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Short communication: The effects of cabergoline administration at dry-off of lactating cows on udder engorgement, milk leakages, and lying behavior

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ABSTRACT

Cabergoline is an ergot derivative with high affinity for the D_2 dopamine receptors whose dopaminergic effects cause inhibition of prolactin (PRL) secretion; thus, it could be considered a molecule that acts as a potential dry-off facilitator. One hundred ninety-nine Holstein cows (102 primiparous; 97 multiparous) producing ≥18 kg/d at dry-off were split in 2 treatments to evaluate the effects of diminishing PRL secretion at dry-off (between 70 and 50 d from the expecting calving date) on udder engorgement, milk leakage, and cow well-being after dry-off. Treatments consisted of a single i.m. injection of 5 mL of a solution containing 5.6 mg of cabergoline (CAB; Velactis, Ceva Santé Animal, Libourne, France) or 5 mL of saline solution as a placebo (CTRL). Each animal was evaluated for presence or absence of milk leakages during the 4 d following dry-off and udder engorgement was determined using a digital algometer. Lying behavior was recorded during 10 d after dry-off. Twenty-five cows from each treatment were randomly chosen and blood sampled at 3 and 15 d after dry-off, and again at 5 and 3 d before the expected calving date to determine serum PRL concentrations. Cows on CAB had lower serum PRL concentrations than cows on CTRL at 3 and 15 d after dry-off. Average udder engorgement was lower for cows on CAB than for cows on CTRL following dry-off, and it decreased as days after dry-off increased. The overall incidence of milk leakage in cows on CAB (3.1 ± 0.88%) was 73.5% of that obtained in cows on CTRL (11.7 ± 1.64%); cows on CAB had 0.2 lower odds of incurring milk leakage than cows on CTRL. The day following dry-off, CAB cows lied about 1.5 h/d more than cows on CTRL. We conclude that i.m. administration of 5.6 mg of cabergoline at dry-off effectively reduces PRL secretion, udder engorgement, and milk leakages, and improves lying time the day following dry-off.
Key words: involution, mammary gland, prolactin

Short Communication

With increasing milk production, drying off has become a challenging period for dairy cows. In fact, it is not difficult to find cows producing more than 30 kg/d at dry-off. During this period, the cow is highly susceptible to new IMI (Eberhart, 1986), and this risk is thought to increase as the level of milk production at dry-off increases (Rajala-Schultz et al., 2005) because the gland continues to temporally produce milk, which accumulates in the udder and may lead to leakages (Klaas et al., 2005). Furthermore, accumulation of milk at dry-off may lead to discomfort and pain (O'Driscoll et al., 2011), and it has been postulated that increased udder pressure between milkings may alter lying time and patterns of dairy cows (Österman and Redbo, 2001). However, little information is available about changes in lying patterns of dairy cows around dry-off. One study (Leitner et al., 2007) reported that cows receiving a treatment that reduced milk production at dry-off had longer lying bouts during the 7 d following dry-off compared with control cows.

A potential method to facilitate dry-off would consist of inducing a direct cessation of milk production by interfering with hormonal signals. For instance, intramammary infusions of CN hydrolysate have been shown to reduce milk secretion in dairy cows (Leitner et al., 2007; Ponchon et al., 2014). Also, blocking the release of prolactin (**PRL**) by binding dopamine D_2 receptors using quinagolide has been shown to decrease milk production in both early- (Lacasse et al., 2011) and late-lactation (Ollier et al., 2013) cows and to hasten the involution of the mammary gland at dry-off (Ollier et al., 2014). A similar strategy would consist of administering cabergoline at dry-off. Cabergoline is an ergot derivative with high affinity for D_2 dopamine receptors, which cause inhibition of PRL secretion (Romagnoli et

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al., 2009). In nonruminant animals, cabergoline has a much longer half-life (~70 h) than quinagolide (17 h), and it also has less adverse effects than quinagolide (Kasum et al., 2014). However, in cattle, half-life of cabergoline has been reported to be ~20 h (Velactis; European Medicines Agency, 2014). The hypothesis behind the current study was that the use of cabergoline would cease milk synthesis, resulting in a reduction in udder engorgement and milk leakages and an improvement in the well-being of the cow that would be evident through increased lying times and longer lying bouts after dry-off. Thus, the objectives of our study were to evaluate responses of high-yielding cows treated with cabergoline at dry-off versus untreated cows on udder engorgement, milk leakages, and cow well-being.

One hundred ninety-nine female Holstein cows (102 primiparous; 97 multiparous) were enrolled in this study. Animals were housed in a commercial farm in north-central Spain (SAT La Travesía, Cortes, Spain). All procedures were approved and supervised by the Animal Care Committee of IRTA. All cows were fed once daily (ad libitum) until dry-off time when they were abruptly changed to a dry-cow ration and moved from freestall pens to bedded packs. While lactating, cows were milked in a rotary parlor 3 times a day at 0600, 1400, and 2200 h. The study followed a complete randomized block design. Randomization was performed using a computerized random generation number for each block. Block was the week of enrollment (cows were dried on Tuesdays). For a cow to be included in our study, she had to be free of mastitis, between 70 and 50 d before the expecting calving date, and producing an average of ≥18 kg/d for the last 3 d before drying-off. All cows were dried-off abruptly. At drying time (right after the last milking), 99 cows received an i.m. injection of 5 mL of a solution containing 5.6 mg of cabergoline (Velactis, Ceva Santé Animal, Libourne, France; **CAB**) and the remaining 100 cows received an i.m. injection of 5 mL of the same excipient used in CAB as a placebo (**CTRL**). After the last milking, each quarter was infused with 7 mL of a solution containing 0.6 g of cloxacillin benzathine (Orbenin Extra, Zoetis, Madrid, Spain).

After drying, cows were brought back to the milking parlor at 1100 h (at a different time than when they were typically milked), with all the equipment (except the rotary table) turned-off and thus without the noise of the vacuum pumps, pulsators, and so on; then, each animal was evaluated for presence or absence of milk leakages during the 4 d following drying-off. Milk leakage was defined as milk dropping or flowing from the teat. During this time, udder engorgement was also determined using a digital algometer (Commander, JTech Medical Industries, Midvale, UT) that was modified by welding a 2-cm washer at 2 cm from the tip of the algometer. The measure consisted of applying force to the caudo-ventral side of the rear left and right half udders using the modified algometer, and to stop applying force when the skin of the udder made contact with the washer. The repeatability of the measures obtained by the modified algometer was tested in a pretrial study that involved 20 lactating cows. Udder firmness of each cow was measured using the modified algometer described above for 5 consecutive days on the caudo-ventral side of the rear right and left udders 30 min before and 30 min after milking. Udder pressure before and after milking was 43.5 ± 1.17 and 20.6 ± 0.66 kg·m/s^2 (mean ± SD), respectively, with 100 and 95% of the values falling within 2 and 1.2 standard deviations above and below the average, respectively. Therefore, the repeatability of this technique was considered acceptable under the criterion of British Standards Institution (BSI, 1975), that sustains that 95% of values should be within the range of 2 standard deviations above and below the average.

At dry-off, all cows were equipped with a HOBO Pendant G Acceleration Data Loggers (Onset Computer Corporation, Bourne, MA) on the right hind leg using cohesive bandages to record total daily lying time on an individual basis at 1-min intervals to estimate number and duration of lying bouts and total daily lying time (Ledgerwood et al., 2010). Lastly, 25 cows from each treatment were randomly chosen and blood sampled from the tail vein at dry-off at 3 and 15 d after dry-off, and again at 5 and 3 d before the expected calving date. These samples were subsequently analyzed for serum PRL concentrations using a bovine ELISA kit (Cusabio, Hubei, China) with intra- and interassay coefficients of variation of <15%.

Milk leakage was treated as a binary response variable and analyzed using a mixed-effects logistic regression model, including the random effect of cow and the fixed effects of treatment, parity, and days relative to dry-off, plus their interactions. Milk production at dry-off entered the model as a covariate. Udder engorgement, lying behavior, and blood data were analyzed using a linear mixed-effects model with the same fixed effects described above. In both models, day entered the analysis as a repeated measure.

Average milk production at dry-off did not differ (P = 0.91) between treatment groups, and it was 24.5 ± 0.37 and 24.5 ± 0.38 for cows on CTRL and CAB, respectively (the lowest value for both groups was 18.0 kg/d, and the greatest value was 35.0 and 34.0 kg/d for CTRL and CAB cows, respectively). Also, length of the dry period did not differ (P = 0.76) between treatments, and it was 58.7 ± 0.70 and 58.8 ± 0.70 d for CTRL and CAB cows, respectively (the lowest value