J. Dairy Sci. 98:1–12
http://dx.doi.org/10.3168/jds.2014-8841

Patterns of circulating serotonin and related metabolites in multiparous dairy cows in the peripartum period

S. A. E. Moore,* J. Laporta,* T. D. Crenshaw,† and L. L. Hernandez*[1]
*Department of Dairy Science, and
†Department of Animal Science, University of Wisconsin-Madison, Madison 53706

ABSTRACT

Dairy cows are challenged to maintain Ca and glucose homeostasis during the transition period. Serotonin (5-HT) is a monoamine that modulates Ca and glucose homeostasis in rodents. Serotonin is positively correlated with Ca and glucose status in dairy cows on d 1 of lactation. However, the pattern of circulating concentrations of 5-HT over the course of a 305-d lactation is unknown. In this observational, longitudinal study, we examined the metabolite patterns of 5-HT, Ca, glucose, parathyroid hormone-related protein, and β-hydroxybutyrate on 2 commercial dairy farms in south-central Wisconsin. Cows sampled on farm 1 were multiparous Jersey cows (n = 30) that calved within a 23-d period; cows on farm 2 were multiparous Holstein cows (n = 35) that calved within a 20-d period. Blood samples were collected daily between d −5 and d 10 relative to parturition and on d 30, 60, 90, 150, and 300 of lactation. Farms 1 and 2 were analyzed individually because of the presence of a farm effect in the initial analysis; a time effect was present on both farms. Concentrations of 5-HT decreased near parturition compared with prepartum by 57.9 and 29.5% on farm 1 and 2, respectively. Transition period 5-HT nadirs were observed on d 1 on farm 1, and on d 1 and 9 on farm 2. Serotonin recovered to prepartum concentrations by d 5 on farm 1. On farm 2, 5-HT recovered to prepartum concentrations by d 4, with a subsequent decrease of 34.6% on d 9 to a level similar to that observed on d 1. Furthermore, 5-HT increased markedly in cows on both farms near peak lactation (d 60, 90, and 150) and decreased on d 300. Compared with prepartum concentrations, Ca decreased by 34.2 and 11.2% on farms 1 and 2, respectively. Circulating total Ca nadir was observed on d 1 on both farms. Circulating 5-HT and circulating Ca were positively correlated during the early lactation period (d 1 to 5 and d 6 to 10) on farm 1 (r = 0.31 and r = 0.22, respectively) and d 6 to 10 on farm 2 (r = 0.16). Circulating 5-HT and glucose were negatively correlated during the early lactation period (d 1 to 5) on farm 1 (r = −0.21) and during mid-lactation (d 30 to 150) on farm 2 (r = −0.26). Milk 5-HT and milk total Ca were positively correlated on farm 2 (r = 0.34). These results demonstrate that 5-HT concentrations change dynamically throughout the transition period, with a pattern similar to that of total Ca concentrations. Further research using controlled experiments should be aimed at discerning the association between 5-HT and Ca and between 5-HT and glucose in dairy cows.

Key words: calcium, lactation, hypocalcemia, serotonin

INTRODUCTION

Dairy cows are challenged to maintain Ca and glucose homeostasis during the transition period. The transition period is defined as 3 wk prepartum through 3 wk postpartum (Grummer, 1995). Subclinical hypocalcemia (total blood Ca = 1.4–2.0 m*M*) affects 25% of primiparous and 47% of multiparous cows postpartum. In addition, clinical hypocalcemia (total blood Ca <1.4 m*M*) is observed in 5 to 10% of all dairy cows (Reinhardt et al., 2011). Hypocalcemia is associated with an increased risk of production losses, displaced abomasum, metritis, reproductive deficiencies, and ketosis (Adams et al., 1996). Jersey cows have a 2.25 times greater risk of developing hypocalcemia than Holstein cows (Lean et al., 2006). In addition, milk from Jersey cows contains approximately 36% more Ca than Holstein milk (Czerniewicz et al., 2006).

Serotonin (5-hydroxytryptamine; **5-HT**) is a monoamine that modulates Ca and glucose homeostasis in rodents (Laporta et al., 2013a,b). Serotonin mediates numerous processes in the mammary gland, including tight junction permeability, parathyroid hormone-related protein (**PTHrP**) production, and Ca and glucose transporter expression (Matsuda et al., 2004; Stull et al., 2007; Hernandez et al., 2012; Laporta et al., 2013a,b). Serotonin and PTHrP are known activators

Received September 10, 2014.
Accepted February 23, 2015.
[1]Corresponding author: llhernandez@wisc.edu

of the cytokine receptor activator of nuclear factor-κB ligand pathway (Hernandez et al., 2012). Activation of this pathway increases bone demineralization and Ca resorption to meet demands when circulating Ca levels are insufficient (Wysolmerski, 2002, 2010; Chabbi-Achengli et al., 2012).

Feeding a 5-HT precursor, 5-hydroxytryptophan, increased osteoclast number and size, as well as serum total Ca concentrations in a murine model (Laporta et al., 2013b). Parathyroid hormone-related protein concentrations were also increased. Serotonin may regulate glucose homeostasis, as liver mRNA expression of gluconeogenic and glycolytic enzymes were greater in 5-hydroxytryptophan–supplemented animals (Laporta et al., 2013a). On d 1 of lactation, 5-HT was positively correlated with Ca and PTHrP concentrations and negatively correlated with ketosis severity in dairy cows (Laporta et al., 2013c).

The potential use of 5-HT in the dairy industry is an exciting possibility. However, 5-HT has not been evaluated temporally in the dairy cow to date. To effectively study 5-HT in dairy cows, the temporal changes that occur in dairy cows not subjected to treatment need to be established. Therefore, the experiment herein was designed as a longitudinal observational study in multiparous Jersey and Holstein dairy cows maintained on 2 dairy farms in south-central Wisconsin. The results obtained from this experiment will be used to design and conduct future experiments that use 5-HT as a modulator of transition-related health issues in dairy cows as a method to improve the well-being and profitability of dairy cows.

MATERIALS AND METHODS

The College of Agriculture and Life Sciences Animal Care and Use Committee at the University of Wisconsin-Madison approved all experimental procedures used on animals in this study. All protocol (A01489) guidelines for the care and use of animals were strictly followed.

Animals

Multiparous cows were housed on 2 privately owned commercial dairy farms in south central Wisconsin. Farm 1 housed multiparous Jersey animals (n = 30; mean parity = 3.2; average daily milk yield = 30.3 kg; daily ECM yield = 39.0 kg). Breakdown of cows by parity were as follows: second lactation (7), third lactation (16), fourth lactation (4), sixth lactation (2), and seventh lactation (1). Cows were housed in a compost bedding pack barn until d 5 postpartum and then housed in a freestall barn through the remainder of the trial. A TMR formulated to meet or exceed NRC recommendations (NRC, 2001) was fed once daily at 0700 h throughout the experiment and animals had ad libitum access to water. The prefresh ration on this farm was formulated as a 41% forage (corn silage, grass hay, alfalfa haylage) to 59% concentrate (oat hulls, soy hulls, canola meal, corn distillers, mineral-protein mix) ratio with a DCAD of 1.127 mEq/100 g of DM. Cows were milked twice daily at 0500 and 1700 h during lactation.

Farm 2 housed Holstein cows. Multiparous cows (n = 35; mean parity = 2.8; average daily milk yield = 47.2 kg; daily ECM yield = 48.9 kg) were housed in a freestall barn through the entirety of the trial. Breakdown of cows by parity were as follows: second lactation (20), third lactation (8), fourth lactation (3), fifth lactation (3), and sixth lactation (1). Cows were fed a TMR formulated to meet or exceed NRC recommendations (NRC, 2001) once daily at 0800 h throughout the experiment and animals had ad libitum access to water. The prefresh ration on this farm was formulated as a 41% forage (corn silage, alfalfa haylage, straw) to 58% concentrate (malt sprouts, wet molasses, mineral protein mix) ratio with a DCAD of −11 mEq/100 g of DM. The DM target was 14 kg of feed per day. Cows were milked 3 times daily at 0400, 1200, and 2000 h during lactation.

Enrollment in the study began on farm 1 on January 22, 2013, and on farm 2 on February 13, 2013. Cows calved within a 23-d and 20-d period on farm 1 and farm 2, respectively. Animals on both dairies were appropriately treated for disease symptoms (i.e., hypocalcemia, ketosis, mastitis) when intervention was deemed necessary by the farm staff, and all animals were included in the study unless they left the herd before conclusion of the study.

Blood and Milk Samples

Blood serum and plasma samples were harvested from blood collected via the coccygeal vein on d −5, −4, −3, −2, −1, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10, relative to parturition (**DRTP**). Samples were also collected on d 30 ± 2, d 60 ± 2, d 90 ± 2, d 150 ± 2, and d 300 ± 2 DRTP. Collection took place immediately following the time of first milking of the stated day for both dry and lactating cows. Whole blood for serum harvest was collected in an evacuated 10-mL Clot Activator BD Vacutainer Serum Plus Blood Collection Tubes (367820, Becton Dickinson and Co., Franklin Lakes, NJ). Whole blood taken for plasma harvest was collected in an evacuated 10-mL BD Vacutainer with lithium heparin (367880, Becton Dickinson and Co.).