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Feed intake is related to changes in plasma nonesterified fatty acid concentration and hepatic acetyl CoA content following feeding in lactating dairy cows

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ABSTRACT

The relationship between hepatic acetyl CoA (AcCoA) content and dry matter intake (DMI) was evaluated using 28 multiparous Holstein cows; 14 were early postpartum (PP; 12.6 ± 3.8 d in milk) and 14 were late-lactation cows (LL; 269 ± 30 d in milk). Cows were fed once daily, and DMI was determined for the first 4 h after feeding. Liver and blood samples were collected before feeding and 4 h after feeding. Feed intake over the 4-h period ranged from 3.7 to 9.6 kg of dry matter and was similar for the 2 stages of lactation. Before feeding, hepatic AcCoA content was greater for PP compared with LL cows (34.4 vs. 12.5 nmol/g), and decreased over the 4 h after feeding for PP only (28.7 vs. 34.4 nmol/g). The range for change in AcCoA over the 4-h period was wide for both PP (−24.3 to 10.4 nmol/g) and LL (−5.7 to 16.1 nmol/g), and was related negatively to DMI at 4 h for both PP ($R^2 = 0.55$) and LL ($R^2 = 0.31$). The reduction in plasma NEFA concentration over the 4-h period was greater for PP than LL cows (−681 vs. −47 μEq/L), and was related to DMI at 4 h for both PP and LL (both $R^2 = 0.38$). Greater DMI among cowsover the first 4 h after feeding might have been from a sharper reduction in supply of AcCoA in the liver for oxidation during meals because of the reduction in plasma NEFA concentration. Consistent with this is that the change in AcCoA was positively related to the reduction in plasma NEFA concentration for PP cows ($R^2 = 0.31$). However, change in plasma NEFA concentration was not related to change in hepatic AcCoA in LL cows, indicating that the pool of AcCoA in LL cows is not as dependent on NEFA flux to the liver as that of PP cows. Further research is required to determine production and fate of AcCoA within the timeframe of meals and the effects of feeding on energy charge in hepatic tissue.

Key words: acetyl CoA, late lactation, metabolic control of intake, nonesterified fatty acid, postpartum

INTRODUCTION

Various fuels including FA, lactate, and AA enter the tricarboxylic acid cycle for oxidation through acetyl CoA (**AcCoA**). Hepatic content of AcCoA is elevated during the lipolytic state when flux of NEFA to the liver and β-oxidation increase greatly (Reynolds et al., 2003). During a meal, anapleurosis of the tricarboxylic acid cycle in hepatocytes will increase oxidation of AcCoA, generating reducing equivalents and CO_2, and increasing ATP production, possibly decreasing feed intake (Allen and Piantoni, 2013). Propionate enters the tricarboxylic acid cycle through succinyl CoA and is considered a primary anapleurotic metabolite, especially during meals (Allen et al., 2009). The hypophagic effects of propionate infusions have been associated with the size of the existing pool of hepatic AcCoA among early-lactation cows (Stocks and Allen, 2012, 2013). Stocks and Allen (2012) showed that the decrease in DMI observed with propionic acid infusions was positively related to hepatic AcCoA content in early-postpartum cows. In addition, it was shown in a later study that propionic acid infusions decreased DMI in postpartum dairy cows but only over the first 4 h after feeding and not the remaining 20 h, and more so in cows with higher hepatic AcCoA content (Stocks and Allen, 2013). Because propionate flux to the liver increases dramatically within the time frame of meals (Benson et al., 2002), its central role for stimulating satiety in dairy cattle by increasing oxidation of AcCoA in the tricarboxylic acid cycle has been suggested (Allen, 2000; Allen et al., 2005). Moreover, Oba and Allen (2003) showed that intraruminal infusions of propionate were more hypophagic in early- than in mid-lactation cows. Because late-lactation cows are not in a lipolytic state, their hepatic pool of AcCoA is not expected to be large, and therefore, control of intake in these cows might be less affected by propionate flux to the liver compared with early-lactation cows.

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Extensive research in laboratory animals supports the theory that oxidation of fuels in the liver affects feed intake (Friedman et al., 1986), and this mechanism has been proposed to be conserved in ruminants (Allen et al., 2005). Fuels that can be extracted from the blood and oxidized in the ruminant liver include propionate, butyrate, NEFA, AA, glycerol, and lactate. Fuels are oxidized in the tricarboxylic acid cycle, generating CO_2 and reducing equivalents that will then feed into the oxidative phosphorylation cascade, generating ATP, and possibly increasing hepatic energy status and contributing to satiety (Allen and Piantoni, 2013). The energy status of the liver, determined by the balance between the rate of production and utilization of high-energy bonds, and not the oxidation of fuels or ATP production per se, is likely the signal that affects feed intake (Friedman, 1997; Friedman et al., 1999). During a meal, anapleurosis of the tricarboxylic acid cycle from propionate will initially be offset by catapleurosis of intermediates such as malate for glucose production until the gluconeogenic pathway is saturated. At this point, oxidation of AcCoA will increase due to increased supply of tricarboxylic acid cycle intermediates (Allen et al., 2009), likely increasing ATP production and contributing to satiety. Re-entry of tricarboxylic acid cycle intermediates into the mitochondria as pyruvate might contribute to AcCoA supply as their concentrations in the cytosol build up when the gluconeogenic pathway is saturated from continuous flux of propionate to the liver during a meal, especially for cows in late lactation with lower hepatic acetyl CoA content.

The objective of this experiment was to evaluate the relationship between hepatic AcCoA and DMI in early postpartum and late-lactation dairy cows. We hypothesized that (1) hepatic AcCoA will be higher for early postpartum than late-lactation cows, (2) hepatic AcCoA will decrease after feeding regardless of stage of lactation, and (3) a greater decrease in hepatic AcCoA will be related to lower DMI during the first 4 h after feeding.

MATERIALS AND METHODS

Animal Housing and Care

All experimental procedures were approved by the Institutional Animal Care and Use Committee at Michigan State University (East Lansing). All cows were housed in the same tie-stall throughout the experiment. Cows were fed once daily (1000 h) at 115% of expected intake and milked twice daily (0500 and 1630 h). The amounts of feed offered and refused were weighed for each cow daily.

Design and Treatment Diets

Twenty-eight multiparous Holstein cows at the Michigan State University Dairy Field Laboratory, consisting of 14 early postpartum (**PP**) cows with the following characteristics: 12.6 ± 3.8 DIM, 48.5 ± 7.9 kg 3.5% FCM, 85.8 ± 94 × 1,000/mL SCC, 2.70 ± 0.45 BCS, and 709 ± 42 kg of BW (all means ± SD), and 14 late-lactation (**LL**) cows with the following characteristics: 269 ± 30 DIM, 31.4 ± 5.9 kg 3.5% FCM, 137 ± 96 × 1,000/mL SCC, 2.90 ± 0.52 BCS, and 744 ± 50 kg of BW (all means ± SD), were used in a randomized block design experiment. Cows were blocked by date of parturition of PP cows. Postpartum cows were between 3 and 14 DIM, and LL cows were over 200 DIM at the beginning of the experiment. Depending on the number of PP cows in each block, LL cows were chosen from the herd based on stable milk yield, DMI, and health. The experiment was conducted over a period of 2 mo with 3 blocks containing 6, 10, and 12 cows each. Within blocks, cows were paired by stage of lactation (each pair contained 1 PP and 1 LL cow). No other criteria were used for the pairing, but stage of lactation and cows were randomly assigned to alternate stalls by stage of lactation. The experiment lasted 4 d for each block of cows: cows were adjusted to stalls for the first 3 d and feeding behavior was recorded and samples collected on d 4. On d 4, feeding was staggered by pair to allow for biopsies to be performed 4 h after feeding. A postpartum or late-lactation diet was offered to the cows depending on their stage of lactation. The ingredient and nutrient composition of the diets fed as TMR are reported in Table 1. Diets were formulated to meet requirements according to NRC (2001).

Data and Sample Collection

Feed offered and refused was recorded throughout the experiment. However, only feed offered and refused recorded on d 4 was used for statistical analyses. Milk yield was recorded and milk samples were collected at each milking on d 4 for composition analyses. Body weight and BCS (Wildman et al., 1982) were recorded once per block. To characterize diets, a TMR sample was collected once per block.

On d 4 of the experiment, feed refused was also recorded at 4 h after feeding, and blood and liver samples were collected before and 4 h after feeding for each cow. Blood samples were collected by venipuncture of coccygeal vessels before liver biopsies into 2 evacuated tubes, one containing potassium EDTA and the other containing potassium oxalate with sodium fluoride as a glycolytic inhibitor. Both tubes were centrifuged at