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Effect of a single injection of cabergoline at dry off on udder characteristics in high-yielding dairy cows

S. Bertulat,* N. Isaka,† A. de Prado,† A. Lopez,† T. Hetreau,‡ and W. Heuwieser*¹

*Clinic for Animal Reproduction, Faculty of Veterinary Medicine, Freie Universität Berlin, Koenigschweg 65, 14163 Berlin, Germany

†CEVA Santé Animale, 10 Avenue de la Ballastière, 33500 Libourne, France

‡Centre d'élevage Lucien Biset, 845 Route de l'École d'Agriculture, 74330 Poisy, France

ABSTRACT

In recent years, relationships between high milk yield at dry off, higher prevalence for new intramammary infections, and stress were evaluated. Considering increasing milk yield, dry off methods need to be refined to ensure udder health and animal welfare, especially in high-yielding dairy cows. The present work evaluated the effect of a single cabergoline injection (Velactis, Ceva Santé Animale, Libourne, France) at dry off on udder pressure, milk leakage, and signs of udder pain after dry off. A total of 234 high-yielding (≥ 16 kg of milk/d) dairy cows was enrolled 7 d before and followed up until 14 d after dry off. Cows were dried off without preparation (i.e., no feed change or intermittent milking before dry off) and treated with a single i.m. injection of 5.6 mg of cabergoline ($n = 115$) or placebo ($n = 119$) after last milking. Udder characteristics were measured 4 d before (i.e., before and after milking) and 1, 2, 3, 7, 10, and 14 d after dry off. Udder pressure was evaluated utilizing a hand-held dynamometer. Milk leakage and signs of udder pain were noted as binary variables. Whereas udder pressure baseline values after last milking did not differ between treatment groups (0.541 ± 0.15 kg), cabergoline significantly reduced udder pressure in primiparous but not in multiparous cows after dry off. Differences between cabergoline- and placebo-treated primiparous cows could be evaluated until 3 d after dry off. The first day after dry off, udder pressure in placebo- and cabergoline-treated cows increased by 115% and 42.3%, respectively. Whereas pressure values in placebo cows were highest on the first day after dry off (1.16 ± 0.61 kg) and slowly decreased afterward, udder pressure in cows treated with cabergoline had a slower increase and peak only 2 d after dry off (0.94 ± 0.44 kg). Furthermore, cabergoline caused a reduction of milk leakage, a known factor

for new intramammary infections. Only 11.3% of cows treated with cabergoline showed milk leakage compared with 21.0% placebo-treated cows. Additionally, cows with placebo treatment were 2.8 times as likely to show signs of udder pain compared with cows treated with cabergoline. An effect of cabergoline on udder pressure, milk leakage, and udder pain was limited to the first week after dry off. Our data provide evidence that a single injection of cabergoline reduces risk factors for udder health and animal welfare problems around dry off in high-yielding dairy cows with more than 16 kg of milk/d. Further research is warranted, however, to investigate if cabergoline at dry off can also be used to reduce new intramammary infection rates and improve animal welfare after dry off.

Key words: dairy cow, dry off, cabergoline, milk leakage, prolactin-release inhibitor

INTRODUCTION

It is well documented that dry cow management and the dry period can have a distinct effect on animal health (Kim and Suh, 2003), milk production (Annen et al., 2004; Andersen et al., 2005), and fertility (Beever, 2006) of dairy cows in the following lactation. Although milk yield per cow per year has increased during the last 4 decades by 30 to 50% (Thornton, 2010; Zobel et al., 2015), dry off procedures hardly changed. A sudden dry off is still the most common management practice on commercial dairy farms (Dingwell et al., 2001; Bertulat et al., 2015), whereas milk yield at dry off changed from below 9 (Natzke et al., 1975) to 24 to 30 kg/d (Annen et al., 2004; Chapinal et al., 2014).

Several studies indicated adverse effects of high milk yield before dry off. Bertulat et al. (2013) analyzed the effect of milk yield on udder pressure, milk leakage, and stress levels after sudden dry off. It was shown that high-yielding dairy cows had higher udder pressure and elevated stress levels compared with low-yielding cows. This association between milk yield, udder pressure, and discomfort (i.e., altered standing-lying behavior)

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¹Corresponding author: w.heuwieser@fu-berlin.de

after cessation of milking was described by O'Driscoll et al. (2011) as well, albeit not in cows that were dried off but cows with an omission of a scheduled milking event. Another study implicated that a sudden dry off in high-yielding dairy cows provokes signs of distress, which were associated with neutrophilia in milk (Silanikove et al., 2013).

Rajala-Schultz et al. (2005) demonstrated a relationship between milk yield and IMI after dry off. The authors argued that high milk yield causes milk leakage (Rovai et al., 2007), and therefore a slower formation of the keratin plug. Consequently, the teat canal remains open for bacterial entry for a longer period of time (Dingwell et al., 2004; Rajala-Schultz et al., 2005). Milk leakage is a major cause for IMI both during lactation and after dry off (Schukken et al., 1993; Waage et al., 1998; Pezeshki et al., 2010), and has been demonstrated to occur more often after sudden dry off than after gradual cessation of milking (Zobel et al., 2013). In cows with sudden dry off the prevalence was higher in high- compared with low-yielding cows (Bertulat et al., 2013). Considering these relationships and the ongoing increase of milk yield, strategies to facilitate an efficacious dry off procedure and to reduce udder pressure and milk leakage are necessary.

Several management methods are known to reduce milk secretion before and immediately after dry off (Bertulat et al., 2015). Valizadeh et al. (2008) compared the effect of 2 different hay diets before dry off and showed that both were efficient in decreasing milk production. These results were supported by Tucker et al. (2009), who demonstrated that feed restriction and gradual cessation of milking had a negative effect on milk yield before dry off. Furthermore, Tucker et al. (2009) reported a decreased prevalence of milk leakage and IMI after dry off in cows with reduced feed intake, but not after gradual cessation of milking. In contrast to Tucker et al. (2009), Zobel et al. (2013) found less milk leakage in cows with gradual dry off compared with cows that were dried off abruptly. Milk yield before dry off, however, was distinctively higher than in the study population used by Tucker et al. (2009), and both groups (i.e., abrupt and gradual dry off) were fed a low-energy diet. An explanation for these findings was provided by Bushe and Oliver (1987), who investigated the effect of different dry off methods on milk composition after dry off and the ability to inhibit growth of coliform mastitis pathogens and, thus, prevent new IMI. Whereas no differences between cows that were dried off abruptly or by gradual cessation of milking were noted, cows that were milked intermittently and fed a hay diet had higher concentrations of somatic cells, lactoferrin, IgG, and BSA and had a higher inhibitory

activity to in vitro growth of *Escherichia coli* (Bushe and Oliver, 1987).

Feed restriction, however, has several disadvantages. Tucker et al. (2009), as well as Valizadeh et al. (2008), reported that cows exposed to reduced feed intake had a greater frequency of vocalization and probably suffered from hunger. Furthermore, severe feed restriction (i.e., straw diet) caused increased cortisol levels, affected nonesterified fatty acid, BHB, and urea concentrations (Odensten et al., 2005, 2007). These metabolic imbalances indicate a negative energy balance that might cause an impairment of udder defense mechanisms (O'Rourke, 2009). In the studies presented by Odensten et al. (2005, 2007), udder health, however, was neither improved nor deteriorated by feed restriction.

Recently, some studies explored pharmacological options to hasten mammary gland involution. Casein hydrolysate was shown to have a positive effect on udder pressure and resting behavior in high-yielding dairy cows (Leitner et al., 2007) and hastened mammary gland involution (Ponchon et al., 2014). Furthermore, other studies have shown that the innate immune system of the mammary gland is activated by casein hydrolysate, which might potentially prevent bacterial infection (Silanikove et al., 2005). To our knowledge, data from field studies on the efficacy of casein hydrolysate, however, have not been published.

Furthermore, systemic application of prolactin-release inhibitors and their effects on mammary gland involution has been investigated. Prolactin-release inhibitors are dopamine D2 receptor agonists, inhibiting the release of prolactin in the pituitary gland. As a result, the galactopoietic effect of prolactin is countered (Lacasse et al., 2012). Quinagolide, a prolactin-release inhibitor shown to reduce milk production (Lacasse et al., 2012; Ollier et al., 2013, 2014), improved resistance to IMI after dry off (Ollier et al., 2015). Although these results are promising, the treatment regimen (i.e., once or twice daily for several days) is hardly adequate for field applications (Ollier et al., 2015).

Cabergoline (**CAB**) is a prolactin-release inhibitor approved to treat false pregnancies in bitches in most European countries (Gobello et al., 2001). Several studies investigated the effect of CAB on milk secretion (Jöchle et al., 1987) and lactation in healthy bitches and those with pseudopregnancies (Arbeiter et al., 1988; Harvey et al., 1997). Furthermore, a case study (Arlt et al., 2011) mentioned the application of CAB in goats with inappropriate lactation syndrome. Therefore, the objective of our study was to evaluate the effect of a single CAB injection at dry off on udder pressure, milk leakage, and udder pain after dry off in high-yielding dairy cows.

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