Intramammary infection rate during the dry period in cows that received blanket dry cow therapy: efficacy of 6 different dry-cow intra-mammary antimicrobial products

I-M Petzer[a*], D C Lourens[a], T J van der Schans[a], J C Watermeyer[a], R van Reenen[a], G H Rautenbach[a] and P Thompson[a]

ABSTRACT

The objectives of this study were to compare the efficacy of 6 different dry-cow intramammary antimicrobial products for the treatment and prevention of mastitis during the dry period in a well-managed high producing Friesland dairy herd, and the influence of treatment on the somatic cell count (SCC) of cows during early lactation.

One of 6 dry-cow intramammary antimicrobial products was randomly allocated to 162 cows due for drying off over a period of 14 months. All cows were sampled twice prior to drying off, and twice after calving for the determination of SCC and presence of micro-organisms. The quarter prevalence of pathogens at drying off and post-calving, the overall quarter cure rate and the rate of new intramammary infections occurring during the dry period were determined.

The overall quarter prevalence of intramammary infections (IMIs) at drying off was 29.78 % and after calving 22.22 %. There was a statistically significant difference ($P < 0.05$) between the prevalence of major and minor pathogens at drying off (7.87 % and 21.91 %) and at calving (4.47 % and 17.75 %). The most prevalent pathogens isolated at drying off (21.14 %) and at calving (16.98 %) were coagulase-negative staphylococci (CNS). The quarter cure rate during the dry period was 83.94 %. The cure rate for the major pathogens (98 %) was significantly better ($P < 0.05$) than that for minor pathogens (78.9 %). The overall quarter cure rate varied from 72.3 % to 93.9 % for the various products. The rate of new quarter infections during the dry period was 17.44 % with a significant difference ($P < 0.05$), between the prevalence of new quarter infections with major (4.32 %) and minor pathogens (13.12 %). CNS was the most prevalent pathogen causing new quarter infections (12.34 %) and the rate of new quarter infections varied from 13.4 % to 24.1 % for the various products.

It is concluded that there is a difference in efficacy between antimicrobial intramammary dry-cow products in their ability to cure and prevent new IMIs during the dry period. Dry-cow products are mainly formulated for efficacy against Gram-positive cocci, while providing no or little protection against Gram-negative bacteria. Therapeutic levels may persist for only 14 to 28 days into the dry period and fail to protect the udder during the last trimester. Dry-cow therapy should, however, always form part of a holistic approach to the dry period which also considers cow factors, dry-cow management, microorganisms and the environment of the dry cow.

Key words: comparative study, cure rates, dairy cow therapy, new intramammary infections, product efficacy.

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INTRODUCTION

Mastitis is a multi-factorial disease and generally results from an interaction between a variety of microbial infections, host factors, environment and management. The importance of the dry period with respect to udder health, productivity, overall health and fertility performance in the next lactation has been widely documented[14,16,25,31,32,54]. The dry period is a period of anatomical, physiological and metabolic change for many body systems, including the mammary gland. The risk of mastitis depends on how well the defence mechanism of the dairy cow can adjust to the challenge as well as the risk from the environment and the microbes.

An important factor that influences the manifestation of clinical mastitis in the next lactation is intramammary infection (IMI), which develops during or persists throughout the dry period[7,36,37,52,55]. In the absence of effective mastitis prevention and control measures during the dry period, more quarters of the udder will be infected at calving compared to the number infected at drying off[11]. From the point of view of mastitis control, most new IMIs occur during the dry period[29,42,48] and cows with a history of mastitis in the previous lactation are twice as likely to develop mastitis in the following lactation. Most new IMIs develop towards the end of lactation, during the initial 3 weeks after drying off and during the final stages of the dry period[9,29,48].

From an udder health perspective, the goal of the dry period is to have as few udder quarters infected in the next lactation as possible and to ensure optimum production of milk with a low somatic cell count (SCC)[14]. Administration of dry-cow antibiotic therapy at the end of lactation is presently an effective way of achieving this goal[14]. However, by placing emphasis on prevention of new infections, udder health can be achieved more rapidly[14] as new IMIs can have a significant impact on milk yield in the next lactation. It therefore relies on an understanding of both the epidemiology of bovine mastitis and the factors affecting the cow's and the udder's susceptibility to mastitogenic pathogens. A holistic approach to management of the dry cow is a vital part of mastitis control and should encompass cow factors, environmental and nutritional management as well as dry-cow therapy.

The objectives of this study were to compare the efficacy of 6 different dry-cow intramammary antimicrobial products for the cure and prevention of new IMIs during the dry period and the influence of treatment on the SCC of cows during the early part of their subsequent lactation.

[a]Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110 South Africa.

*Author for correspondence.
E-mail: inge-marie.petzer@up.ac.za

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Table 1: **Summary of the intra-mammary antibiotic products used in this investigation.**

Product	Composition	Spectrum indicated on the package insert	Effective tissue concentrations*
Product 1	Procaine benzylpenicillin 297.92 mg(300 000 IU), nafcillin 100 mg and hydrostreptomycin 100 mg.	A wide range of bacteria, including penicillin-resistant staphylococci and coliforms	Up to 8 weeks
Product 2	Cephalexin 250 mg and neomycin sulphate 250 mg	Subchronic and subclinical infections	4 weeks
Product 3	Procaine benzylpenicillin 4.9 % m/m and dihydrostreptomycin SO_4 6.5 % m/m	Common forms of bovine mastitis	2 weeks
Product 4	Specially processed cloxacillin 600 mg (benzathine salt) in a long-acting base with 3 % aluminium mono-stearate	Sensitive Gram-positive organisms	Up to 7 weeks
Product 5	Cephalonium, 250 mg in a long-acting base	Gram-positive and Gram-negative bacteria	Up to 10 weeks
Product 6	Cloxacillin (benzathine salt) 500 mg, ampicillin 250 mg (as the trihydrate) in a long-acting base with 3 % aluminium stearate	Gram-positive and Gram-negative organisms	Up to 4 weeks

Adapted from the IVS Desk Reference, 2001/2 (6) (*Effective time is the time during which the tissue concentrations of the active ingredients are above the MIC of most common mastitogenic pathogens).

MATERIALS AND METHODS

The trial herd

The cows used in this study were from a well-managed, high producing Holstein Friesland herd with 340 cows in milk. They were on a total mixed ration system and milked 3 times a day. Dry-off criteria that were used were either 55 days prior to their expected calving date or when milk yield dropped below 10 kg per day. Cows due for drying off were only fed grass hay for 24–48 hours prior to drying off. Dried off cows were kept in kikuyu grass camps where they also calved. They received Multimin+SE, vitamin ADE and Ivomec injections 21 days prior to their expected calving dates and were fed a total mixed ration formulated to meet NRC nutrient requirements for transition cows during the last 3 weeks prior to calving.

Sample size

Quarter milk samples of the herd were taken 4 weeks prior to the start of the trial and indicated that 69.0 % of quarters were normal, 17.7 % had non-specific disturbance and 13.3 % of quarters were infected. The sample size for the trial was calculated based on the prevalence of clinical and subclinical mastitis in the herd. New infection and cure rates were compared between groups using the Fisher Exact Test on the complete results obtained at that stage from 464 quarters. Simulation of further data collection was done by multiplying each cell in the contingency tables by 1.25 and 1.5 (to simulate the collection of 25 % and 50 % more data respectively). This was found to result in very little change in the outcome, with marginal changes in significance.

Experimental design and procedure

All cows due for drying off, regardless of parity and milk yield, were eligible for inclusion in the trial. Cows were randomly allocated to receive treatment with 1 of the 6 dry-cow antibiotic products (see Table 1). Cows were dried off abruptly and were given intramammary treatment in an aseptic manner. Foremilk quarter samples were aseptically collected twice prior to drying off and after calving according to the International Dairy Federation guidelines. The 1st of the 2 samplings was carried out 24 hours prior to drying off by the farm manager and the 2nd at drying off by the trial veterinarian on the weekly herd visits. Cows were sampled as soon as possible after calving, but not longer than 6 days. Bulk milk samples were analysed weekly to monitor the udder health and milk hygiene status. The farm manager collected composite cow samples for the National Milk Recording Scheme from all lactating cows in the herd on a fixed 5-weekly routine. Individual cow SCC data for the 1st 3 milk recording test dates after calving were obtained for analysis.

Clinical observations

The trial veterinarian clinically examined udders and teats at drying off, weekly throughout the dry period and twice after calving.

Laboratory examinations

The laboratory investigation took place in the milk laboratory of the Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria, and composite cow milk samples were analysed by Lactolab (Irene, Centurion).

All milk samples were visually inspected and cultured on bovine blood tryptose agar (BTA) (Columbia Blood Agar Base, CM331 from Oxoid, plus 5 % defibrinated bovine blood), which supports the growth of most mastitogenic bacterial pathogens[46]. Inoculated agar plates were incubated for 18–24 h at 37 ± 1 °C, evaluated for growth, and re-incubated and re-read after a further 24 h[47]. Colonies were identified based on colony morphology, haemolysis, catalase reaction and Gram-staining, CAMP/aesculin hydrolysis test (Columbia Blood Agar Base, CM331 from Oxoid) with ferric citrate and aesculin plus defibrinated bovine blood. The identification of streptococci was confirmed by means of the Streptococcal Grouping Kit (Latex agglutination test) from Oxoid. Gram-positive cocci which tested catalase-positive were tested for coagulase by means of the Staphylase Test from Oxoid. Gram-negative organisms were identified using the API 20E from bioMérieux.

Somatic cell counting was performed with a Fossomatic 90 (The Rhine Ruhr Group) according to the standard method for Somatic cell counting[56].

Data management

Relevant data from each cow and laboratory results were entered, stored and analysed by the Milk Sample Diagnostic computer program (Abaci Systems). Statistical analysis was performed using a commercial statistical analysis software package (NCSS 2001, NCSS, Kaysville, UT, USA). A quarter was considered infected at drying off when a specific udder pathogen was isolated from the milk sample collected immediately prior to treatment. A quarter was regarded as cured when the type of pathogen isolated at drying off was not recovered from the milk sample collected at calving. A new quarter infection acquired during the dry period was recorded when a quarter that was not infected at drying off or a quarter infected with a different pathogen yielded a pathogen at calving.

Statistical analysis

The chi-square test was used and results with a *P*-value of greater than 0.05 were regarded as significant. Each unique pair

Table 2: **Bacteriological results from quarter milk samples, prevalence of IMI at dry-off and after calving, cure rates and new infection rates during the dry period** (n = 648)**.**

Microorganism	Prevalence of quarters with IMI at drying off (%)	Cure rate of IMI during the dry period (%)	Prevalence of quarters with IMI post-calving (%)	Prevalence of quarters with new IMIs post-calving (%)
Major pathogens				
Staphylococcus aureus (STA)	18 (2.78 %)	17 (94.4 %)	15 (2.31 %)	14 (2.16 %)
Streptococcus agalactiae (SAG)	23 (3.55 %)	23 (100.0 %)	11 (1.70 %)	11 (1.70 %)
Streptococcus dysgalactiae (SDY)	10 (1.54 %)	10 (100.0 %)	3 (0.46 %)	3 (0.46 %)
Subtotal	51 (7.87 %)[a]	50 (98.0 %)[a]	29 (4.47 %)[a]	28 (4.32 %)[a]
Minor pathogens				
Coagulase-neg. staphylococci (CNS)	137 (21.14 %)	107 (78.1 %)	110 (16.98 %)	80 (12.34 %)
Enterococcus faecalis (EFA)	2 (0.31 %)	2 (100.0 %)	2 (0.31 %)	2 (0.31 %)
Other	2 (0.31 %)	2 (100.0 %)	2 (0.31 %)	2 (0.31 %)
E. coli	1 (0.15 %)	1 (100.0 %)	0	0
Streptococcus uberis (SUB)	0	0	1 (0.15 %)	1 (0.16 %)
Subtotal	142 (21.91 %)[b]	112 (78.9 %)[b]	115 (17.75 %)[b]	85 (13.12 %)[b]
Total	193 (29.78 %)	162 (83.9 %)	144 (22.22 %)	113 (17.44 %)

Values within a column with different superscripts (a, b) differ significantly ($P < 0.05$).

of treatments was compared using the Fisher exact test in order to determine whether there was a significant difference in the outcome. For the comparison of cure rates only those quarters classified as infected at drying off were included. For the comparison of new infection rates, only those quarters that were not infected at drying off, or that had been infected but subsequently cured, were included. Owing to the random selection of cows, the percentage IMIs differed for each product at commencement of the trial. To compensate for this initial variation, percentage point changes from drying off until calving were calculated for each antimicrobial product, taking both the cure rates and new IMIs into account.

RESULTS

In total, 162 cows (648 quarters) were analysed. Of these, 89 (55 %) cows were at the end of their 1st lactation. Two cows developed clinical mastitis during the dry period and were excluded from the trial. The bacteriological results from quarter milk samples, prevalence of IMI at drying off and after calving, cure rates and new infection rates during the dry period are summarised in Table 2.

The overall prevalence of quarter infection at drying off and after calving was 29.78 % and 22.22 %, respectively. There were statistically significant differences ($P < 0.05$) at drying off (7.87 % and 21.91 %) and after calving (4.47 % and 17.75 %) between the prevalence of major and minor pathogens.

Most (74.47 %) of the IMIs present at calving were new infections and the most prevalent pathogens isolated at drying off (21.14 %) and after calving (16.98 %) were coagulase-negative staphylococci (CNS).

The overall quarter cure rate during the dry period was 83.94 %. The overall cure rate for the major pathogens (98.0 %) was significantly better ($P < 0.05$) than the cure rate for minor pathogens (78.9 %). The cure rate of the major pathogens varied from 94.4 % for *Staphylococcus aureus* (STA) to 100 % for *Streptococcus agalactiae* (SAG) and *Streptococcus dysgalactiae* (SDY). The cure rate of the minor pathogens ranged from 78.1 % for CNS to 100 % for the other minor pathogens.

The quarter new infection rate during the dry period was 17.44 %. That of major pathogens varied from 0.46 % for SDY to 2.16 % and 1.70 % for STA and SAG, respectively. Almost all major pathogens isolated post-calving were derived from new IMIs (96.6 %) while 74.1 % of minor pathogens were new infections. The rate of new IMIs with minor pathogens for the study varied from 0.16 % for SUB to 12.34 % for CNS. The difference between the prevalence of new IMIs with major (4.32 %) and minor pathogens (13.12 %) was statistically significant ($P < 0.05$).

The comparative results of the quarter cure rates and development of new infection during the dry period for the various products are summarised in Table 3.

The cure rates varied between 72.3 % and 93.9 % for the various products, with an average overall cure rate of 83.9 %. The best cure rates of 93.9 % and 91.6 % were significantly better in quarters which received cephalonium or cloxacillin at drying off, compared with those that received benzyl penicillin/dihydrostreptomycin, cloxacillin/ampicillin and procaine benzylpenicillin/nafcillin/hydrostreptomycin combinations ($P < 0.05$).

The rate of new infection for quarters that received intramammary dry-cow treatment varied between 13.4 % and 24.1 % for the different products with an overall rate of new IMIs of 17.4 %. The new infection rate was significantly lower ($P < 0.05$) in quarters that received intramammary cephalonium (13.4 %) and a

Table 3: **Comparative results of quarter cure rates and new IMIs during the dry period for the various products** (n = 648)**.**

Product	Number of IMIs at drying off	Number of IMIs cured (%)	Number of new IMIs at calving (%)
Product 1 (n = 108)	24	19 (79.2 %)[b]	22 (20.4 %)[b]
Product 2 (n = 108)	28	24 (85.7 %)	15 (13.9 %)[a]
Product 3 (n = 100)	29	21 (72.4 %)[b]	16 (16.0 %)
Product 4 (n = 112)	47	43 (91.5 %)[a]	27 (24.1 %)[b]
Product 5 (n = 112)	33	31 (93.9 %)[a]	15 (13.4 %)[a]
Product 6 (n = 108)	32	24 (75.0 %)[b]	18 (16.7 %)
Total	193	162 (83.9 %)	113 (17.4 %)

Values within a column with different superscripts differ significantly ($P < 0.05$).

Table 4: **Relationship between the initial 3 composite cow SCC post-calving and the products.**

Product	First SCC (%) (SCC ≤400 000 cells per mℓ milk)	Second SCC (%) (SCC ≤400 000 cells per mℓ milk)	Third SCC (%) (SCC ≤400 000 cells per mℓ milk)
Product 1	18 (64.3)[b]	17 (63.0)[b]	14 (53.8)[b]
Product 2	21 (84.0)[a]	21 (84.0)[a]	14 (56.0)[b]
Product 3	15 (57.7)[b]	15 (57.7)[b]	16 (69.6)[b]
Product 4	15 (62.0)[b]	13 (54.2)[b]	8 (33.3)[b]
Product 5	16 (64.0)[b]	16 (64.0)[b]	12 (50.0)[b]
Product 6	17 (60.7)[b]	13 (46.4)[b]	11 (45.8)[b]
	102 (66.2)	95 (62.1)	75 (52.1)

Values within a column with different superscripts differ significantly ($P < 0.0$)5.

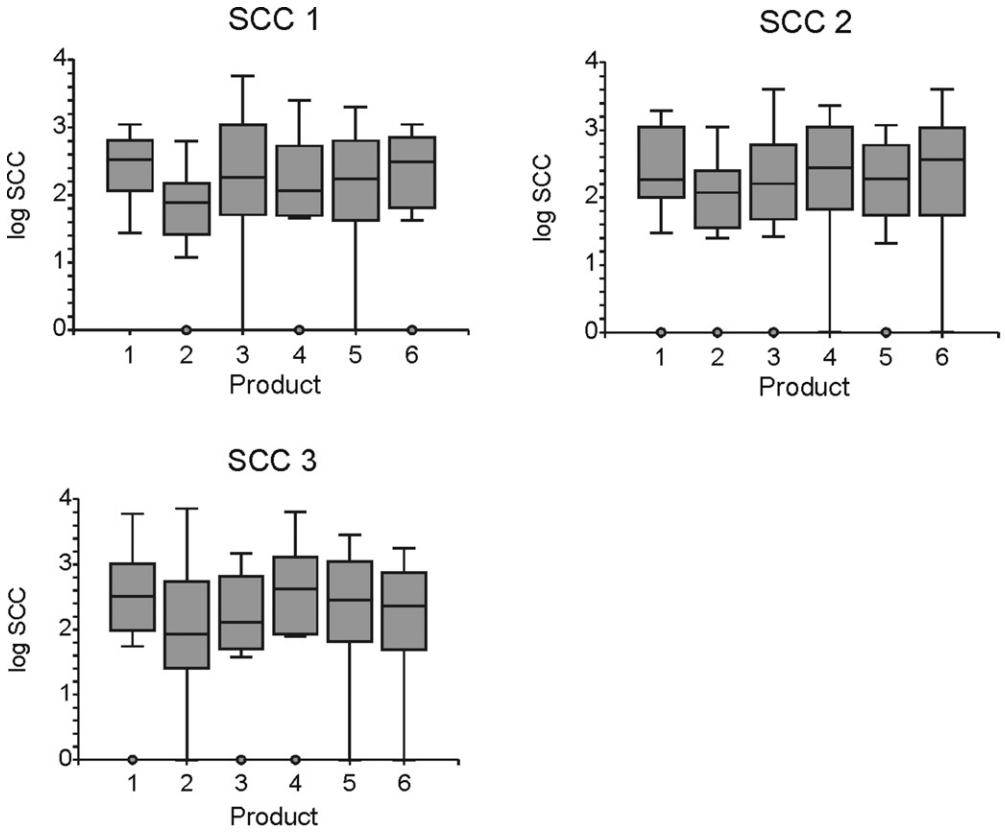

Fig. 1: **Comparison of SCC of cow milk samples** (logarithmic values)**, taken 5 weekly after calving, between the 6 different products studied.**

combination of cephalexin and neomycin (13.9 %), compared with those that received cloxacilin, benzyl penicillin/dihydrostreptomycin, cloxacillin/ampicillin and procaine benzylpenicillin/nafcillin/hydrostreptomycin combinations (range of variation: 16.7 % to 24.1 %; $P < 0.05$).

Table 4 summarises cow SCC per treatment group during the 1st 3 samplings of the South African National Milk Recording Scheme for each cow participating in the trial. Cows treated with product 2 had a significantly lower SCC (<400 000 cells per mℓ) at the 1st and 2nd sampling post-calving than cows treated with the other 5 products.

A Kruskal-Wallis multiple analysis as presented in Fig. 1 confirmed that cows dried off with product 2 had significantly lower SCC at the 1st SCC (SCC1) sampling (Z-value = 2.8133) post-calving than those cows dried off with the other 5 products in this trial. For the 2nd sampling (SCC2) the SCC of cows dried off with product 2 remained significantly lower than those cows dried off with Product 6 (Z-value = 2.1700), while no significant differences were present between products in the 3rd sampling (SCC3) post-calving.

The SCC improved the most from drying off to calving in cows dried off with Product 3 and Product 5 and the least with Product 4.

Product 2 had a significantly lower SCC (<400 000 cells per mℓ) at the 1st and 2nd 5-weekly cow milk samples post-calving than cows treated with the other 5 products, while no significant differences were present between products in the 3rd 5-weekly sampling post-calving.

DISCUSSION

This study recorded the prevalence of intramammary quarter infections at drying off and after calving, the overall cure rate and the rate of new IMIs during the dry period. It also compared the efficacy of 6 dry-cow antibiotic products in eliminating existing infections and preventing new IMIs during the dry period. The primary goal of the dry period, from an udder health perspective, is to minimise the number of quarters infected at the next lactation through the elimination of existing infections and the prevention of new IMIs during the dry period.

Clinical mastitis

The use of dry-cow therapy is usually associated with fewer cases of clinical mastitis during the dry period[2,5] but the control needs to be used in conjunction with dry-cow therapy[12,27,46,57]. The percentage of clinical cases which developed during the dry period in this trial compared favourably with those found in other

studies. Bradley and Green[8] reported 3.12 % of clinical cases, Williamson[58] fewer than 3.9 %, while Berry[5] found none in treated and 9 % in untreated cows. Both these cases occurred towards the end of the dry period, while Williamson[58] found that 83 % occurred within 21 days of drying off.

Prevalence of IMI at drying off and after calving

The recorded overall prevalence of IMIs at drying off and after calving in this study is higher than described in most other studies. Few studies, however, have recorded the quarters prevalence of IMIs at the time of drying off, and estimates vary from 5 % to 28 %[11,14,23,36,47]. The recorded prevalence of IMIs after calving varies between 4 % and 14 %[4,30,36,47,53,58]. østerås[39] recorded new IMI rates during the dry period of between 13.1 % and 24.0 % which is in agreement with the findings of this study. Reasons for variations in results amongst studies can be due to variation in the herd (breed, herd size, management, nutrition, sanitary conditions during the dry period and at calving, environmental and climatic factors), criteria used for the inclusion of cows in the study, sampling methodology and schedules and number of samples. Some variation could also be due to differences in laboratory techniques used for bacteriological culture and in the interpretation of results and differences in the definition of intramammary infections among studies[14]. The most prevalent pathogen isolated at drying off and after calving in this study was CNS, while the prevalence of the major contagious and environmental pathogens was low. This finding correlates with findings of Jones[25] of 10–20 % in well-managed herds. Aarestrup[1] isolated CNS from 70 % of heifers prior to calving.

Cure rate

High cure rates found in this study for SAG and SDY is in agreement with other studies that recorded cure rates of between 60 and 100 %[42,52,54] while the cure rate of STA IMI was substantially higher than previously reported, even though there is no consensus at present as to the exact cure rate of STA intramammary infection during the dry period. A large variation in intramammary overall cure rate was reported by various authors[17,20,35,42,46,52,54,58] of between 21.2 % and 80 %. Rainard[43] estimated that between 70 % and 90 % of infections present at drying off can be eliminated with dry cow therapy and the cure rate of IMI during the dry period was found to vary significantly between major and minor pathogens[14,46]. The reason for the high cure rate for STA in this study could be partly due to the low prevalence of STA (0.58 %) in the trial herd and the high percentage of 1st lactation cows. Newly acquired (<2 weeks duration) STA intramammary infections were found to have a cure rate of 70 %, compared to chronic infections (>4 weeks duration) of 35 %[46,53]. Sandholm[46] reported that each month a STA infection persisted in the udder, the prognosis worsened by 20 % if the original cure was 100 %. The cure rate of STA decreases with the age of the cows (from 81 % for cows <48 months to 55 % for cows >96 months) and with the number of infected quarters (from 73 % for 1 infected quarter to 56 % for 4 infected quarters)[42,46,53].

Historically, CNS have been referred to as minor pathogens based on observations that they caused only modest increases in SCC and were infrequently associated with clinical mastitis[22].

This study found lower cure rates for CNS than those of Sandholm[46] and Eberhart[14] of between 90 % and 100 %. Cure and re-infection during the dry period of CNS cases, however, could not be ruled out, as milk samples were only collected at drying off and after calving and not during the dry period. The cure rate during the dry period of non-agalactiae pathogenic streptococcal IMI was reported to be between 77 % and 90 % [14,53,59], which correlates with the high cure rate found in this trial. However, the sample size was very small.

New IMIs

Østerås[40] recorded new IMI rates during the dry period of between 13.1 % and 24.0 %, which is in agreement with the findings of this study. However, most other studies described lower rates of between 4 % and 14 % [4,30,36,47,52,58]. The expected rate of new IMIs during the dry period in bacteria-negative quarters that were untreated was reported by Eberhart[14] to vary between 8 % and 12 % while Berry[4] reported new infection rates of 34.4 % in untreated cows compared with 10.3 % in treated cows. The reduction of new IMIs during the dry period with dry-cow therapy has been estimated at between 50 % and 80 %[14,45].

The rate of new IMIs is many times higher during the dry period compared with the new infection rate during lactation[32]. It is well known that the beginning and end of the dry period are the highest risk periods for new IMIs[7,8,19,41,42]. A 2nd period of increased susceptibility occurs prior to parturition during the period of colostrogenesis and lactogenesis, while the fully involuted udder is quite resistant to coliform infections, but susceptible to SUB and SAG[15,50,58]. Although the infected mammary gland of the lactating cow is the main source and reservoir of STA, it may also be present on the teat skin and external orifices and lesions of cows, bedding, insects and the water supply[42]. STA present in the upper respiratory tract or ears of humans in close contact with the dairy cows can also be a source of infections for IMI in dairy cows (Petzer, unpubl. data). CNS are opportunistic skin flora pathogens[48] and most developed countries now report CNS as an important cause of IMI[50,53]. The dry period appears to be the origin of many new IMIs with CNS[21]. Much has been debated about the possible protective role that CNS, when present in the teat canal, may play to prevent IMI with major pathogens[34,38,42,43,59]. Contrary to a protective role, research has also shown that infections with CNS may increase the susceptibility of quarters to infections with major pathogens[5,23].

Antimicrobial products

In agreement with previous studies, differences in cure rates and new IMIs were observed in cows treated with various intramammary dry-cow products during this trial. Fox[18] found the cure rate for STA IMI to vary between 5 % (penicillin/dihydrostreptomycin-based product) and 87 % (cephalosporin based product). Ziv[60], however, found no differences in the overall efficacy among 3 products (procaine benzylpenicillin/nafcillin/dihydrostreptomycin; cloxacillin and cephalonium), but found differences in cure rates amongst the herds tested. Da Fonseca[10] found cure rates of IMI treated with gentamycin to be significantly higher ($P < 0.05$) compared with those treated with cloxacillin, but found no difference in the new infection rates between the 2 treatment groups during the dry period.

The effect of duration of effective therapeutic levels (persistency) on cure rate

The 2 products in this trial that contain cloxacillin differed significantly ($P < 0.05$) in their overall cure rates of IMI, *i.e.* 91.5 % and 79.2 %. The difference may be as a result of different durations of effective antimicrobial levels. The more successful product had a higher concentration of cloxacillin (600 mg compared to 500 mg per dose) and claimed a longer withdrawal period (7 weeks compared to 4 weeks). In this trial product 5, which claimed the longest active therapeutic level in the udder, was the most effective in curing IMI. There was, however, no significant relationship between overall cure rates and the withdrawal periods

(Table 3). This finding is supported by other studies[42] that reported, contrary to expectation, that when the efficacy in cure rates with long-acting and short-acting dry-cow antimicrobial intramammary products was compared, short-acting intramammary preparations proved to be more effective. Bradley[7,8] found quarters treated with an extra long-acting (14 weeks) intramammary product reduced new coliform IMIs by 52 %, while Smith[52] used short-acting intramammary products (3 weeks) and reported no reduction in coliform mastitis post-calving. The latter could be explained by the fact that coliform infections that occurred at the end of the dry period mainly lead to IMI post-calving[46].

The 3 pharmacodynamic properties of antibiotics that best describe killing activity are time-dependence, concentration-dependence and persistent effects. Dry-cow intramammary preparations should be time-dependent drugs with prolonged persistent effects, as their purpose is to form a deposit in the lactiferous ducts from where the antibiotic is slowly released, without causing unacceptable tissue irritation[23,46]. Most intramammary dry-cow preparations persist only for 14 to 28 days[14,52]. Aminoglycosides are concentration-dependent drugs, where fluctuations in tissue concentration levels are necessary for optimum efficacy. The mechanism of action of the aminoglycoside group is through the inhibition of bacterial protein synthesis. Aminoglycosides do penetrate cells, but at a very slow rate. The environment within the lysosomes is acidic (pH = 5), which reduces the action of aminoglycosides greatly. Aminoglycosides are therefore not ideal for dry-cow formulations. Penicillins are time-dependent in their killing and have minimal persistent effects. Intramammary dry-cow remedies contain mostly narrow spectrum penicillins (penicillin, cloxacillin, oxacillin and nafcillin) and cephalosporins. These dry-cow preparations are designed to eliminate contagious mammary gland pathogens such as STA and SAG and to prevent their infection during the early dry period. In intensive systems, where dairy cows are confined to small areas, environmental infections increase during the dry period. Most dry-cow remedies are reasonably effective against environmental streptococci, but are ineffective against coliform bacteria.

The effect of product composition on cure rate

Antimicrobial products used in this trial differed in their composition and efficacy to cure IMIs and their ability to prevent new IMIs. It should be borne in mind that almost all microorganisms isolated were Gram-positive. Cure rates during the dry period were the highest with cephalonium and the lowest with a combination of cloxacillin/ampicillin. The lowest percentage of new IMIs was observed with cephalonium and a combination of cephalexin/neomycin (Table 3). Of interest was an observation that the 2 products with the highest overall cure rates both contained only 1 antimicrobial agent, compared with the other 4 products, which were combinations of 2 or more. All the intramammary dry-cow antibiotics used in this trial were from the β-lactam (Procaine benzylpenicillin, ampicillin, cloxacillin, nafcillin and cephalosporins) and aminoglycoside groups (dihydrostreptomycin and neomycin sulphate) or combinations thereof.

The efficacy of antimicrobial products to cure IMI during the dry period

Dry-cow treatment was originally developed as a control measure for summer mastitis[41] and adopted as a cornerstone of mastitis control strategies in the 1960s. It is still considered to be the most effective practice for eliminating existing, mainly contagious, IMI during the early dry period, even in herds with a low cell count[28]. Its efficacy and advantages are well known[4,6,17,19,24,33,46]. Mastitogenic pathogens that were highly susceptible to antibiotics were practically eliminated from the cow population while at the same time resistant bacteria became dominant. In a similar way, Gram-positive infections become less frequent when teat dipping is practised, while the prevalence of acute Gram-negative infections, coliforms and Gram-positive infections, *i.e.* SUB, seem to increase[7,46].

Prevention of new IMIs

No significant relationship was found between overall new IMIs during the dry period and the duration of the claimed therapeutic effect of the products. The most to least successful product in preventing new IMIs during the dry period claimed effective therapeutic levels for 10 weeks, 4 weeks, 2 weeks, 4 weeks, 8 weeks and 7 weeks, respectively. With the exception of product 5 with a 10-week action, the short-acting products were most effective in preventing new IMIs. This finding corresponds with the findings of Radostits[42] and Østerås[38]. Østerås[38] found that short-acting, compared to long-acting preparations, had a significantly better effect in preventing new infection with STA and SDY in cows with fewer than 3 infected quarters. Ziv[60] found 7.8 %, 6.9 % and 6.7 % new STA intramammary infections in cows treated with cloxacillin, procaine benzylpenicillin/nafcillin/hydrostreptomycin and cephalonium, respectively.

The effect of dry-cow treatment with various products on somatic cell counts post-calving

There is a strong correlation (r = 0.86) between SCC of quarter milk and those of composite milk samples[21]. The dilution of the high SCC milk from infected quarters with low SCC is an important consideration in the interpretation of the composite sample SCC. Increased SCC values signal udder disease, decrease in milk yield, change in milk composition, and an increase in cost of production and thus less profit[49]. According to Barkema[3] and Renau[44], quarter milk somatic cell counts, as of day 3 after calving, can be used to give an indication of IMI. The SCC from uninfected cows should be less than 300 000 by day 5 *post partum*[44]. The major factor affecting SCC in milk is IMI[13]. Other factors are often implicated in increased SCC, but few have a significant impact[14,21,26,42].

CONCLUSION

To eliminate mainly existing IMIs and in preventing new IMIs, blanket anti-micrbial intra-mammary dry-cow therapy remains a fundamental part of a successful mastitis control programme[14,45]. Administration of intramammary therapy at drying off appears to be an effective therapy to cure existing infections and prevent new IMIs during the dry period. However, results also illustrate that, despite the advantages, there are shortcomings.

The overall cure rate of IMI observed during the dry period was high, as well as the cure rate for IMI with major pathogens. Significant differences were observed between both the cure rates and rate of IMI for the 6 antimicrobial products used for intramammary treatment in this trial. The overall improvement in the intramammary infection rate from drying off to calving was relatively low. However, a large variation in the percentage point change of IMI from drying off till calving was shown between dry-cow therapeutic products. IMI increased in cows treated with product 1 while it decreased up to 51.49 % with cows treated with product 5. No clear correlation between the ability of products to cure existing and prevent new IMIs during the dry period and the effective duration of therapeutic levels was observed.

A difference on the level of SCC post-calving was shown between the 6 intramammary therapeutic dry cow products.

Cows treated with 1 of the 6 products (product 2) had significantly lower SCC at the 1st and 2nd 5 weekly cow milk samples post-calving than cows treated with the other products.

The results of this study emphasise the variability of the response amongst drugs. The emphasis must be on the multifactorial nature of IMI and the adoption of a holistic method to control IMI. Although dry-cow therapy is necessary, it is also necessary to manipulate indirect factors. If key components such as the primary and secondary defence mechanisms of cows and bacterial exposure of the cow are controlled, the prevalence of IMIs can be minimised, the success of dry-cow treatment will be improved and the losses due to mastitis will be limited. The prophylactic use of antibiotics in food-producing animals is likely to become more restricted in the future due to public concerns (antibiotic resistance and residues in the food chain). As a consequence, there is a growing demand for effective alternatives to antibiotic treatments, such as teat sealants (internal and external) and vaccines.

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