputs by improvements in efficiency. Capturing these efficiencies can provide a balance between meeting animal needs and minimizing environmental impacts. This presentation will provide examples of how over-supplementation of nutrients precludes adaptive improvements in efficiency, leading to substantial environmental impacts and economic losses.

Background: Pelvic organ prolapses in sows – a challenging problem.

Certainly, POP in sows have increasingly gained national attention over the past decade. This complex condition negatively impacts animal welfare and raises concerns animal staff morale and negative economic impacts in the swine industry. Ample descriptions of the complex problem and prevalence among herds have been compiled (Pittman, 2017; Supakorn et al., 2017; Chipman et al., 2018). More recent efforts have provided substantial contributions to allow a better understanding of the problem (Kiefer et al., 2020; Kiefer et al., 2021). However, very limited efforts have focused on identifying failures in underlying physiological processes that result in POP. Understanding these processes will hopefully lead to effective interventions to prevent POP.

Our recent efforts in sow nutrition research have focused on one of the many physiological processes purported as a potential underlying contributor to POP. Over the past decade, as the prevalence of POP increased, we were frequently queried about the potential for a disruption in Ca homeostasis as an underlying mechanism leading to POP in sows. Due to increased Ca demand associated with gestation and lactation phases, reproducing mammals are more vulnerable to develop disorders of Ca homeostasis (Horst *et al*., 2005). However, only limited evidence is available to support the spontaneous occurrence of hypocalcemia in sows. This report provides a brief overview of our research results that relate to Ca homeostasis in sows and some practical insights gained from these experiments. An unexpected outcome from the initial experiments focused on Ca homeostasis was evidence for a failure of sows to maintain P homeostasis during lactation. In a separate presentation at this conference, Mariola Grez Capdeville has summarized our recent research efforts on P adequacy.

Calcium homeostasis in sows

The perception that disruption of Ca homeostasis around parturition may be a predisposing factor for POP in sows is likely extrapolated from clinical evidence in dairy cows. The consequences of a disruption in Ca homeostasis around calving are well established for dairy cows (Horst et al., 2005; Goff, 2008; Goff, 2020). In context of the current presentation, an increased prevalence of uterine prolapses is one clinical outcome of hypocalcemia in dairy cows. Major insights into nutritional management strategies developed for dairy cows involved observations that excess dietary Ca supplements during the transition phase increased the prevalence of hypocalcemia. The excess Ca supplements are thought to suppress two major pathways involved in Ca homeostasis, intestinal Ca absorption and bone Ca remodeling. Applications from dairy cow research involve a reduction in dietary Ca supplementations during the transition phase to stimulate intestinal absorption and acidification of the transition cow diet by altering cation-anion balance to stimulate bone remodeling. These strategies have proven effective for dairy cows.

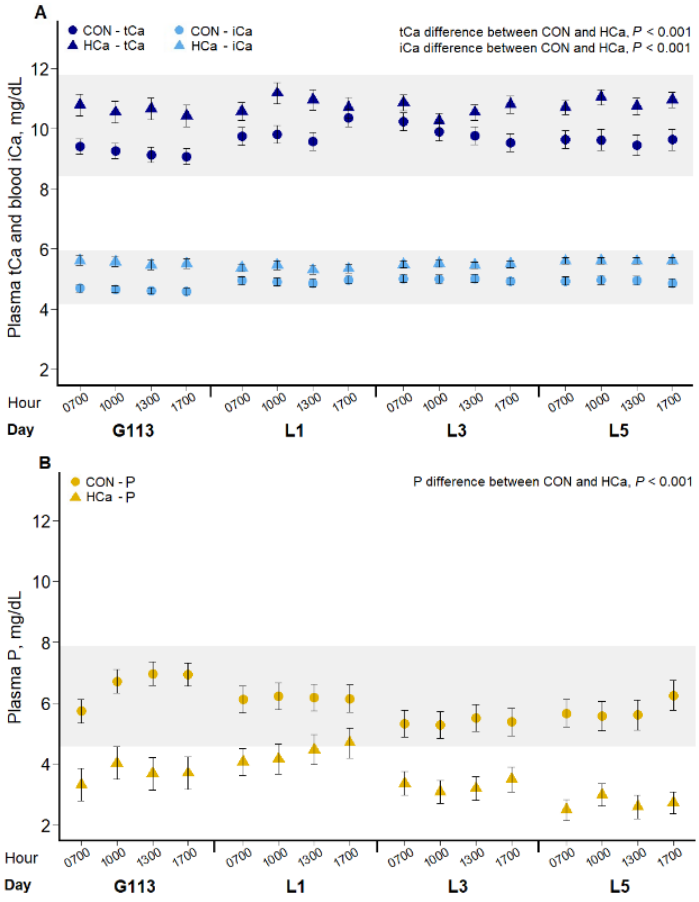

Figure 1. Plasma total Ca (tCa), ionized Ca (iCa) concentrations (Panel A), and P concentrations (Panel B) from sows fed adequate (CON, 0.65%) or excess Ca (HCa, 1.75%) diets. Samples were collected at day 113 of gestation (G113) and days 1, 3, and 5 of lactation (L1, L3, and L5) at 4 different hours within a day (0700, 1000, 1300, and 1700 h). Shaded areas represent the physiological range for total Ca (8.5 to 11.8 mg/dL), iCa (4.3 to 5.9 mg/dL), and P (4.6 to 7.9 mg/dL). Differences were detected ($P < 0.001$) between dietary treatments for total Ca and P plasma concentrations. Plasma P tended to decrease from L1 to L5 ($P = 0.057$). From Grez-Capdeville and Crenshaw, 2020).

Our recent efforts to assess the potential for a disruption of Ca homeostasis in sows at parturition have considered insights gained from studies with dairy cows. We designed an experiment to increase the potential for a disruption in Ca homeostasis by feeding a diet with excess Ca. In this experiment, multiparous sows were fed control diets (0.65% Ca, 0.38% STTD P and 0.67% Ca, 0.38% STTD P in gestation and lactation, respectively); or diets with excess Ca (1.75% Ca, 0.46% STTD P and 1.75% Ca,

0.45% STTD P in gestation and lactation, respectively). These diets were fed during the last 4 weeks of gestation and during a 4-week lactation phase to assess hypocalcemic responses in the peripartum period. Blood samples were collected at 15-minute intervals at 0700, 1000, 1300 and 1700 h on gestation day 113 and lactation days 1, 3, and 5. In addition to total Ca (tCa), ionized Ca (iCa), and P plasma concentrations, venous blood pH, blood gases, electrolytes, glucose, and lactate) were analyzed. Results for plasma tCa, iCa, and P concentrations are shown in **Figure 1**.

Complete results have been reported (Grez-Capdeville and Crenshaw, 2020). Unlike similar studies in dairy cows, no clinical signs of Ca metabolism disorders were observed. No evidence for hypocalcemia was detected in peripartum sows fed control or excessive Ca diets. Sows fed excessive Ca diets had greater concentrations of plasma tCa than sows fed control diets. Unexpectedly, concentrations of plasma P in sows fed diets with excess Ca were lower than concentrations in sows fed control diets. Plasma P tended to decrease as day of lactation increased. Differences between dietary treatments for blood pH, gases, electrolytes, and metabolites were not detected. These results imply that excess Ca in late gestation diets did not result in hypocalcemia during the peripartum period. However, the plasma P concentrations of sows fed diets with excess Ca were below normal physiological ranges, which raised concerns for the effects of excess dietary Ca on regulation of P homeostasis. Subsequent experiments have focused on P homeostasis and methods to assess P requirements in sows. (Grez-Capdeville and Crenshaw. 2021)

Further considerations of the sow's ability to adapt physiological mechanisms and maintain Ca homeostasis during the peripartum period were provided in a recent study (Darriet et al., 2017), which focused on alterations in dietary cation-anion balance. Two experiments were conducted to assess the efficacy of an anionic mineral supplement (CAD-MATE, Granco Minerals, Petersburg, VA) to stimulate mobilization of Ca during the peripartum period in sows. As with dairy cows, the addition of an anionic mineral supplement effectively induced a metabolic acid load in gestating sows. The acid load was compensated, primarily by increased renal ammonium excretion. However, sows fed diets supplemented with 2.5% CAD-MATE also mobilized body Ca stores. The mobilization of Ca reserves was consistent with responses by dairy cows to altered dietary cation-anion balance. Common nutritional management strategies applied to dairy cows involve alterations of dietary cation-anion balance to induce acidogenic stimulation of bone remodeling. The increased bone remodeling supplies a readily exchangeable Ca pool in the body to prevent hypocalcemia. In our studies, none of the sows were hypocalcemic, even the sows fed control, non-supplemented diets.

An overall conclusion from our studies might be simply stated as: ***Sows are not cows***. The susceptibility of dairy cows to hypocalcemia in the peripartum period is often attributed to the rapid demand for Ca at the onset of lactation. Likewise, the reproducing sow has dramatic Ca demands for fetal development and milk production. Yet, our efforts to induce hypocalcemia in the sow, using treatment strategies know to increase the prevalence of hypocalcemia in dairy cows, did not provide evidence that hypocalcemia was a concern for sows during the peripartum period. One obvious explanation relates to the dietary acid load. Typical diets fed to gestating sows are acidogenic, while diets with greater forge concentrations fed to dairy cows are more alkalinogenic. Additional homeostatic mechanisms may also contribute to the apparent resiliency of the sow to hypocalcemia.

Intrinsic pathways for regulation of homeostasis

The results from our studies on hypocalcemia illustrate the importance of understanding the homeostatic mechanisms involved in nutrient use. Applications of these principles are critical for development of nutritional strategies to improve sow reproductive productivity and health, rather than a simple reliance on intuitive assumptions. The intuitive assumptions might follow a progression in extrapolation of hypocalcemic responses that leads to POP in one species, the dairy cow, to inferences that a similar response would occur in another species, the sow. Continued intuitive extrapolations may also lead to assumptions that hypocalcemia in sows can simply be resolved by adding more Ca to the diet. These intuitive assumptions appear to be commonly applied in diet fortification strategies for sows, especially strategies applied to mineral and vitamin supplements. Instead, diet fortification strategies for sows should be based on applications gained from an understanding of intrinsic mechanisms involved in

nutrient homeostasis. Thus, more effective strategies can be developed to reduce POP, and perhaps other clinical disorders in sows.

Intuitive assumptions often result in an over-supplementation of nutrients. The over-supplementation precludes the animal's adaptive improvements in efficiency of nutrient use, which, with some nutrients such as P, will lead to substantial environmental impacts and economic losses. The following examples illustrate the ability of animals to adapt to marginal nutrient inputs by improvements in efficiency, without reduced productivity.

Both macro- and micro- minerals, and fat-soluble vitamins are nutrients with intrinsic pathways that can be optimized for improvements in efficiency. Over-supplementation of these nutrients often precludes adaptive improvements in nutrient efficiency. In some nutrients, over-supplementation may lead to substantial negative complications due to imbalances with other nutrients. Additionally, the over-supplementation often has negative environmental consequences and contributes to economic losses. One example is the over-supplementation of dietary P. A 0.10% excess P supplementation to diets for the entire U.S. sow herd for only one reproductive cycle equates to an excess of 4,745 metric tons of P that must be accommodated in manure nutrient management plans. Additionally, feeding excess dietary P activates intrinsic pathways involved in the maintenance of P homeostasis. The excess P stimulates FGF-23 release from bone that targets both GI tract to down-regulate P absorption and the kidney to upregulate urinary P excretion. In the kidney, FGF-23 down-regulates the conversion of 25-OH vitamin D into the active vitamin D hormone, 1,25 $(OH)_2$ vitamin D. Thus, animals fed excess P may display "normal" serum 25-OH vitamin D concentrations, however, the active vitamin D hormone is not sufficient to meet animal needs. The FGF-23, P, vitamin D axis for regulation of P homeostasis is discussed in detail in an earlier review (Crenshaw et al., 2011).

Similar regulations of intrinsic pathways are evident for trace minerals, especially Fe, Zn and Mn. Over-supplementation of these trace minerals will inhibit pathways for active absorption of the specific mineral and will often induce feed-back inhibition of pathways linked to homeostatic regulation of associated minerals. In a study to assess the trace mineral status of sows over seven parities (Crenshaw et al, 2013), no evidence was detected for a depletion of trace mineral reserves in the highly productive sows that were fed a constant, relatively moderate concentration of minerals. Adaptative mechanisms were apparently available to allow an improvement in nutrient use as the sows progressed and maintained productivity.

In conclusion, capturing intrinsic pathways to improve nutrient efficiencies by gestating sows provide opportunities for significant impacts on the balance between meeting animal needs and minimizing environmental impacts. As a society and industry our research efforts and practical applications must focus on positive ways to capture nutrient efficiency, especially in fortifications of minerals and vitamins, to promote a sustainable industry.

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