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Effect of trace mineral supplementation on selected minerals, energy metabolites, oxidative stress, and immune parameters and its association with uterine diseases in dairy cattle

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ABSTRACT

The objective of this study was to evaluate the relationship between selected minerals' serum levels, energy metabolites, oxidative stress indicators, IL-8 and haptoglobin levels, and the potential for uterine diseases. Additionally, we investigated the effect of injectable trace mineral supplementation (ITMS) on metabolism, immune function, and animal health under field conditions involving a dairy herd with high milk production. The study was conducted in 1 dairy farm located near Ithaca, New York, with 270 multiparous cows were enrolled from October 3, 2012 until January 10, 2013. Cows were randomly allocated into 1 of 2 treatments groups: ITMS or control. Cows randomly assigned to the ITMS group received 2 injections of trace minerals at 230 and 260 d of gestation; each injection contained 300 mg of Zn, 50 mg of Mn, 25 mg of Se, and 75 mg of Cu. Retained placenta (RP) and metritis were diagnosed and treated by trained farm personnel. Clinical endometritis evaluation was performed by the investigators. Blood mineral levels, plasma nonesterified fatty acids and serum β-hydroxybutyrate concentrations, plasma IL-8 concentrations, serum haptoglobin concentration, and serum superoxidase dismutase and plasma glutathione peroxidase activities were measured at various time points before and after calving. Four groups of mixed general linear models were fitted to the data using MIXED procedure of SAS. Injectable trace mineral-supplemented cows had increased serum concentration of Cu, Se, and Zn. Conversely, ITMS did not affect energy metabolites or immune and oxidative stress parameters. Serum concentration of Ca, Cu, K, Mg, Mo, Ps, Pt, Se, and Zn varied according to days relative to parturition. Cows with RP had reduced serum concentrations of Ca, Mg, Mo, and Zn when compared with cows without RP. Cows affected with metritis had significantly lower serum concentrations of Ca, Mo, soluble P, total P, Se, and Zn than nonaffected cows. Serum concentration of Ca, Cu, Mo, and Zn were reduced in cows diagnosed with endometritis in comparison to nonaffected ones.

Key words: retained placenta, metritis, mineral, oxidative stress

INTRODUCTION

Postpartum uterine diseases, such as metritis, endometritis, and retained placenta (**RP**), are important for animal welfare reasons, as they contribute to cow discomfort and elimination from the herd and are associated with profoundly affected reproductive performance, reduced milk yield, and treatment costs. Metritis and endometritis are commonly associated with mixed bacterial infection of the uterus, including *Escherichia coli*, *Trueperella pyogenes*, and *Fusobacterium necrophorum* (Bicalho et al., 2012). A contributory factor increasing susceptibility to bacterial infections and metritis development are the challenges observed during the periparturient period leading to physiological stress (Drackley, 1999), which dramatically alters metabolism to supply the mammary gland with nutrients for milk synthesis (Bauman and Currie, 1980; Goff et al., 2002). Additionally, the high nutritional requirements for parturition and initiation of lactation causes reduced DMI, negative energy balance (Roche et al., 2009), and oxidative stress, which altogether also contribute to dairy cows increased susceptibility to develop uterine diseases (Sordillo and Aitken, 2009).

For instance, subclinical mineral deficiency of Se has been associated with immunosuppression (Sordillo and Aitken, 2009) and reproductive failure (Spears and Weiss, 2008), subclinical deficiency of Zn was associated with impaired growth (Enjalbert et al., 2006), and subclinical deficiency of Ca was associated with decreased milk production (Oetzel, 2013). Cows with subclinical hypocalcemia have reduced blood neutrophil counts as

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well as impaired neutrophil function and increased incidence of metritis compared with normocalcemic cows (Martinez et al., 2012). Additionally, other trace minerals, such as Se, can be effective in reducing oxidative stress, and have a tremendous effect on bovine immune system and on the severity of metritis (Sordillo, 2013). Moreover, an association between a greater degree of negative energy balance (characterized by elevated prepartum NEFA concentration and postpartum BHBA concentration) and decreased immune response in cows that developed uterine disease compared with healthy cows has been reported (Cai et al., 1994; Kimura et al., 1999; Hammon et al., 2006; Galvão et al., 2010).

Machado et al. (2013) evaluated the effect of injectable trace mineral supplementation (**ITMS**) in a large multifarm clinical trial that enrolled over 1,400 cows and reported that cows injected with trace minerals at drying off and during the transition period were at significantly lower risk of stillbirth parturition, endometritis, and clinical and subclinical mastitis. Additionally, it was observed that ITMS decreased the presence of *T. pyogenes* and *F. necrophorum* in the uterus at 35 DIM (Machado et al., 2012). Although these studies provided some useful information regarding the potential benefits ITMS might have for transition cows, it also created questions regarding the possible biological mechanisms that led to the observed effects.

Considering the benefits of trace minerals and other minerals to physiological processes, energy metabolism, and immune status, we hypothesized that occurrence of uterine diseases would be associated with mineral levels, energy metabolites, and markers of immune function and supplementation with ITMS would mitigate the negative effects of mineral deficiencies on homeostasis, immune function, and development of diseases. Therefore, the objective of the present study was to evaluate the relationship between selected serum mineral levels, energy metabolites, oxidative stress indicators, IL-8 and haptoglobin levels, and the potential for uterine diseases. Additionally, we investigated the effect of ITMS on metabolism, immune function, and animal health under field conditions involving a dairy herd with high milk production.

MATERIALS AND METHODS

Farm and Management

This study was conducted in a dairy farm located near Ithaca, New York. Cows were enrolled from October 3, 2012 until January 10, 2013; the follow-up period continued until July 1, 2013. This farm was selected because of its long working relationship with the Ambulatory and Production Medicine Clinic at Cornell University. The farm milked 3,300 Holstein cows 3 times daily in a double 52-stall parallel milking parlor. The cows were housed in freestall barns, with concrete stalls covered with mattresses and bedded with manure solids. All cows were offered a TMR consisting of approximately 55% forage (corn silage, haylage, and wheat straw) and 45% concentrate (corn meal, soybean meal, canola, cottonseed, and citrus pulp) on a DM basis. The diet was formulated to meet or exceed the NRC nutrient requirements for lactating Holstein cows weighing 650 kg and producing 45 kg of 3.5% FCM (NRC, 2001). The chemical compositions (mineral and vitamins) of prefresh and lactating cow diets for study farm are presented in Table 1. The farm reproductive management used a combination of Presynch, Ovsynch, Resynch and detection of estrus, with 25 to 30% of cows bred via timed AI and the remainder bred after detection of estrus solely by activity monitors (Alpro; DeLaval, Kansas City, MO).

Study Design and Treatments

A total of 270 cows were enrolled in the study. A complete randomized field trial study design was used; cows were randomly allocated into 1 of 2 treatments groups: ITMS or control. All dry cows that were available during the enrollment period were included in the study (Figure 1). Randomization was completed in Excel (Microsoft, Redmond, WA) using the random number function and imported into the farm's Dairy Comp 305 program (Valley Agricultural Software, Tulare, CA). Cows that were randomly assigned to the treatment group received 2 injections of trace minerals (Multimin North America, Inc., Fort Collins, Co) at 230 and 260 d of gestation; each injection contained 300 mg of Zn, 50 mg of Mn, 25 mg of Se, and 75 mg of Cu. Blood samples were collected from coccygeal vein or artery using a Vacutainer tube without anticoagulant (for serum), a Vacutainer tube with lithium heparin (for plasma), and a 20-gauge × 2.54-cm Vacutainer needle (Becton, Dickinson and Company, Franklin Lakes, NJ). After collection, all blood samples were transported to the laboratory on ice and spun in a centrifuge at 2,000 × g for 15 min at 4°C, and the serum and plasma were harvested and frozen at −80°C. Serum and plasma samples were collected at 230 ± 3 d of gestation, 260 ± 3 d of gestation, 274 ± 3 d of gestation, 3 ± 2 DIM, 7 ± 2 DIM, 14 ± 2 DIM, and 25 ± 3 DIM. Body condition scores were determined for all study cows at blood collection time by a single investigator blinded to treatment group using a 5-point scale with a quarter-point system, as previously described (Edmonson et al., 1989).