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Residue concentration of cefquinome after intramammary dry cow therapy and short dry periods

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ABSTRACT

Short dry periods and their effects on milk production, reproductive performance, as well as cow and udder health have been widely studied. A dearth of information is available about the consequences of short dry periods on the residue concentrations of dry cow antibiotics in milk after calving. The objective of our study was to determine the residue concentration of a dry cow antibiotic in milk after short dry periods during the colostrum period and early lactation. Quarters of 19 dry cows were treated with an intramammary (IMM) dry cow antibiotic containing 150 mg of cefquinome on d 21, 14, and 7 before calculated calving date. One quarter of each cow did not receive treatment and served as negative control. After calving, quarter foremilk samples were collected twice daily until 21 d and once daily until 36 d after IMM dry cow treatment (i.e., end of withdrawal period). A total of 588 foremilk samples from odd milking numbers were chosen for the determination of the residue concentration of cefquinome using HPLC–tandem mass spectrometry until the residue concentration fell below the limit of quantification (1 ng/g), which occurred at the latest in milking number 37. The dry period length of the treated quarters was categorized in 3 dry period groups ranging from 1 to 7 d (4.8 ± 2.4), 8 to 14 d (11.5 ± 2.3), and 15 to 26 d (19.5 ± 3.3; ±SEM), in dry period group 1, 2, and 3, respectively. In dry period group 1, the cefquinome concentration increased after calving until the third milking and decreased considerably until the fifth milking. In dry period group 2, the cefquinome concentration peaked at the second milking and decreased considerably until the fifth milking as well. There was no increase in cefquinome after calving in dry period group 3. Up to the 37th milking, the cefquinome concentration was higher in dry period group 1 than in dry period group 2 and 3. On average, 31.3 ± 1.2, 19.0 ± 1.1, and 6.7 ± 0.8 milkings and 19.4 ± 0.4, 20.6 ± 0.5, and 24.1 ± 0.7 d after treatment were necessary for the concentration of cefquinome to fall below the maximum residue limit (MRL) in dry period group 1, 2, and 3, respectively. These results indicate that shorter dry periods lead initially to higher cefquinome residues in milk. The residue concentration after experimental short dry periods still falls below the MRL within the recommended withdrawal period for milk of 36 d after IMM dry cow treatment. For the sake of food safety and economics, these short dry periods should not be used in the dry cow management, as they lead up to a maximum of 31.3 ± 1.2 milkings and 19.4 ± 0.4 d after treatment with cefquinome residues above the MRL. Therefore, a considerable number of milkings have to be discarded due to long withdrawal periods after calving.

Key words: dry period, antibiotic residue, cefquinome, withdrawal period

INTRODUCTION

An effective dry cow management including treatment with an antibiotic or internal teat sealant is an essential part of the international mastitis control program recommended by the National Mastitis Council (NMC, 2006). According to the US National Animal Health Monitoring System, about 93.0% of US dairy cows received an intramammary dry ow antibiotic and averaged a dry period of 57.1 d (Lombard et al., 2015). A survey on commercial dairy farms in northern Germany revealed a blanket dry cow therapy on 79.6% of the farms and an average dry period of 7 wk (Bertulat et al., 2015). Short dry periods of 35 d or less were used in only 3.7% of the participating dairy farms (Bertulat et al., 2015). Short dry periods are considered a management strategy that could facilitate dry off and the transition period for high-producing cows (Lefebvre and Santschi, 2012).

Recently, several studies investigated the effects of short dry periods on production (Kuhn et al., 2006),

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reproductive performance (Shoshani et al., 2014), energy balance during early lactation (van Knegsel et al., 2014), and udder health (Church et al., 2008). A dry off 31 to 40 d before calving has been associated with maximized lifetime production after second or later lactation (Kuhn et al., 2006) and improved reproductive performance without any loss in colostrum quality (Shoshani et al., 2014). Furthermore, a dry period length of 30 d resulted in an improved energy balance of dairy cows in early lactation (van Knegsel et al., 2014) without any untoward effects on udder health (Church et al., 2008).

Santschi and Lefebvre (2014), however, hypothesized that short dry periods can be a risk factor for antibiotic residues in early lactation when cows calve early. To avoid antibiotic residues, withdrawal periods for milk are determined utilizing the time to safe concentration method, which calculates the number of milkings necessary for the residue concentration in milk to fall below the maximum residue limit (CVMP, 2000). For dry cow antibiotics, withdrawal periods for milk depend on the dry period length; thus, the residue depletion during the dry period and postcalving is considered (CVMP, 2006).

The potential effect of shortening the residue depletion during the dry period on the residue concentration of dry cow antibiotics after calving has not yet been investigated. Church et al. (2008) measured antibiotic residues in foremilk samples both from cows with regular dry period length (45 or 60 d) that had been treated with a dry cow antibiotic and from cows with short dry periods (30 d) that had received a lactating cow antibiotic at dry off. Those authors did not find greater risk for antibiotic residues after short dry periods when cows were treated with a lactating cow antibiotic. When dry cow antibiotics are used, however, the risk for antibiotic residues after short dry periods might be greater, as antibiotics are pharmacologically designed to reach high and prolonged concentrations throughout the udder (Ehinger et al., 2006). Therefore, the objective of our study was to investigate the residue concentration of a dry cow antibiotic containing 150 mg of cefquinome during the colostrum period and early lactation in quarter foremilk samples after short dry periods.

MATERIALS AND METHODS

Animals and Eligibility Criteria

The study was conducted between November 2014 and May 2015 at the Clinic for Animal Reproduction (Freie Universität Berlin, Berlin, Germany). To reduce the number of study animals, and in agreement with previous studies that suggested that udder quarters can be considered as independent entities (Schukken et al., 1993; Lindmark-Månsson et al., 2006), we choose a quarter-based approach. Previously dried-off cows (i.e., abrupt dry off with blanket dry cow treatment containing 150 mg of cefquinome at least 57 d before calculated calving date) from a commercial dairy farm were selected and treated again with an intramammary (**IMM**) dry cow antibiotic in an extra-label manner within 21 d before calculated calving (i.e., 280 d after artificial insemination). This approach was favored because it minimized the effect and potential confounding of milk leakage on the residue concentration after calving, as milk leakage occurs most frequently within the first week after dry off (Bertulat et al., 2013). One quarter of each cow was not treated and served as a negative control (i.e., control quarters) to allow a quantification of potential residues from the first dry cow treatment and to determine if antibiotic concentrations could distribute among quarters.

Overall, 19 healthy, multiparous dry Holstein-Friesian and Holstein-Friesian crossbreed dairy cows were enrolled in the study 21 d before calculated calving date and followed until the end of the withdrawal period of the second dry cow treatment (i.e., maximum of 35 d after calving). We only enrolled dry cows with a calculated dry period length of at least 57 d. This allowed a 36-d withdrawal period for the first dry cow treatment plus 21 d between second dry cow treatment and calculated calving. All cows were managed according to the guidelines set by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (Hellmann and Radeloff, 2000). The experimental procedures reported herein were conducted with the approval of the Institutional Animal Care and Use Committee of Freie Universität Berlin. Enrolled cows were in good health (e.g., no mastitis, metabolic, or infectious disease) and had 4 functional quarters. Cows with clinical mastitis within the past 3 mo or antibiotic treatment (i.e., IMM or systemic) other than dry cow therapy within the past 2 mo before enrolment were excluded from the study.

During their study period, cows were housed in groups of 4 or less in a freestall barn with 6 cubicles equipped with chopped straw-lime-water mixture and smooth concrete floor. For calving, cows were transferred to a calving pen after signs of imminent parturition (i.e., tail raising, vaginal discharge, abdominal contraction) had been identified. The calving pen (3.50 $\times$ 3.10 m) was equipped with rubber mats and deep-straw bedding and was separated from the study cows by 2 metal fences. After calving, the cows and calves were separated immediately and cows were transferred back to the study group.