J. Dairy Sci. 99:1–13
http://dx.doi.org/10.3168/jds.2016-11711

Effect of reducing milk production using a prolactin-release inhibitor or a glucocorticoid on metabolism and immune functions in cows subjected to acute nutritional stress

S. Ollier,* F. Beaudoin,* N. Vanacker,*† and P. Lacasse*[1]
*Sherbrooke Research and Development Centre, Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8
†Département de biologie, Faculté des sciences, Université de Sherbrooke, Sherbrooke, QC, Canada J1K 2R1

ABSTRACT

When cows are unable to consume enough feed to support milk production, they often fall into severe negative energy balance. This leads to a weakened immune system and increases their susceptibility to infectious diseases. Reducing the milk production of cows subjected to acute nutritional stress decreases their energy deficit. The aim of this study was to compare the effects on metabolism and immune function of reducing milk production using quinagolide (a prolactin-release inhibitor) or dexamethasone in feed-restricted cows. A total of 23 cows in early/mid-lactation were fed for 5 d at 55.9% of their previous dry matter intake to subject them to acute nutritional stress. After 1 d of feed restriction and for 4 d afterward (d 2 to 5), cows received twice-daily i.m. injections of water (control group; n = 8), 2 mg of quinagolide (QN group; n = 7), or water after a first injection of 20 mg of dexamethasone (DEX group; n = 8). Feed restriction decreased milk production, but the decrease was greater in the QN and DEX cows than in the control cows on d 2 and 3. As expected, feed restriction reduced the energy balance, but the reduction was lower in the QN cows than in the control cows. Feed restriction decreased plasma glucose concentration and increased plasma nonesterified fatty acid (NEFA) and β-hydroxybutyrate (BHB) concentrations. The QN cows had higher glucose concentration and lower BHB concentration than the control cows. The NEFA concentration was also lower in the QN cows than in the control cows on d 2. Dexamethasone injection induced transient hyperglycemia concomitant with a reduction in milk lactose concentration; it also decreased BHB concentration and decreased NEFA initially but increased it later. Feed restriction and quinagolide injections did not affect the blood concentration or activity of polymorphonuclear leukocytes (PMN), whereas dexamethasone injection increased PMN blood concentration but decreased the proportion of PMN capable of inducing oxidative burst. Incubation of peripheral blood mononuclear cells in serum harvested on d 2 of the restriction period reduced their ability to react to mitogen-induced proliferation, and injection of quinagolide or dexamethasone could not alleviate this effect. This experiment shows that prolactin-release inhibition could be an alternative to dexamethasone for reducing milk production and energy deficit in cows under acute nutritional stress, without disturbing immune function.
Key words: quinagolide, dexamethasone, negative energy balance, dairy cow

INTRODUCTION

In a number of situations, including surgery, inability to stand up, milk fever, and ketosis, cows may be unable to eat enough to support milk production. Consequently, high-yielding cows fall into severe negative energy balance and must mobilize body reserves extensively to balance the deficit between nutrient intake and the nutrients required for milk production. Cows in an energy deficit have a weakened immune system, which increases their susceptibility to infectious diseases such as mastitis and metritis (Suriyasathaporn et al., 2000; Sheldon, 2004; Goff, 2006). Indeed, blood nonesterified fatty acid (**NEFA**) and BHB concentrations increase when cows are in negative energy balance, and glucose concentration decreases (Chilliard et al., 1998); these changes in metabolite concentrations may affect the immune functions of leukocytes (reviewed in Ingvartsen and Moyes, 2013). Therefore, strategies that improve energy status may limit immunosuppression in cows subjected to acute nutritional stress.

Reducing the milk production of cows under acute nutritional stress decreases their energy deficit. Glucocorticoids such as dexamethasone are used to treat disorders such as ketosis, mastitis, respiratory tract diseases, udder edema, and musculoskeletal inflamma-

Received July 6, 2016.
Accepted September 2, 2016.
[1]Corresponding author: Pierre.Lacasse@agr.gc.ca

tion. Large doses of glucocorticoids inhibit milk synthesis (Braun et al., 1970; van der Kolk, 1990) and are sometimes used to temporarily reduce milk production in cows under acute nutritional stress. However, glucocorticoids are potent immunosuppressants and increase the risk of infection (Roth and Kaeberle, 1982). Recent studies by our team have shown that quinagolide, a potent and specific inhibitor of prolactin (**PRL**), can also reduce milk production in lactating cows (Lacasse et al., 2011) without causing metabolic disturbance or immunosuppression (Ollier et al., 2014). These findings suggest that an inhibition of the lactogenic signal via PRL could be used to temporarily decrease milk production in lactating cows at high risk of becoming ill. The aim of the present study was to compare the effects on metabolism and immune function of reducing milk production using quinagolide or dexamethasone in feed-restricted cows.

MATERIALS AND METHODS

Animals and Experimental Design

This experiment was conducted in accordance with the guidelines of the Canadian Council on Animal Care (1993). Twenty-three multiparous Holstein cows (99 ± 4 DIM) were housed in individual tie stalls at Agriculture and Agri-Food Canada's Sherbrooke Research and Development Centre (Sherbrooke, QC, Canada). All the cows were subjected to acute nutritional stress by severely restricting their feed for 5 d. They were fed at 55.9 ± 0.4% of their DMI of the previous week. After 1 d of feed restriction and for the remainder of the feed-restriction period, the cows were assigned to 1 of 3 groups as follows: the control group (n = 8) received twice-daily i.m. injections of water (B. Braun Medical Inc., Scarborough, ON, Canada), the quinagolide group (**QN** group; n = 7) received twice-daily i.m. injections of 2 mg of quinagolide (Ferring, Wallisellen, Switzerland), and the dexamethasone group (**DEX** group; n = 8) received the same water injections as the control cows after an initial injection of 20 mg of dexamethasone sodium phosphate (Vétoquinol N.A. Inc., Lavaltrie, QC, Canada). To facilitate experiment management, 2 blocks of cows were studied separately: the first block consisted of 4 control, 3 QN, and 4 DEX cows, and the second block consisted of 4 control, 4 QN, and 4 DEX cows. Before, during, and after the feed-restriction period, all animals were fed a TMR containing (on a DM basis) 36.6% grass silage, 24.4% corn silage, 18.7% corn grain, 10.6% soybean meal, 1.8% beet pulp, 3.0% chopped dry hay, 3.2% non-mineral supplement, and 1.7% mineral supplement. The composition of the TMR is presented in Table 1. Feed intake was recorded daily for each cow from 10 d before feed restriction until 20 d after, and each cow's BW was determined at the start and end of the experiment.

Table 1. Composition of the diet (% of DM unless otherwise noted)

Chemical composition	Value
CP	18.3 ± 0.2
ADF	22.1 ± 0.6
NDF	33.1 ± 1.2
P	0.43 ± 0.01
K	1.85 ± 0.04
Ca	0.89 ± 0.03
NE_L (Mcal/kg of DM)	1.53 ± 0.01

Milk Collection and Energy Balance

The cows were milked twice daily, and milk yield was recorded at each milking from 15 d before feed restriction until 20 d after. Milk samples were collected at the a.m. milking on d −6, −2, −1, 1 (after 1 d of feed restriction), 2 (after 1 d of injections), 3, 4, 5, 6, 12, and 19. Milk fat, protein, lactose, and BHB concentrations and SCC were determined in a commercial laboratory (Valacta Inc., Ste-Anne-de-Bellevue, QC, Canada). Energy balance was estimated as the difference between energy consumed and the sum of energy required for maintenance and milk production, based on milk yield, milk composition, BW, and feed intake, using the NRC equations (National Research Council, 2001).

Blood Collection

Caudal blood samples were taken just before milk collection on d −6, −2, −1, 1, 2, 3, 4, 5, 6, 12, and 19 in Vacutainer collection tubes without additives and in EDTA-coated Vacutainer tubes (BD, Mississauga, ON, Canada). The blood tubes without additives were left at room temperature for approximately 2 h to allow clotting before centrifugation (1,900 × *g*, 4°C, 15 min). Then, the serum was stored at −20°C until determination of PRL, cortisol, urea, and serum amyloid A concentrations. The blood tubes containing EDTA were placed on ice immediately after collection and centrifuged (1,900 × *g*, 4°C, 15 min) within 30 min. Then, the plasma was stored at −20°C until determination of glucose, NEFA, BHB, lactose, and tumor necrosis factor α (**TNF-α**) concentrations.

Jugular blood samples were taken on d −6, 1, 2, and 4 using Vacutainer collection tubes without additives (BD). The tubes were left at room temperature for approximately 2 h to allow clotting before centrifugation (1,900 × *g*, 4°C, 15 min). Then, the serum was stored at −20°C until peripheral blood mononuclear