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Hypophagic effects of propionate increase with elevated hepatic acetyl coenzyme A concentration for cows in the early postpartum period

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ABSTRACT

Thirty multiparous lactating dairy cows were used in a randomized block design experiment to evaluate factors related to the degree of hypophagia from intraruminal infusion of propionate. Cows between 3 and 40 d postpartum at the start of the experiment were blocked by calving date and randomly assigned to treatment. Treatments were 1.0 mol/L propionic acid or 1.0 mol/L acetic acid adjusted to pH 6 with sodium hydroxide and infused at 0.5 mol of volatile fatty acid/h from 6 h before feeding until 12 h after feeding. Propionate infusion decreased dry matter intake by 20.0%, total metabolizable energy intake by 22.5%, and plasma β-hydroxybutyrate concentration by 54.3% compared with acetate infusion. Effects of treatment on dry matter intake were related to concentration of acetyl coenzyme A (CoA) in the liver; hypophagic effects of propionate compared with acetate increased as liver acetyl CoA concentration increased. Hypophagic effects of propionate are greater for cows with elevated concentrations of acetyl CoA in the liver.
Key words: dairy cow, propionic acid, dry matter intake

INTRODUCTION

Research in rodents suggests that meals can be terminated by a signal carried from the liver to the brain via vagal afferents, which is affected by hepatic oxidation of fuels and generation of ATP (Langhans and Scharrer, 1992; Friedman, 1995). Allen et al. (2005) suggested that, of fuels metabolized by the ruminant liver, propionate is likely a primary satiety signal because (1) its flux to the liver increases greatly during meals (Benson et al., 2002), (2) hepatic extraction of propionate from the portal vein exceeds 70% (Reynolds et al., 2003), and (3) hypophagic effects of propionate are eliminated by hepatic vagotomy (Anil and Forbes, 1980). Propionate might stimulate satiety by its oxidation via conversion to acetyl CoA if its uptake by the liver exceeds gluconeogenic flux, or by stimulation of oxidation by anapleurosis of an existing pool of acetyl CoA derived from other fuels (Allen et al., 2009).

Increasing ruminal starch fermentation increases propionate flux to the liver by increasing production of VFA as well as propionate as a fraction of total VFA (Davis, 1967). Increased ruminal starch fermentation reduced feed intake of lactating cows in several experiments reported in the literature, as reviewed by Allen (2000). An experiment from our laboratory demonstrated that a more rapidly fermented starch source almost doubled the fractional rate of starch digestion in the rumen and reduced feed intake 8% because of a 17% reduction in meal size compared with a less fermentable starch source (Oba and Allen, 2003a). The reduction in meal size might be because hepatic oxidation was stimulated by propionate (Allen, 2000).

Hypophagic effects of propionate are greater for cows in the immediate postpartum period compared with those in mid lactation (Oba and Allen, 2003b). Beginning prepartum and for several weeks postpartum (**PP**), cows are in a lipolytic state, when energy requirements for milk production increase at a greater rate than energy consumed. Hyperlipidemia in the periparturient period is initially caused by a reduction in plasma insulin concentration combined with a reduction in insulin sensitivity of adipose tissues (Bell, 1995). Uptake of NEFA by the liver increases greatly (Reynolds et al., 2003), resulting in increased FA oxidation, buildup of acetyl CoA, and hepatic export of ketones. Hepatic oxidation of FA and generation of ATP might suppress feed intake in the periparturient period, and hypophagic effects of propionate may be enhanced because propionate uptake by the liver stimulates oxidation of the existing pool of acetyl CoA (Allen et al., 2009).

The objective of this experiment was to evaluate the relationship between hypophagia from intraruminal infusion of propionate relative to acetate and characteristics of cows in the PP period that are in a lipolytic state. We hypothesized that hypophagic effects of propionate increase when hepatic acetyl CoA concentration is elevated. Propionate is expected to

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stimulate oxidation of acetyl CoA in the tri-carboxylic acid cycle, causing satiety sooner and decreasing meal size for cows with elevated acetyl CoA concentration in the liver. Understanding the mechanisms controlling energy intake during the peripartum period in cows is vital to maintaining healthy, productive cows.

MATERIALS AND METHODS

Animals, Housing, and Diets

The Institutional Animal Care and Use Committee at Michigan State University approved all experimental procedures for this experiment. Thirty lactating Holstein cows were ruminally cannulated at least 45 d before calving. Cows were housed in individual tie stalls for the duration of the experiment. Cows were fed once daily (1200 h) at 115% of expected intake and received a common experimental diet from parturition through the end of the experiment. The experimental diet (Table 1) was composed of corn silage, alfalfa silage, alfalfa hay, ground corn, soybean meal, soy hulls, and a vitamin and mineral mix and formulated to meet requirements for absorbed protein, minerals, and vitamins (NRC, 2001).

Experimental Design and Treatments

The experiment was a randomized block design with a covariate period. Cows were between 3 and 40 d PP at the start of the experiment and were assigned to block by calving date, and then randomly assigned to treatment within a block. The experiment was conducted with 5 blocks of cows containing from 4 to 8 cows each within the same calendar year. The length of the experiment was 3 d for each block of cows, including a covariate day to establish baseline values for all measurements on d 1. Day 2 of the experiment was a rest day with no treatment or sampling. Treatments were propionic or acetic acids (1 mol/L, adjusted to pH 6.0 ± 0.1 with sodium hydroxide) continuously infused into the rumen at 0.5 mol of VFA/h from 0600 h to 2400 h (9 mol/18-h infusion) on d 3 of the experiment. Solutions were infused at 500 mL/h using peristaltic pumps (#78016-30, Cole-Parmer Instrument, Vernon Hills, IL) with Tygon tubing (1.6 mm i.d.) from individual containers that were manually refilled with 500 mL of treatments hourly to ensure accurate infusion rates per hour. Infusions began 6 h before feeding to reach a steady-state VFA concentration in the rumen before starting the monitoring of feeding behavior.

Table 1. Ingredients and nutrient composition of experimental diet (% of dietary DM except for DM)

Item	Value
Diet ingredient	
Corn silage	38.7
Alfalfa silage	30.2
Alfalfa hay	6.0
Ground corn	10.9
Soybean meal	6.9
Soy hulls	4.2
Vitamin and mineral mix[1]	4.0
Nutrient composition	
DM	51.0
OM	92.2
Starch	19.2
NDF	37.1
ADF	27.5
CP	15.9
Ether extract	3.7

[1]Vitamin and mineral mix contained 24.8% ground corn grain, 21.5% dehydrated cane molasses, 11.2% limestone, 9.6% blood meal, 9.0% sodium bicarbonate, 6.6% dicalcium phosphate, 4.2% ReaShure choline (Balchem Corp., New Hampton, NY), 3.1% magnesium sulfate, 2.8% salt, 2.0% animal fat, 1.5% niacin, 1.3% trace mineral mix, 0.95% biotin, 0.70% Yeast Plus (Chr. Hansen, Milwaukee, WI), 0.54% vitamin ADE premix, 0.32% selenium yeast, and 0.09% Rumensin 90 (Elanco Animal Health, Indianapolis, IN).

Data and Sample Collection

Cows were blocked from feed from 1000 to 1200 h daily to allow for weighing of orts, collection of orts samples, and offering feed. Samples of all diet ingredients (0.5 kg), the TMR (0.5 kg), and orts (12.5% of the remaining feed) were collected daily and composited into one sample per cow per block for analysis. Body weight and BCS were recorded on d 1 of the experiment. Body condition was scored by 3 trained investigators on a 5-point scale, where 1 = thin and 5 = fat, as described by Wildman et al. (1982). Cows were milked twice daily at 0400 and 1700 h in the milking parlor, with the exception of the covariate day and infusion day, when cows were milked in their stalls. Milk samples were collected from each milking during the covariate day and analyzed for fat, true protein, lactose, and SNF by Michigan DHIA (AOAC, 1997).

Blood, rumen, and fecal samples were collected every 6 h for 24 h (n = 4) during the covariate day. Rumen fluid samples were collected from 5 different sites in the rumen, squeezed through a nylon screen, and pH was determined immediately. Samples were then frozen at −20°C for later analysis of VFA and ammonia-N concentrations. Fecal samples were collected and frozen at −20°C for later analysis to determine diet digestibility for use in calculating ME intake. Blood samples were collected via coccygeal venipuncture into 2 Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ): 1 with potassium EDTA and 1 with potassium oxalate and sodium fluoride (as a glycolytic inhibitor). Blood samples