Effects of Prepartum Intramammary Antibiotic Therapy on Udder Health, Milk Production, and Reproductive Performance in Dairy Heifers

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ABSTRACT

Preparturient heifers ($n = 561$) from 9 herds in 6 US states and 1 Canadian province were enrolled in a study to test the hypothesis that prepartum intramammary therapy would cure existing intramammary infections (IMI) and lead to increased milk production, reduced linear somatic cell count (LSCC), and improved reproductive performance. Mammary secretions were collected 10 to 21 d before expected calving from each quarter. Heifers were then assigned by identification number to receive intramammary therapy consisting of infusion of one tube per mammary quarter of a lactating cow commercial antibiotic preparation containing cephalapirin or to a nontreated control group. Overall, 34.1% of mammary quarters were infected with a mastitis pathogen before parturition and 63.4% of heifers had at least one mammary quarter infected. The coagulase-negative staphylococci (CNS) caused the majority (74.8%) of prepartum IMI. Coagulase-positive staphylococci, environmental streptococci, and coliforms accounted for 24.5% of prepartum infections. Treatment had a significant effect on the cure rate of infected mammary quarters. Mammary quarters that were infected prepartum and treated with antibiotics had a 59.5% efficacy of cure rate and the percentage reduction in heifers with IMI was 51.9. Control quarters had a spontaneous cure rate of 31.7%. Treatment did not significantly affect milk production or LSCC in the first 200 d of lactation; however, there was a significant treatment by herd interaction for milk production. Quarters cured of either CNS or major pathogens had a lower LSCC in the first 200 d of lactation. No significant effect on services per conception or days open between treat-

ment and control groups was observed. This trial demonstrated that prepartum intramammary antibiotic therapy did reduce the number of heifer IMI postpartum. Milk production, LSCC, and reproductive performance during the first 200 d of the first lactation were not significantly affected by treatment. Given these results, use of prepartum intramammary antibiotic therapy in heifers as a universal strategy to increase milk production in first-lactation dairy cows may not be warranted.

Key words: mastitis, antibiotic treatment, heifer, health

INTRODUCTION

Mastitis causes the greatest economic loss to the dairy industry today (DeGraves and Fetrow, 1993). Although losses have been well characterized in mature cows, the prevalence of IMI in primigravid heifers has been a more recent focus of study (Oliver and Mitchell, 1983; Trinidad et al., 1990a; Matthews et al., 1992; Nickerson et al., 1995). As many as half of all mammary quarters in heifers may have IMI at first parturition (Fox et al., 1995). Antibiotic treatment of multiparous dairy cows following the last milking of lactation (dry cow treatment) is a common and cost-effective means to aid in control of mastitis (DeGraves and Fetrow, 1993). It would be expected that similar prepartum treatment of heifers might be successful in reducing IMI at parturition given that mastitis pathogens isolated from mammary glands of heifers preterm were susceptible to antibiotics used to treat mastitis pathogens (Watts et al., 1995).

Researchers in Louisiana (Trinidad et al., 1990b; Owens et al., 1991) studied the effects of dry cow antibiotic preparations given intramammarily at various stages of gestation. Results of those studies demonstrated that use of intramammary antibiotics significantly reduced

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the prevalence of mastitis pathogens at calving and 2 mo into the first lactation. Based on these initial studies, the researchers suggested that administration of antibiotics should be done 20 wk (Trinidad et al., 1990b) or 10 to 12 wk (Owens et al., 1991) before expected calving to obtain the greatest cure rate and minimize the chance of antibiotic residues in milk at calving. Subsequent research (Owens et al., 2001) indicated that approximately 12 wk before expected calving date might be the best time to treat mammary glands of heifers with intramammary dry cow antibiotic preparations. The efficacy of treatment on existing IMI was not different between trimesters of pregnancy. However, there were fewer new coagulase-positive staphylococcal IMI established after treatment and before calving in the group treated from 12 to 2 wk before calving. Thus, these researchers concluded that treatment during the last trimester of pregnancy would presumably lead to less new IMI after prepartum therapy.

The efficacy of lactating cow antibiotic therapy on heifer IMI has been studied (Oliver et al., 1992, 1997, 2003, 2004). When administered 7 to 14 d before expected calving, antibiotic preparations approved for use in lactating cows containing cloxacillin, cephalixin, pirimycin, or penicillin-novobiocin were all effective at eliminating prepartum IMI in heifers (Oliver et al., 1992, 2004). Fewer episodes of antibiotic residues (inhibitors) in mammary secretions at calving and during early lactation were observed with treatment 14 d before expected calving (Oliver et al., 1992, 1997). The type of antibiotic used to treat heifers affected the length of time that residues were detected in milk. Generally, inhibitors were not detected at 3 d after parturition, a time when milk is often deemed free of colostral content and added to the bulk tank for human consumption.

Treatment during the last trimester of pregnancy seems most advantageous given the success of therapy during this time and the more intensive management of heifers during the peripartum period. Several studies on efficacy of periparturient intramammary treatment of heifers suggests this approach could effectively reduce IMI at calving. However, only one study in a single herd (Oliver et al., 2003) demonstrated that this approach is economically viable as demonstrated by an increase in milk production and a decrease in SCC. Data from a preliminary report from the Netherlands suggest that prepartum intramammary therapy in heifers from herds with reportedly higher prevalence of IMI may result in higher yields of milk during the first lactation than controls, but this relationship did not hold true in herds with reportedly low IMI prevalence (Sampimon and Sol, 2005). Thus, the success of such

therapy might differ depending on prevalence of mastitis across herds.

The purpose of the current study was to test the hypothesis that intramammary therapy of heifers preterm is effective in enhancing the clearance of IMI, increasing milk production, and decreasing SCC, using several herds in multiple locations across North America. We were also interested in determining the effect of intramammary therapy of heifers preterm on postpartum reproductive performance based on previous studies that suggested that clinical and subclinical mastitis in lactating cows had a negative effect on reproductive performance (Barker et al., 1998; Schrick et al., 2001).

MATERIALS AND METHODS

This project was developed and conducted by participants in USDA Regional Research Project NE-1009. Heifers ($n = 561$) were included from 9 farms in 7 locations as indicated in Table 1. All herds were enrolled in a production testing program. Animals were assigned to treatment group by cow identification number with odd-numbered heifers serving as untreated control animals and even-numbered heifers used as treatment animals. Collection of mammary secretions from each quarter was done aseptically according to National Mastitis Council guidelines (Hogan et al., 1999). In brief, mammary quarter secretion samples were collected in duplicate between 10 and 21 d before expected calving from all heifers. Teat ends were wiped with individual disposable paper towels and scrubbed with cotton pads soaked in 70% isopropyl alcohol, and the first few streams of foremilk were discarded at postpartum collections. Immediately following mammary secretion collection, intramammary infusion of a commercially available lactating cow antibiotic formulation containing 200 mg of cephalixin sodium (Cefa-Lak, Fort Dodge Animal Health, Fort Dodge, IA) was made using the partial insertion method in all mammary quarters of treatment heifers. Controls did not receive a placebo treatment. Following infusion of treated heifers, and sampling in control animals, each teat was dipped in a polymer-based barrier teat dip (Stronghold, West Agro Inc., Kansas City, MO). Mammary quarter foremilk samples were collected aseptically within the first 3 d after calving. Aseptically collected mammary quarter foremilk samples were also collected at 1 to 7 d postpartum (wk 1), 7 to 14 d postpartum (wk 2) and 14 to 21 d postpartum (wk 3).

Milk samples were stored at -5°C until cultured. A 10- μL aliquot from each milk sample thawed at ambient temperature was spread on blood agar plates and incubated for 48 h at 37°C . After incubation, plates

Table 1. Intramammary infections in heifers pre- and postpartum: Efficacy of treatment on cure rate for all pathogens¹

Herd ²	Infected quarters		Cured quarters		Efficacy, ³ %	95% CI	P-value (χ^2)
	Treated	Control	Treated	Control			
A	51	49	39	15	60.0	37.7, 74.4	<0.0001
B	12	19	11	3	82.8	50.7, 94.0	<0.0001
C	6	8	6	3	62.5	8.3, 84.7	0.0157
D	57	77	43	7	88.0	75.2, 94.1	<0.0001
E	25	23	23	5	76.4	48.3, 89.2	<0.0001
F	137	126	106	58	40.5	26.6, 51.8	<0.0001
G	26	34	24	15	52.1	28.8, 67.7	0.0001
H	27	33	23	11	60.9	35.0, 76.4	<0.0001
I	33	19	24	6	56.6	13.1, 78.3	0.0038
Total	374	388	299	123	59.5	52.8, 65.15	<0.0001

¹Pathogens considered were major (coagulase-positive staphylococci, streptococcal spp., and coliforms) and CNS. Other pathogens from 5 IMI (2 *Pseudomonas* spp., 1 *Lactobacillus* sp., 1 *Serratia marcescens*, and 1 *Pasteurella* sp.) were not included in the analysis.

²Herds included in study: Louisiana State University; The Ohio State University; University of Tennessee Dairy Experiment Station; University of Tennessee Middle Tennessee Experiment Station; University of Connecticut; Washington State University; University of Guelph (Ponsonby and Elora); and Cornell.

³Efficacy = $100 \times (1 - \text{cure risk ratio})$ where cure risk ratio = percentage control quarters cured/ percentage treated quarters cured. For the total overall comparisons the efficacy and P-value were compiled using the Mantel-Haenszel χ^2 test as no significant heterogeneity of effects between herds existed.

were observed and organisms identified presumptively (Hogan et al., 1999) as coagulase-positive staphylococci, CNS, *Streptococcus* species, and coliforms based on colony morphology, reaction on Christie, Atkins, and Munch-Peterson-esculin agar plates and MacConkey agar, catalase and coagulase test reactions, and Gram stain. Isolates that could not be identified by these presumptive techniques were classified as "other." Coliforms, streptococcal species, and coagulase-positive staphylococci were considered major. A sample was considered contaminated when 3 or more dissimilar colony types were isolated. A mammary quarter was considered infected prepartum if the same pathogen was isolated from duplicate samples. If only a single prepartum sample could be obtained, results of the single sample were considered to determine the presence of an IMI. A mammary quarter was characterized as having a new infection if the same pathogen was isolated from 2 of 3 samples collected during early lactation that was not present in prepartum samples. A mammary quarter remained infected if the same organism that was present prepartum was isolated during early lactation. If any quarter sample taken on d 7 or 14 was contaminated, a new sample was not taken, and the mammary quarter was not disqualified from the study. If the final mammary quarter milk sample taken at 3 wk postpartum was contaminated, a new mammary quarter milk sample was taken immediately following diagnosis of contamination. If a follow-up sample after a contaminated sample at the 3-wk period was not taken, data from the mammary quarter were not included in the analysis. A mammary quarter was considered cured if

the pathogen present before calving was not isolated in any of the samples obtained during early lactation.

Production testing records including milk yield, milk SCC, services per conception, and days open were obtained for the first 200 DIM. Any clinical mastitis event and subsequent treatment were also recorded. Milk SCC was transformed to linear SCC (LSCC) using the linear SCC formula: $\text{LSCC} = [\text{LOGe}(\text{SCC})/0.6931] - 3.6439$.

All statistical analyses were done using SAS (version 8.0, SAS Institute Inc., Cary, NC). Frequency tables of cure by treatment by herd were prepared, and the Cochran-Mantel-Haenszel χ^2 test with herds as strata was used to analyze the statistical significance of intramammary treatment on bacterial cure. The treatment efficacy, by individual herd and for all herds combined, were computed using the formula: $100 \times (1 - \text{cure risk ratio})$, where the cure risk ratio was defined as the percentage of control mammary quarters cured postpartum divided by the percentage of treated quarters cured (Orenstein et al., 1985, 1988).

Milk production and LSCC were analyzed by a model for repeated measures (PROC MIXED). Milk production and LSCC were regressed against the effects of treatment (control or treated), herd, herd $\times$ treatment interaction, days between first sampling prepartum and parturition (interval), interval $\times$ treatment interaction, and DIM at production test. The quadratic effect of DIM was also included in the model. Herd, treatment, and cow were categorical variables and interval and DIM were considered as continuous variables. Cow within herd by treatment was used as the error term

Table 2. Intramammary infections in heifers pre- and postpartum: Efficacy of treatment on cure rate for CNS

Herd ¹	Infected quarters		Cured quarters		Efficacy, ² %	95% CI	P-value (χ^2)
	Treated	Control	Treated	Control			
A	42	39	32	14	52.9	26.0, 70.0	0.0001
B	11	15	10	2	85.3	46.0, 96.0	0.0002
C	4	7	4	2	71	7.8, 91.1	0.0133
D	43	47	35	5	86.9	69.7, 94.4	<0.0001
E	23	22	21	4	80.1	51.3, 91.9	<0.0001
F	104	84	84	46	32.2	15.9, 45.4	0.0001
G	12	17	11	8	48.2	11.4, 69.8	0.0128
H	24	32	21	10	64.3	39.0, 79.1	<0.0001
I	26	18	19	5	62.0	17.0, 82.6	0.003
Total	289	281	237	96	57.5	49.8, 64.1	<0.0001

¹Herds included in study: Louisiana State University; The Ohio State University; University of Tennessee Dairy Experiment Station; University of Tennessee Middle Tennessee Experiment Station; University of Connecticut; Washington State University; University of Guelph (Ponsonby and Elora); and Cornell University.

²Efficacy = $100 \times (1 - \text{cure risk ratio})$ where cure risk ratio = percentage control quarters cured/percentage treated quarters cured. For the total overall comparisons the efficacy and P-value were compiled using the Mantel-Haenszel χ^2 test because no significant heterogeneity of effects between herds existed.

to test the significance of the effects of herd, treatment, and herd $\times$ treatment interaction on milk production and LSCC. The repeated measure, time (DIM), was fitted as a covariate along with treatment by DIM, and interval, and these were tested using the residual mean square. The effect of cure on milk production and LSCC was tested in a data set in which only information from mammary quarters that had preparturient infections was included. The independent effects of herd, treatment, interval, cured, and pathogen type (CNS or major mastitis pathogen), cured by pathogen type interaction, DIM, and DIM $\times$ DIM were considered.

Mammary quarters that were not infected prepartum and those quarters cured postpartum were eligible for new IMI. The difference in new infections between treatment and control mammary quarters was evaluated using χ^2 analysis.

To test significance of differences between treatments in calving to conception interval (days open), survival analysis (PROC PHREG) with herds as strata was used. Animals were censored at 200 DIM if they had not conceived by that time. Animals that were culled were censored at their cull date or 200 DIM, whichever came first. Finally, animals that were still open but had not reached 200 DIM by the time the analysis was conducted were censored at their last date on record. To test for significance between treatment groups in number of services per conception, a frequency table of number of services per conception was prepared and tested for significance using the Cochran-Armitage trend test.

RESULTS

Complete records from 561 heifers were used, 286 in treatment and 275 in control groups. Coagulase-nega-

tive staphylococci caused the majority of IMI: 570 out of 762 infected quarters (74.8%). Coagulase-positive staphylococci, environmental streptococci, and coliforms accounted for 24.5% of prepartum infections. Treated mammary quarters had a significantly higher cure rate than control quarters in all herds (Table 1). Cure rates in treated and control mammary quarters were 79.9 and 31.7%, respectively. The efficacy of cure for treated vs. controls was 59.5% and was statistically significant ($P < 0.0001$). Although treatment efficacy was significant in all herds, there were some apparent differences among herds. The greatest cure rate of treated over control mammary quarters was seen in herd D (88.0%) and the lowest was in herd F (40.5%). Cure rate was analyzed by pathogen type. Infections were separated into those caused by major pathogens (coagulase-positive staphylococci, environmental streptococci, and coliforms) and CNS. Five heifers had IMI with pathogens in the "other" category. Two heifers had IMI with *Pseudomonas* spp. and 1 with a *Lactobacillus* sp.; these IMI were cured. One heifer had a *Pasteurella* sp. IMI and 1 had a *Serratia marcescens* IMI; neither was cured by treatment. These 5 "other" IMI were not included in the analysis. Treatment had a significant effect ($P < 0.0001$) on curing CNS infections (Table 2) and overall treatment efficacy was 57.5%. The highest treatment efficacy was in herd D (86.9%) and the lowest treatment efficacy was in herd F (32.2%).

Four of the 9 herds had significantly ($P < 0.05$) higher cure rates for major pathogens in treated mammary quarters than in controls (Table 3). In one herd (B), no mammary quarters of treated animals were infected with a major pathogen prepartum, and, therefore, an efficacy of treatment could not be calculated. In 2 herds

Table 3. Intramammary infections in heifers pre- and postpartum: Efficacy of treatment on cure rate for major pathogens¹

Herd ²	Infected quarters		Cured quarters		Efficacy, ³ %	95% CI	P-value (χ^2)
	Treated	Control	Treated	Control			
A	9	10	7	1	87.1	13.8, 93.6	0.0028
B	0	4	0	1	* ⁴	*	*
C	2	1	2	1	*	*	*
D	14	27	8	1	93.5	53.3, 99.1	<0.0001
E	2	1	2	1	*	*	*
F	33	41	22	12	56.1	25.4, 74.2	0.0013
G	14	17	13	7	55.8	20.0, 75.3	0.0028
H	3	1	2	1	*	*	0.505
I	7	1	5	1	*	*	0.5371
Total	84	103	61	26	60.0	44.7, 71.1	<0.0001

¹Major pathogens are coagulase-positive staphylococci, streptococcal species, and coliforms.

²Herds included in study: Louisiana State University; The Ohio State University; University of Tennessee Dairy Experiment Station; University of Tennessee Middle Tennessee Experiment Station; University of Connecticut; Washington State University; University of Guelph (Ponsonby and Elora); and Cornell University.

³Efficacy = $100 \times (1 - \text{cure risk ratio})$ where cure risk ratio = percentage control quarters cured/percentage treated quarters cured. For the total overall comparisons the efficacy and P-value were compiled using the Mantel-Haenszel χ^2 test because no significant heterogeneity of effects between herds existed.

⁴Those values signified by an asterisk (*) were undefined because the cure risk ratio could not be computed when no infections were present in mammary quarters of either control or treated animals or when 100% of IMI were cured in all animals. When the number of IMI was too small for the purposes of making clinically valid comparisons, the ratio was not computed.

(C and E), all of the treatment and control quarters infected prepartum were cured of major pathogen IMI postpartum. In herds H and I, the number of IMI by major pathogens was too small to warrant clinically valid comparisons. Overall, when controlling for herd effects, the treatment effect on major pathogen cure was highly significant ($P < 0.0001$), with an efficacy of 60%.

The minimum and maximum milk production (kg/heifer per day) by herd was 14.23 and 33.67; overall, milk production varied by herd (Table 4). Treatment had no significant effect on milk production in the first 200 DIM ($P = 0.7234$; Table 4). Treated animals pro-

duced an average of 28.1 kg (± 9.03) on test day whereas control animals produced an average of 27.8 (± 8.51) kg of milk on test day (Table 5). There were significant differences in milk production between herds ($P < 0.0001$) and a significant herd by treatment interaction ($P < 0.05$). Control heifers produced more milk in 5 herds (C, D, E, G, and I), whereas treated heifers produced more milk during the study period in 4 herds (A, B, F, and H). The variable interval, the time between treatment or first sampling, and parturition, significantly impacted milk production, but the effect of treatment by interval was not significant (Table 4). The mean ($\pm$ SD) interval between treatment and parturition was 13.1 (± 6.1) d. As the interval between time of treatment and parturition increased, milk production increased; the regression coefficient was 0.074. There

Table 4. Repeated measures mixed model with production as the dependent variable and regressed against the independent variables (herd, treatment, DIM, and interval)

Independent variables	Degrees of freedom	F-value	P > F
Herd	8	142.52	<0.0001
Treatment ¹	1	0.13	0.7234
Herd $\times$ Treatment	8	2.50	0.0108
DIM	1	263.83	<0.0001
DIM $\times$ DIM	1	217.38	<0.0001
Interval ²	1	6.58	0.0104
Interval $\times$ Treatment	1	0.89	0.4441

¹Treated animals received intramammary antibiotic therapy 10 to 21 days before expected calving. Control animals received no intramammary treatment.

²Interval is the period between first sampling before parturition (day of treatment for treated animals) and parturition.

Table 5. Mean ($\pm$ SD) milk production and milk linear SCC for cows that were treated and control, and for cows with mammary quarters cured of an IMI caused by a major or minor pathogen¹

Parameter	Production	Linear SCC
Control (no treatment)	27.8 (± 8.51)	2.85 (± 2.01)
Treatment	28.1 (± 9.03)	2.53 (± 1.95)
Not cured of minor pathogen	26.9 (± 9.05)	3.07 (± 1.84)
Cured of minor pathogen	27.8 (± 8.74)	2.34 (± 1.86)
Not cured of major pathogen	24.1 (± 9.34)	4.51 (± 1.93)
Cured of major pathogen	26.4 (± 9.27)	2.36 (± 1.83)

¹Pathogen was classified as either a major (coagulase-positive staphylococci, streptococcal species, and coliforms) or minor (CNS) pathogen.

Table 6. Repeated measures mixed model with Linear SCC as the dependent variable, and regressed against independent variables (herd, treatment, DIM, and interval)

Independent variables	Degrees of freedom	F-value	P > F
Herd	8	11.01	<0.0001
Treatment ¹	1	1.55	0.2135
Treatment × Herd	8	0.18	0.9942
DIM	1	38.77	<0.0001
DIM × DIM	1	36.52	<0.0001
Interval ²	1	2.05	0.1278
Interval × Treatment	1	3.28	0.0702

¹Treated animals received intramammary antibiotic therapy 14 d before expected calving. Control animals received no intramammary treatment.

²Interval is the period between first sampling before parturition (day of treatment for treated animals) and parturition.

were significant linear and quadratic effects of DIM on production ($P < 0.0001$) with regression coefficients of 0.12 and -0.0005 , respectively.

There were no significant differences in the LSCC of treated animals compared with control animals ($P = 0.2135$, Table 6). The mean LSCC was 2.85 for control heifers during the first lactation as compared with 2.53 for treated heifers (Table 5). Linear and quadratic effects of DIM were significant ($P < 0.0001$); regression coefficients were -0.015 and 0.00007 , respectively. No other independent variables had a significant effect on LSCC as modeled (Table 6).

Pathogen type did not significantly affect milk production (Table 7). Milk production of heifers with cured mammary quarters produced more milk than those without cures (Table 5) although differences were not significant (Table 7). The interaction between cured and pathogen type was also not significant (Table 7). Effects of cure and pathogen type did significantly affect LSCC

Table 7. Repeated measures mixed model with milk production as the dependent variable, and regressed against independent variables (herd, treatment, DIM, cured, and pathogen type)

Independent variables	Degrees of freedom	F-value	P > F
Herd	8	82.82	<0.0001
Treatment ¹	1	1.38	0.2406
DIM	1	392.57	<0.0001
DIM × DIM	1	319.92	<0.0001
Cured	1	1.28	0.2584
Pathogen ²	1	0.74	0.8459
Cured × Pathogen	1	0.04	0.9011

¹Treated animals received intramammary antibiotic therapy 10–21 days prior to expected calving. Control animals received no intramammary treatment.

²Pathogen was classified as either major (coagulase-positive staphylococci, streptococcal species, and coliforms) or minor (CNS) pathogen.

Table 8. Repeated measures mixed model with linear SCC as the dependent variable, and regressed against independent variables (herd, treatment, DIM, cured, and pathogen type)

Independent variables	Degrees of freedom	F-value	P > F
Herd	8	15.05	<0.0001
Treatment ¹	1	0.44	0.5064
DIM	1	63.27	<0.0001
DIM × DIM	1	57.30	<0.0001
Cured	1	53.47	<0.0001
Pathogen ²	1	9.18	0.0025
Cured × Pathogen	1	15.31	<0.0001

¹Treated animals received intramammary antibiotic therapy 10 to 21 d before expected calving. Control animals received no intramammary treatment.

²Pathogen was classified as either major (coagulase-positive staphylococci, streptococcal species, and coliforms) or minor (CNS) pathogen.

(Table 8). Heifers with mammary quarters with major pathogen IMI that were not cured had the highest LSCC, whereas those with cured major or cured minor pathogen IMI had the lowest LSCC (Table 5).

Intramammary antibiotic therapy had no significant ($P = 0.3867$) effect on reproductive performance as measured by days open. The median days open for control animals was 128 d [95% confidence interval (CI): 106, 144] and 136 d (95% CI: 122, 152) for treatment animals. There was no difference ($P = 0.3039$) between control and treatment groups regarding the number of services per conception: 1.88 ± 1.26 vs. 2.02 ± 1.15 .

Heifers treated with antibiotics prepartum had fewer new IMI in the first 3 wk of lactation (Table 9). Only 2.6% of treated quarters had a new IMI in the first 3 wk postpartum whereas 7.8% of control quarters had a new mastitis-causing pathogen isolated from at least 2 of 3 consecutive postpartum milk samples. The overall relative risk of a new IMI in the first 3 wk of lactation for control heifers, as compared with treated heifers, was 66.4% ($P < 0.0001$, Table 9). At the start of the study, 60.8% (174/285) of treated heifers had IMI, as opposed to 62.5% (175/275) of controls. Overall, there was a 51.9% reduction in heifers with IMI when heifers receiving treatment were compared with controls (Table 10). Individually, reduction in heifers with IMI was found in 8 of 9 herds (Table 10).

DISCUSSION

It was hypothesized that antibiotic treatment of mammary quarters would significantly improve cure rate resulting in increased milk production, decreased SCC, and improved reproductive performance during the first lactation. A commercial intramammary product containing 200 mg of cephapirin sodium was chosen given the success this formulation had in curing infec-

Table 9. New intramammary infections in heifers: Treatment quarters vs. control quarters (no. of eligible quarters in parentheses)

Herd ¹	Treated quarters	Control quarters	Relative risk, ² %	95% CI	P-value (χ^2)
A	4 (156)	3 (127)	8.5	376.2, -75.3	0.9201
B	2 (84)	10 (12)	-81.7	-18.9, -95.9	0.0105
C	2 (26)	0 (63)	*	*	*
D	1 (55)	5 (63)	-77.1	90.9, -97.2	0.1313
E	0 (23)	5 (17)	*	*	*
F	3 (65)	10 (72)	-66.8	15.5, -90.4	0.0644
G	3 (194)	8 (174)	-66.4	24.8, -90.9	0.0861
H	1 (49)	4 (43)	-78.1	88.9, -97.5	0.1253
I	4 (111)	10 (121)	-56.4	35.1, -85.9	0.1364
Total	20 (763)	55 (706)	-66.4	-38.0, 78.4	<0.0001

¹Herds included in study: Louisiana State University; The Ohio State University; University of Tennessee Dairy Experiment Station; University of Tennessee Middle Tennessee Experiment Station; University of Connecticut; Washington State University; University of Guelph (Ponsonby and Elora); and Cornell University.

²Relative risk of a mammary quarter not treated becoming infected. Relative risk = (1/Mantel Haenszel Cohort Relative Risk Value) - 1. For the total overall comparisons, the relative risk and P-value were compiled using the Mantel-Haenszel χ^2 test because no significant heterogeneity of effects between herds existed.

*Undefined because relative risk could not be computed when no infections were present in mammary quarters of either control or treated animals.

tions in heifers when treated 14 d before expected parturition (Oliver et al., 2003). Moreover to maintain uniformity and reduce the number of variables between herds, it was important that all treated heifers in the study would receive the same product. Intramammary antibiotic treatment was effective in curing prepartum IMI. Most IMI were caused by CNS and cure rate of CNS IMI in treated mammary glands was 57.5% greater than in control glands. This finding agrees with previous research in which CNS was the most commonly

isolated pathogen from heifer mammary glands and cure rates in prepartum antibiotic-treated mammary quarters were 30.5 to 76.2% higher than untreated control quarters (Trinidad et al., 1990b; Oliver et al., 1992, 1997, 2004; Owens et al., 2001).

Overall, the major pathogen cure rate in treated mammary quarters was significantly greater than in control quarters. This agrees with previous findings that have shown that prepartum intramammary antibiotic therapy in heifers is efficacious against major

Table 10. The number of heifers in treated and control groups with intramammary infections before and after parturition

Herd ¹	No. of heifers enrolled		No. of heifers with IMI prepartum		No. of heifers with IMI postpartum		Difference, ² %
	Treated	Control	Treated	Control	Treated	Control	
A	53	45	23	23	17	11	54.5
B	24	24	8	14	1	13	-92.3
C	8	5	5	3	0	3	*
D	28	35	24	27	10	25	-60.0
E	12	10	12	10	2	10	-80.0
F	51	50	48	47	20	33	-39.4
G	55	52	19	20	2	13	-84.6
H	19	19	14	13	3	11	-72.7
I	36	35	21	15	7	10	-30.0
Total	286	275	174	172	62	129	51.9

¹Herds included in study: Louisiana State University; The Ohio State University; University of Tennessee Dairy Experiment Station; University of Tennessee Middle Tennessee Experiment Station; University of Connecticut; Washington State University; University of Guelph (Ponsonby and Elora); and Cornell University.

²Difference = IMI in treated as compared with control heifers for 3 wk postpartum = $100 \times [(\text{no. of IMI in treated heifers} - \text{no. of IMI in control heifers}) / \text{no. of IMI in control heifers}]$.

*Undefined because relative risk could not be computed when no infections were present in mammary quarters of either control or treated animals.

pathogens such as *Staph. aureus* (Trinidad et al., 1990b; Owens et al., 1991, 2001; Oliver et al., 1997, 2004) and environmental streptococci (Oliver et al., 1997, 2004; Owens et al., 2001). However, major pathogen infections were rare in some herds, meaning that calculation of treatment efficacy values and making valid clinical comparisons was difficult.

The effect of fewer infections postpartum and significantly improved prepartum cure of IMI did not result in improved postpartum milk yield in treated animals. Cure, but not treatment, was associated with a significant reduction in LSCC. This is in partial agreement with a previous report by Oliver et al. (2003) on intramammary antibiotic therapy in prepartum heifers. They found that the majority of heifer IMI were caused by CNS, as in the current study. However, Oliver and coworkers (2003) also reported that heifers treated with intramammary antibiotic 7 and 14 d before expected calving had significantly higher milk production and lower SCC score than control animals. The interval between treatment and parturition was a significant variable affecting the current trial and that of Oliver et al. (2003). In the current trial, cows were enrolled 10 to 21 d before their expected due dates, and the average interval was 13.1 d. The interval in the trial by Oliver and coworkers (2003) was 7 to 14 d, and was likely shorter. But data from this study suggest that longer intervals resulted in more milk produced postpartum. Curing infections earlier may lead to less loss of mammary parenchyma due to IMI. Moreover, the effect of herd differences may account for the different production responses to treatment in this and other reports (Oliver et al., 2003; Sampimon and Sol, 2005). Data from the current study indicate the interaction of treatment by herd significantly affected the dependent variable milk production. In 56% of herds (5 of 9) on average, control heifers produced more milk than treated animals, whereas the opposite was true for the remaining herds. In Sampimon and Sol's (2005) multiple herd study there was very little difference between milk production in heifers postpartum in herds with apparent lower prevalence of heifer IMI. However, in herds with apparently higher heifer IMI, the production response might be significantly greater in prepartum treated heifers.

Schrick et al. (2001) found that animals with clinical and subclinical mastitis before first service had increased days open (110.0 ± 6.9 and 107.7 ± 6.9 d, respectively) compared with cows that did not have a mastitis pathogen (where days open was 85.4 ± 5.8 d). These authors report that cows with clinical and subclinical mastitis also had an increase in services per conception, 2.1 ± 0.2 and 2.1 ± 0.1 , respectively, which contrasts with cows without mastitis with services per conception

of 1.6 ± 0.2 . Heifers were only a small fraction of the data set analyzed. In a study with only primiparous cattle, Schrick et al. (2002) reviewed the records of animals from a previous study (Oliver et al., 1997) to determine if prepartum treatment of heifers with intramammary antibiotics had an effect on reproductive performance. There was no difference found in days open or services per conception when records were analyzed by treatment. Control, cephalixin-treated, and cloxacillin-treated animals had days open of 72.8 ± 3.8 , 72.1 ± 3.1 , and 75.3 ± 3.6 , respectively. Services per conception were 1.5 ± 0.3 for control animals, 1.6 ± 0.2 for cephalixin-treated animals, and 1.6 ± 0.3 for cloxacillin-treated animals. The findings in the current study concurred, because there were no significant differences in reproductive parameters between treated and control animals. Additionally, in the current study, there was no significant difference found in either days open or services per conception between treated and untreated animals in the first lactation across all herds.

There was a prophylactic effect on new IMI due to treatment. New IMI in the first 3 wk postpartum was not as prevalent in treated quarters as it was in control quarters. This is similar to previous research in which a prophylactic effect of intramammary antibiotic therapy administered as dry cow therapy was found (Ward and Schultz, 1973). When all mammary quarters were treated with a dry cow antibiotic at dry-off, only 5.6% of quarters had a new IMI in the first month of the next lactation compared with 9.5% of untreated mammary quarters. Overall, treatment in this study reduced the number of heifers with IMI postpartum by approximately 52%, with the greatest decline in streptococci.

Results of milk production from the current study would indicate that prepartum treatment of primiparous cows was not uniformly efficacious across herds. Therefore, adoption of this therapy as a general management practice to increase milk production in first-lactation cows is not warranted. Data from this and other studies indicate that such treatment of heifers has different levels of success in affecting milk production across different herds. Moreover, the CNS account for the large majority of postpartum heifer IMI. The CNS are a large group of heterogeneous mastitis pathogens in which each species within the group might not respond equally to a single regimen of therapy. Thus, future studies could be directed at determining the herd factors and the heifer factors that might influence the success of prepartum intramammary therapy, the differences in CNS responses to therapy, and strategies that can be used to prevent prepartum heifer IMI.

CONCLUSIONS

Intramammary antibiotic therapy administered to heifers 10 to 21 d before expected calving aids in curing

IMI before the first lactation. Such therapy led to a significant decrease in IMI at calving (cures) and decreased prevalence of IMI for the first 21 DIM (prophylaxis). However, treatment prepartum was not associated with a significant increase in milk production or a significant decrease in LSCC. However, cure of IMI was associated with a significant decrease in LSCC but not with an increase in milk production. Given these mixed results, in which treatment on the one hand had a significant positive effect on cure of IMI but on the other hand did not improve production or LSCC, we suggest that preterm therapy in heifers should be practiced with caution. The data would not support the universal adoption of preterm intramammary therapy in heifers to be on par with standard dry cow therapy. However, intramammary antibiotic therapy administered to heifers within 1 to 3 wk before expected calving might have value in a herd when a significant proportion of heifers have IMI.

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