Effect of an Intramammary Teat Seal and Dry Cow Antibiotic in Relation to Dry Period Length on Postpartum Mastitis

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ABSTRACT

Infusion of either a long-acting antibiotic preparation (ceftiofur) or the same antibiotic preparation combined with an internal teat sealant (bismuth subnitrate) were compared for the effect on new intramammary infections at calving and clinical mastitis in the first 100 d of lactation, in relation to dry period length. For all cows, a significant reduction in the incidence of new infections in quarters at calving (3.7 vs. 7.3%) was found for the combination treatment group (150 cows) compared with the antibiotic-alone treatment (133 cows). With a dry period of 10 wk or longer, significantly fewer new quarter infections (3.8 vs. 11.4%) were found in those cows receiving the combination treatment compared with antibiotic treatment alone. When the dry period was less than 10 wk, the incidence of new infections in quarters treated with the combination treatment was lower than for the antibiotic treatment alone (3.7 vs. 6%) but this was not a statistically significant difference. Fewer infections caused by *Streptococcus uberis* and coagulase-negative staphylococci were found in cows receiving the combination treatment compared with the antibiotic treatment alone (not significant). Coliform isolates were less likely in cows receiving the combination treatment with the longer dry period but the numbers of new intramammary coliform infections were low for both dry period categories. Few infections were caused by coagulase-negative staphylococci. The incidence of clinical mastitis in the first 100 d of lactation in quarters infected at calving was significantly lower (4 vs. 15 cases) for the combination treatment than for the antibiotic treatment alone for both dry period lengths. The clinical incidence in quarters in which a pathogen was not detected in either of the samples taken after calving was comparable between groups. No significant difference was found in the total clinical incidence after calving for both groups irrespective of dry period length.

Key words: OrbeSeal, intramammary infection, mastitis

INTRODUCTION

In the United Kingdom the use of some form of dry cow prophylaxis for all dairy cows, in all seasons, is the recommended practice at the end of lactation for all cows to be retained. Recent evaluations of the effectiveness of dry cow antibiotic treatment have confirmed that it has significant value in preventing new infections during the dry period and at calving (Hassan et al., 1999; Berry and Hillerton, 2002b; Huxley et al., 2002). However, new infections occur in antibiotic-treated cows, raising concerns over the effectiveness against certain pathogens and as a prophylactic, especially when the dry period is especially long (Bradley and Green, 2000; Berry and Hillerton, 2002b). Previous studies on different dry cow strategies have not considered whether length of the dry period may be a significant factor in new infection incidence but have reported wide variations in the dry period lengths for the cows studied (Berry and Hillerton 2002a,b; Godden et al., 2003). Economic analysis indicates that a dry period between 4 and 8 wk may be an optimum length but many factors may interfere with this aim (Coppock et al., 1974; Sorenson and Enevoldsen, 1991; Rougier et al., 1999). This may result in dry period lengths longer than the stated withholding periods for any of the dry cow antibiotic products available in the United Kingdom. This is a potential problem when a requirement of mastitis control is to prevent new infections during the dry period. Furthermore, the current economics of European dairy farming, with a relatively low price for milk and high production costs, require regular appraisal of all costs, including total dry cow antibiotic therapy, and their benefits.

Various types of external teat seals have been used in combination with dry cow antibiotics but need frequent application, particularly toward the end of the dry period (Hemling et al., 2000; Timms, 2000). An inert internal teat sealant, made from the inert salt bismuth subnitrate in a paraffin base, is marketed in the United Kingdom as OrbeSeal (Pfizer Animal Health Ltd., Sandwich, Kent, UK) for use in uninfected cows with

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a composite milk cell count less than 200,000 cells/mL. OrbeSeal is administered at drying off and forms an artificial barrier within the teat canal and lower teat sinus to prevent invasion by bacteria.

OrbeSeal has also been used in combination with an antibiotic (Meaney, 1977; Woolford et al., 1998; Godden et al., 2003) or the bacteriocin lactacin 3147 (Ryan et al., 1998). In a study in New Zealand, under an extensive grazing system, no significant difference was found between the combination treatment group and the OrbeSeal or dry cow antibiotic groups in the rate of new IMI at calving (Woolford et al., 1998). However, the combination treatment was shown to prevent significantly more new infections at calving than the antibiotic alone in an intensive housing situation in the United States (Godden et al., 2003).

In this study, the combination of OrbeSeal and a cephalosporin-based dry cow antibiotic was compared with the cephalosporin-based dry cow product alone on the rate of new IMI and on clinical mastitis postpartum, for varying dry period lengths, over 2 yr, in the United Kingdom.

MATERIALS AND METHODS

Trial Design

All cows due to recalve into the Institute for Animal Health (IAH) herd were used for a selective dry cow trial from April 2003 to April 2005. Cows were assigned, using a random number allocation table, to 1 of 2 groups: treatment with Cepravin (Schering Plough Animal Health Ltd., Uxbridge, UK) or OrbeSeal (Pfizer Ltd., Sandwich, UK) and Cepravin combined. Cepravin is a long-acting cephalonium-based product with a claim of effective levels of antibiotic up to 10 wk after infusion and a milk-withholding period of 54 d (National Office of Animal Health, 2006).

All eligible cows were dried off abruptly at the end of the designated milking. After cluster removal, the teats were cleaned using cotton wool pledgets soaked in 70% ethanol solution until the pledgets were no longer visibly dirty. The dry cow treatments were infused using a partial insertion technique. For those cows receiving both Cepravin and OrbeSeal, the Cepravin was administered first, followed by the OrbeSeal (single intramammary syringe of both Cepravin and OrbeSeal). Eligible cows were those that were uninfected with *Streptococcus* spp., *Staphylococcus aureus*, coliform spp., or *Arcanobacterium pyogenes* at drying off. Infected cows were excluded from the analysis to avoid possible overestimation of infections at calving, because differentiation to distinguish between infections present at drying off and at calving was not carried out. Cows were eligible for drying off on either the minimum

numbers of days before expected calving date (approximately 8 wk) or when yield dropped below 10 kg/d. This meant that for some cows, the predicted dry cow period could be considerably longer than the aim of 8 wk. This herd had a low level of infections at drying off and generally cows were not dried off early due to IMI.

Any cow that required medical or surgical intervention within 14 d after calving was excluded from the trial. All cows had a winter housing period on sand-bedded cubicles and a summer grazing period on grass. All cows were managed as a single husbandry group, monitored for at least 100 d after calving, and were under natural exposure to infection. The sampling routine consisted of single quarter samples taken 1 wk before drying off, at drying off, at calving, and approximately 1 wk after calving with extra confirmatory samples after calving as necessary. All quarters detected as having clinical signs of mastitis were sampled before treatment. Sampling and bacteriological examination of the milk were carried out according to IDF recommendations (IDF, 1981) with selected extra testing (Berry and Hillerton, 2002a,b).

Definitions

When the same pathogen was isolated from 2 consecutive samples or 2 out of 3 samples, or in one sample from a quarter with clinical signs of mastitis, this was defined as an infection (IDF, 1981). Clinical mastitis occurred when visible changes in the milk were seen, such as watery milk, clots, or flakes, and changes in the udder such as swelling or heat. These were detected by the farm staff or at one of the routine sampling times. A new infection at calving was defined as isolation of a pathogen not present in either pre-dry period sample.

The cows were allocated by dry period length to 1 of 2 groups: cows dry for fewer than 10 wk and those dry for 10 wk or more.

Statistical Analyses

The data were analyzed using the Minitab statistical computer package (release 12.21; Minitab Inc., State College, PA) and SAS system (Version 8; SAS Institute, Cary, NC). Fisher's exact and χ^2 tests were carried out to determine if there was an effect of treatment on the probability of infection.

Quarter interdependence was not considered in the analysis because our previous study (Berry et al., 2003) had demonstrated that this was not a factor if all quarters within the cow were treated prophylactically and this had not been taken into consideration by other studies on internal teat sealants (Huxley et al., 2002; Berry et al., 2003; Godden et al., 2003).

Table 1. Quarters with an IMI at calving (% of total quarters in parentheses) for the whole dry period and by dry period length

Treatment ¹	Total		Dry period <10 wk		Dry period ≥10 wk		Total quarters
	Uninfected	Infected	Uninfected	Infected	Uninfected	Infected	
Antibiotic	492 (92.7)	39 ^a (7.3)	375 (94)	24 ^b (6)	117 (88.6)	15 ^c (11.4)	531
Antibiotic and teat sealant	574 (96.3)	22 ^a (3.7)	421 (96.3)	16 ^b (3.7)	153 (96.2)	6 ^c (3.8)	596
Total	1,066	61	796	40	270	21	1,127

^a $\chi^2 = 7.321$; $P = 0.007$.

^b $\chi^2 = 2.536$; $P = 0.111$.

^c $\chi^2 = 6.205$; $P = 0.013$.

¹Antibiotic = Cephalexin (Schering Plough Animal Health Ltd., Uxbridge, UK); teat sealant = OrbeSeal (Pfizer Animal Health Ltd., Sandwich, Kent, UK).

RESULTS

Two hundred eighty-three cows completed the trial to give eligible data for 1,127 quarters, with 150 cows treated with a combination of Cephalexin and OrbeSeal and 133 cows treated with Cephalexin only. Any cows calving with an infection in a quarter that was detected as infected at drying off were excluded from the analysis.

No clinical cases of mastitis were detected in either group during the dry period. Those quarters treated with the combination of products had a significantly lower incidence of a new IMI at calving compared with those treated only with the antibiotic (3.7 vs. 7.3%, $P = 0.012$; Table 1). Two hundred ten cows had a dry period of less than 10 wk, and 73 cows had a dry period of 10 wk or longer. When the dry period was 10 wk or longer, significantly fewer new quarter infections were found in those cows treated with the combination treatment compared with antibiotic treatment alone (3.8 vs. 11.4%, $P = 0.019$; Table 1). The incidence of new infections in quarters treated with the combination treatment was lower than for the antibiotic treatment alone (3.7 vs. 6%) when the dry period was less than 10 wk; this was not a statistically significant difference.

Fewer new infections were caused by *Streptococcus uberis* and CNS, as determined in the calving samples, in cows receiving the combination treatment compared with the antibiotic treatment alone, but this was not a significant difference (Table 2). Fewer new coliform isolates occurred only in the combination treatment of the longer dry period, but the numbers of new intramammary coliform infections were low for both dry period categories. The numbers of infections caused by CNS were low in all groups.

The incidence of clinical mastitis in the first 100 d of lactation in quarters detected as having an infection at calving was significantly lower for the combination treatment than for the antibiotic treatment alone for

both dry period lengths (4 vs. 15 cases, $P = 0.034$ and $P = 0.04$ for dry period <10 wk and ≥10 wk, respectively; Table 3).

The clinical incidence in quarters in which a pathogen was not detected in either of the samples taken after calving was comparable between groups (24 cases in the combination treatment and 21 in the antibiotic treatment; Table 4). Slightly more clinical cases attributable to coliform infections were detected in the combination group for both dry period lengths and more clinical cases with *Strep. uberis* were also detected in the combination group. Numbers were similar for clinical cases in which no isolate was found in both treatment groups. The total clinical incidence after calving for both groups was 28 in the combination group and 36 in the antibiotic-alone group. There was no significant difference between groups for all dry period lengths or for the dry periods of <10 wk and ≥10 wk ($P = 0.132$, $P = 0.535$, and $P = 0.061$, respectively).

DISCUSSION

A much lower incidence of new infections at calving was found in both treatment groups compared with other trials in the United States and the United Kingdom (Godden et al., 2003; Bradley et al., 2005) but levels were similar to those reported in a study conducted in New Zealand (Woolford et al., 1998). This may be a reflection of management within the herd (the herd studied here was a research herd, albeit one run on commercial lines) or in the definition of infection. This herd has an extremely low prevalence of infections caused by *Staph. aureus* (<1%) and clinical cases were predominantly due to environmental infections. In this study an infection was defined as isolation of the same pathogen in 2 out of 3 consecutive samples and with a short sampling period (less than 2 wk between the 3 samples). Previous studies have reported infections using isolation of bacteria at one time point only. This

Table 2. Pathogens causing IMI at calving¹

Pathogen type	Dry period <10 wk		Dry period ≥10 wk		Total
	Antibiotic	Combination	Antibiotic	Combination	
<i>Streptococcus uberis</i>	11 ^a	6 ^a	6 ^b	2 ^b	25
Coliforms	2	2	3	0	7
<i>Arcanobacterium pyogenes</i>	1	0	0	0	1
<i>Streptococcus dysgalactiae</i>	0	0	1	0	1
Enterococci	2	2	0	0	4
CNS	8	6	5	4	23
Total	24	16	15	6	61

^a*P* = 0.7471 (Fisher's exact).^b*P* = 1.0000 (Fisher's exact).¹Antibiotic = Cepravin (Schering Plough Animal Health Ltd., Uxbridge, UK); teat sealant = OrbeSeal (Pfizer Animal Health Ltd., Sandwich, Kent, UK). Combination = antibiotic plus teat sealant.

can lead to overestimation of numbers, as reported by the International Dairy Federation (IDF, 1987).

Positive benefits from using an internal teat sealant either in combination with an antibiotic or alone have been reported previously but have varied as to whether this effect was for a lower prevalence of infections at calving and/or a lower incidence of clinical infections (Woolford et al., 1998; Berry and Hillerton, 2002a; Huxley et al., 2002; Godden et al., 2003; Bradley et al., 2005). Huxley et al. (2002) compared an internal teat sealant alone with an antibiotic in cows with a low cell count at drying off. A lower prevalence of infections in samples taken at calving for cows treated with an internal teat sealant treatment was reported, when the definition of infection was 1 isolate from 2 samples, but there was no significant difference in clinical cases for the first months after calving. Similar cure rates for existing infections for both treatments over the dry period were reported, which is unusual for a nonantibiotic treatment. Bradley et al. (2005) compared a combination of antibiotic and internal teat sealant with antibiotic alone in high cell count cows. No significant difference in infection status at calving was reported (with no

definition of infection given) but a significant reduction was found in clinical incidence using the combination treatment in the first 2 mo after calving. Godden et al. (2003) reported on 2 US herds using a total confinement system for cows with a dry period of between 28 and 100 d allocated to either a combination treatment or an antibiotic treatment. Infection levels reported for postcalving were higher (>20%) than in the present study, but at both time points, the combination group had a significantly lower infection level. A significantly lower clinical incidence was reported for the combination treatment in the first 60 d after calving.

The present study found a significantly lower incidence of clinical mastitis using the combination treatment compared with antibiotic alone for those quarters detected as infected at calving and some of this may be a carryover effect from the lower incidence in infections in the combination group at calving. The total clinical mastitis incidence, including cases not detected as infected at calving, was not significantly different between the 2 groups, although a lower clinical incidence occurred with the combination group. Previous studies have also found a significantly lower clinical incidence

Table 3. Clinical mastitis incidence and pathogen in quarters infected at calving¹

Pathogen type	Dry period <10 wk		Dry period ≥10 wk		Total
	Antibiotic	Combination	Antibiotic	Combination	
<i>Streptococcus uberis</i>	7	3	2	0	12
Coliforms	1	0	2	0	3
<i>Arcanobacterium pyogenes</i>	1	0	0	0	1
<i>Streptococcus dysgalactiae</i>	0	0	1	0	1
<i>Streptococcus faecalis</i>	1	0	0	0	1
CNS	0	0	0	1	1
Total	10 ^a	3 ^a	5 ^b	1 ^b	19

^a $\chi^2 = 4.512$; *P* = 0.034.^b $\chi^2 = 4.210$; *P* = 0.040.¹Antibiotic = Cepravin (Schering Plough Animal Health Ltd., Uxbridge, UK); teat sealant = OrbeSeal (Pfizer Animal Health Ltd., Sandwich, Kent, UK). Combination = antibiotic plus teat sealant.

Table 4. Clinical mastitis incidence and pathogen type in quarters not detected as infected at calving in the first 100 d of lactation¹

Pathogen type	Dry period <10 wk		Dry period ≥10 wk		Total
	Antibiotic	Combination	Antibiotic	Combination	
<i>Streptococcus uberis</i>	1	5	2	1	9
Coliforms	4	7	2	3	16
<i>Streptococcus faecalis</i>	0	0	1	0	1
No pathogen isolated	6	5	1	1	13
CNS	2	2	1	0	5
<i>Corynebacterium</i> spp.	1	0	0	0	1
Total	14	19	7	5	45

¹Antibiotic = Cepravin (Schering Plough Animal Health Ltd., Uxbridge, UK); teat sealant = OrbeSeal (Pfizer Animal Health Ltd., Sandwich, Kent, UK). Combination = antibiotic plus teat sealant.

in the combination treatment but have usually compared the total clinical incidence rather than attributing clinical cases to those quarters known to be infected at calving (Godden et al., 2003; Bradley et al., 2005).

The level of isolation of CNS reported in this study was lower than that reported previously (Godden et al., 2003). This may be a reflection that, although the current study was carried out on a herd run on commercial lines, some milking practices may have been applied more diligently, such as postmilking teat disinfection, or that with the definition of an infection used in this study, the same isolate was found in both samples taken after calving was more precise. The definition of infection used in this study and that sampling points after calving could be up to 2 wk after calving also may have resulted in a lower number of infections. It has been reported that CNS infections can rapidly self-cure soon after calving (Oliver and Jayarao, 1997).

The length of the dry period has been indicated as a risk factor for new infection rates—the longer the dry period, the greater the new infections acquired—although this was in selective dry cow treatment studies and only demonstrated in antibiotic-treated cows and not untreated control cows (Rindsig et al., 1978; Berry and Hillerton, 2002b). The length of the dry period has not been explored in previous studies using an internal teat sealant. This study clearly demonstrates that for cows with a longer dry period, the combination of dry cow antibiotic and teat sealant resulted in significantly fewer new infections at calving and subsequent clinical cases attributable to these infections. In the United Kingdom, more than 24% of cows have a dry period between 8 and 10 wk, and a further 27% have a dry period exceeding 10 wk (M. Blanchard, National Milk Records, Chippenham, UK; personal communication), and cows with longer dry periods are reported as also occurring in the United States (Kuhn et al., 2005). Dry cow formulations available in the United Kingdom have a range of withholding periods from 28 to 54 d. This range indicates the period during which milk may have

antibiotic levels higher than the maximum permitted but does not indicate the period in which antibiotic levels are above the MIC. Thus, many cows may not have adequate antibiotic protection for the whole dry period. This may be a concern for all herds, not only those where management results in a long dry period for some cows. Cows with infections at calving have been reported as having a reduction in yield in that lactation (Neave et al., 1950). A recent US study on dry period length (Kuhn et al., 2006) highlighted lactation yield losses for cows with a dry period longer than 70 d. One factor may be that antibiotic levels become inadequate or below MIC and some of the yield loss may be a response to infection acquired during the dry period and persisting into lactation. The present study suggests that the precalving risk period for new infections remains a problem even in cows treated with antibiotics, and that this risk increases with a longer dry period.

The economics of choosing among dry cow treatments vary with the individual herd situation. Previously, it was shown that it might not always be the most economical decision to use a combination of dry cow antibiotic and internal teat sealant on all cows (Berry et al., 2004). The present study indicates that for those cows with a longer dry period, a combination may be the most effective choice and may be more economically viable.

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