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Effect of prolactin-release inhibition on milk production and mammary gland involution at drying-off in cows

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ABSTRACT

The end of each lactation is a challenging period for high-yielding cows as they are often dried off while still producing significant quantities of milk and, consequently, are highly susceptible to new intramammary infections. Once involution is complete, the mammary gland becomes much more resistant to infection. Therefore, it is critically important to develop strategies aimed at reducing milk production before drying-off and to accelerate mammary gland involution. This study assessed the effect of inhibition of the lactogenic signal driven by prolactin (PRL) on milk production and concentrations of involution markers in mammary secretions. Sixteen Holstein cows in late lactation were assigned to treatments based on milk yield, somatic cell count, and parity. Of those cows, 8 received twice-daily intramuscular injections (2 mg per injection) of quinagolide, a specific inhibitor of PRL release, from 4 d before drying-off to 3 d after (Quin). The other 8 cows received injections of the solvent (water, control). Blood and milk (mammary secretion) samples were collected on the last 5 d before and on d 1, 3, 5, 7, 10, and 14 after the last milking. Additionally, on the day preceding the first injection and on the following day, several blood samples were collected around milking time. Quinagolide reduced basal serum PRL concentrations on all injection days as well as PRL released in blood during milking. The PRL inhibitor decreased milk production before drying-off, which averaged, over the last 3 d of lactation, 19.3 and 15.5 kg/d for the control and Quin cows, respectively. Quinagolide had no significant effect on milk citrate:lactoferrin and Na:K ratios, which decreased and increased, respectively, during the first 2 wk of the dry period. Nevertheless, the increases in the number of somatic cells and bovine serum albumin concentration during early involution were greater and matrix metalloproteinase-2 activity tended to be greater in mammary secretions of the Quin cows compared with the control cows. This experiment shows that inhibition of PRL release decreases milk production of cows in late lactation. Changes in the composition of mammary secretions suggest that this approach also hastens mammary gland involution.
Key words: quinagolide, dry period, dairy cow

INTRODUCTION

The lactation cycle of the dairy cow requires a dry period for optimal milk production in the following lactation. Although this period is critical for mammary gland remodeling, the cow is highly susceptible to new IMI during the early dry period (see review: Dingwell et al., 2003). After drying-off, although milk is not being removed, the mammary gland temporarily continues to synthesize milk, which accumulates in the udder. The resulting increase in mammary pressure may cause leakage of milk via the teats, allowing microorganisms to gain entry into the mammary gland. In addition, at the beginning of involution, mammary gland secretions contain low concentrations of natural protective factors, such as immune cells, immunoglobulins, and lactoferrin, as well as high concentrations of fat, casein, lactose, and citrate, which can interfere with the defense capacity of the gland and provide an excellent medium for bacterial growth (see reviews: Oliver and Sordillo, 1989; Collier et al., 2012). Once involution is completed, within 30 d after cessation of milking, the mammary gland becomes much more resistant to new IMI because of a low fluid volume in the udder and a medium unfavorable for bacterial growth (see review: Burvenich et al., 2007). With increasing milk production, drying-off has become a challenging period for the dairy cow. Rajala-Schultz et al. (2005) established that the risk of IMI at calving increases by 77% for every 5 kg of milk produced above 12.5 kg when milking is stopped. As it is now common to dry off cows that are still producing 30 kg/d, it is important to develop strategies that reduce milk production before drying-off and to hasten mammary gland involution.

One method commonly used to reduce milk production is a drastic reduction in feed supply in the days

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that precede drying-off. This strategy constitutes metabolic stress, however, especially in high-yielding cows. Another method that is effective in reducing milk production before drying-off is intermittent milking, but its association with a reduction in IMI at calving has not been clearly proven (Dingwell et al., 2003; Newman et al., 2010). Drying-off could be facilitated by decreasing the lactogenic signals driving milk production. Prolactin (**PRL**) is a hormone known to be mammogenic and lactogenic in both monogastric and ruminant mammals. Lacasse et al. (2011) showed that the inhibition of PRL secretion by quinagolide gradually decreases milk production of cows in early lactation, suggesting also a galactopoietic role of PRL in cows. This approach has never been investigated in late-lactation cows, however. The objective of this study was therefore to assess the effect of inhibition of PRL release by quinagolide on milk production just before drying-off and on concentrations of involution markers in mammary secretions after the last milking.

MATERIALS AND METHODS

Animals and Experimental Design

The experiment was conducted in accordance with the guidelines of the Canadian Council on Animal Care (CCAC, 1993). Sixteen Holstein cows in late lactation (278 ± 7 DIM at drying-off), housed at the Dairy and Swine Research and Development Centre of Agriculture and Agri-Food Canada (Sherbrooke, QC, Canada), were assigned to 2 treatments according to their milk yield, SCC, and parity. Of that number, 8 cows received twice-daily (at 0930 h and 2130 h) i.m. injections of 2 mg of quinagolide (Ferring, Wallisellen, Switzerland) from 4 d before drying-off to 3 d after (**Quin**), and the other 8 received injections of the solvent (water, control treatment). The cows were fed ad libitum a late-lactation diet containing (on a DM basis) 28.7% grass silage, 28.6% corn silage, 5.7% dry hay, 20.9% corn grain, 9.6% soybean meal, 4.7% nonmineral supplement, and 1.9% mineral supplement. After drying-off, the cows were fed a dry-period diet containing (on a DM basis) 62.1% dry hay, 25.5% corn silage, 10.1% soybean meal, and 2.3% mineral supplement. Feed intake was recorded daily throughout the experiment, and each cow's BW was determined at the start and end of the experiment.

Before drying-off, the cows were milked twice daily, at 0800 h and 2030 h, and milk yield was recorded at each milking during the last 2 wk. Milk samples were collected at the a.m. milking on the last 5 d before drying-off (d −5 to d −1). After the last milking, each quarter was treated with dry-cow therapy containing cloxacillin benzathine (Dry-Clox, Boehringer Ingelheim, Burlington, ON, Canada). Mammary secretions (60 mL) were manually collected from 1 quarter at 0800 h on d 1, 3, 5, 7, 10, and 14 after the last milking. The sampled quarter was alternated at each sampling, and the teat was dipped into a teat protection sealant containing 0.1% triclosan (Uddergold Dry, Ecolab Inc., St. Paul, MN) after the sampling. The samples were used to measure SCC, and then skimmed by centrifugation (1,900 × *g*, 4°C, 15 min) and stored at −20°C until determination of BSA, lactoferrin, citrate, Na^+, and K^+ concentrations, and gelatinase activity.

Caudal blood samples were taken just before collection of milk and mammary secretions on d −5, −2, −1, 1, 3, 5, 7, 10, and 14. On d −4 (before the first injection) and d −3 (after 2 injections), several blood samples were collected before and during the a.m. milking (−30, −20, −10, 0, 2, 5, 10, 15, 20, 30, 40, 60, 80, 100, and 120 min relative to the start of milking) from a silastic catheter (i.d. 1.02 mm, o.d. 2.16 mm; Dow Corning Corp., Midland, MI) inserted into the jugular vein. All blood tubes (without additive) were left for approximately 2 h at room temperature for clotting before centrifugation (1,900 × *g*, 4°C, 15 min). Then, the serum was stored at −20°C until determination of PRL concentration.

Serum Prolactin Concentration

Serum PRL concentration was measured by RIA as described by Bernier-Dodier et al. (2011). Bovine PRL, rabbit antiserum specific for bovine PRL, and goat anti-rabbit gamma globulin were purchased from the National Hormone and Peptide Program (Harbor-UCLA Medical Center, Torrance, CA). The intra- and interassay coefficients of variation were 3.1 and 4.1%, respectively.

SCC in Milk and Mammary Secretions

Somatic cell count was determined from fresh whole milk and mammary secretion samples using an automatic cell counter (DeLaval International AB, Tumba, Sweden). Samples of mammary secretions were diluted with commercial, skimmed, microfiltered milk until the SCC obtained was between 100 and 200 cells/μL.

Concentration of BSA in Milk and Mammary Secretions

The concentration of BSA in milk and mammary secretion samples was evaluated by a colorimetric assay as previously described by Bouchard et al. (1999), with some modifications. Briefly, 200 μL of skimmed sample was mixed with 450 μL of water and 450 μL of