

Cephalosporin in Mastitis Therapy

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Introduction

The New York State Mastitis Control Program is operating under the Department of Large Animal Medicine, Obstetrics and Surgery of the New York State Veterinary College at Cornell University, Ithaca, New York. The program furnishes dairymen of New York State diagnostic services relating to prevention, detection, treatment and control of bovine mastitis on both a herd and individual cow basis. Mastitis control personnel visit the dairies, examine the cows physically for udder health and abnormal milk, collect milk samples for bacteriological culturing, and evaluate milking machinery, milking practices and management as it would apply to the production of quality milk. These services are offered to the dairymen in conjunction with their practicing veterinarian, and results of the surveys are returned to the practitioner for application.

At the request of a practicing veterinarian a mastitis survey was conducted on a 96 cow dairy that had a history of repeatedly exceeding the United States Public Health Service standards for bulk tank leucocyte count in milk produced and sold (1,500,000 WBC/ml). The veterinarian and owner had been able to control the leucocyte count below the tolerance level on occasion by physically examining and treating cows positive to the strip plate and California Mastitis Test. The veterinarian felt however that mastitis was not being controlled, rather just the most obvious cases were being discovered and either treated or excluded from the milk being sold.

The initial Mastitis Survey on the entire dairy of 96 cows on March 13, 1973, showed the following:

Table 1

	Cows		Quarters	
	No.	%	No.	%
Negative	6	6		
Str. agalactiae	70	73	153	40
Hemolytic staph	58	60	94	24
Streps - other species	43	45	61	16
E. Coli	3	3	3	1
Abnormal Secretion (Strip Plate)	21	22	27	7
Leucocyte Count Bulk Milk Samples 1,581,032/ml.				

Milking equipment was examined. The vacuum pump and line were found adequate to operate six

milking machines and a milk transfer station. Milking machines were approximately 25 years old and functioning satisfactorily.

The farm is family owned, milking is done by family members, but not always the same people at every milking. The herd is not on a production testing program but the herd average would be estimated at not over 10,000 lbs. milk/cow/year. Most dairy replacements are home raised. Teat dipping after milking to control infection spread and routine dry cow mastitis therapy were not being practiced.

Upon receiving the result of the mastitis survey with the recommendation to treat one or more quarters of 70 of the 96 cows, the owner was reluctant to begin such a drastic solution and with the exception of treating visibly clinical mastitis further action was postponed.

In June of 1973 the owner agreed to have all cows treated with Sodium Cephapirin Intramammary Infusion (Bristol Laboratories), which was currently the subject of a clinical efficacy study designed to support a New Animal Drug Application to be submitted to the Food and Drug Administration by the sponsoring company.

Pharmacology

The first of the cephalosporin group of antibiotics was discovered in the Mediterranean Sea off the coast of Sardinia. Produced by a fungus of the genus *Cephalosporium*, many of the cephalosporin antibiotics possess clinically valuable properties, among them being a broad spectrum of antibacterial activity and resistance to the enzyme penicillinase. Numerous cephalosporin derivatives have been produced biosynthetically. There is some similarity between the basic cephalosporin nucleus and the basic penicillin nucleus.

Sodium cephapirin is a cephalosporin derivative possessing bactericidal activity against gram positive and gram negative organisms, and is not inactivated by strains of staphylococci producing penicillinase. It is, therefore, effective against most penicillin-resistant staphylococci.

Following intramammary infusion of 200 mgm of sodium cephapirin at 12-hour intervals for two treatments, bactericidal levels of the antibiotic (above 0.1 mcg/ml) are present in the milk for 36-48 hours. Trace amounts are detectable for longer

periods and a 96-hour milk withholding time had been established for this product.

The drug is excreted in the urine and detectable amounts can be found in urine from treated cows for 24-48 hours following the last infusion of 200 mgm.

Cows treated with 200 mgm Sodium Cephapirin Intramammary Infusion b.i.d. for two treatments showed no signs of irritation to other investigators and none were observed in this study.

Like penicillins, cephalosporins have the potential of producing allergic reactions, however these are extremely rare. Sodium cephapirin should be administered cautiously to any subject known to be allergic, especially to penicillin.

Methods

The following experimental design for this study was strictly followed:

1. Duplicate individual milk samples from each quarter of each cow in the herd were collected on June 26, 1973, cultured and pathogens and abnormal secretions recorded.
2. At the same time, an evaluation of the leucocyte count in milk from each quarter was made by direct somatic cell count.
3. Each milking cow in the herd was randomly assigned to either Group I or Group II, so that two groups of approximately equal number resulted.
4. All quarters of 42 cows in Group I were treated at consecutive milkings for two treatments on June 26. The 96-hour milk withholding period was strictly observed. Cows in Group II were not treated at this time.
5. On July 17, 1973, twenty days following the last treatment of Group I, duplicate quarter milk samples were collected from both groups, cultured, pathogens and abnormal secretions recorded. Cell counts of all quarters of Group I were estimated by direct somatic cell count. This served as:
 - a. Post treatment cultures for Group I
 - b. Pre-treatment cultures for Group II
6. All quarters of 48 cows in Group II were treated on July 17 in the same manner as Group I on June 26.
7. On August 7, twenty days after the last treatment, duplicate samples from all quarters of Group II were collected and cultured. Abnormal secretions were recorded and cell counts were estimated by direct somatic cell count.

Culture Methods

One hundredth ml. of milk from each quarter sample was streaked with a sterile loop on a quadrant of esculin agar with 5% bovine blood 3 mm. deep in a 100 x 15 mm. plate in a pattern that does not overlap quarters. Plates were inverted and incubated at 37.5°C. for 24 and 48 hours when colony growth was examined and recorded. Pathogens were recorded under four classifications:

- a. *Streptococcus agalactiae*
- b. *Streptococcus* species (other than *S. agalactiae*)
- c. Hemolytic staphylococcus and *Micrococcus*

Staphylococcus aureus

Staphylococcus species

- d. Miscellaneous (Enterobacteriaceae, Pseudomonas, Corynebacterium, Pasteurella, Nocardia, Yeasts, Molds and less common mastitis causing organisms)

Special procedures for further bacterial identification were begun at 24 or 48 hour reading periods as necessary.

All hemolytic staphylococcus infections were tested for antibiotic susceptibility by the Kirby-Bauer method. This was done both pre-treatment and post-treatment. Each isolation was tested for susceptibility to the following antibiotics: Penicillin, Dihydrostreptomycin, Neomycin, Cloxacillin, DiCloxacillin, Lincomycin, Tetracycline, Furacin, Cephalothis (Cephalosporin), Kanamycin, Ampicillin, Erythromycin.

The antibiograms thus produced were used:

1. To determine the susceptibility of staphylococci to the test drug.
2. To identify those strains which were penicillin-resistant.
3. To assist in distinguishing new infections post treatment from original pre-treatment infections by comparing the susceptibility to the various antibiotics.

Untreated cows in Group II of 6/26 were resampled in 20 days. Bacteriological results were compared with original samples for apparent spontaneous recovery, as none of these cows received treatment of any kind during that period.

Table 2
Apparent Spontaneous Cure Rate

Organism	Infected Quarters	Recovered	% Cure
Str. agalactiae	77	7	9
Hemolytic staph	24	6	25
Streps - other other species	18	5	29

Table 3
Treatment Results - Group I: 42 Cows

Organism	Pre-Treatment		Post-Treatment		Cure Rate Qtrs. %
	Cows	Qtrs.	Cows	Qtrs.	
Str. Agalactiae	27	60	0	0	100
Hemolytic Staph	13	18	3	3	83
Streps - Other species	8	9	2	2	78
Negative	5		29		

Six cows harboring pathogens in one or more quarters were treated in Group II, but were dry and at pasture, unable to be sampled post treatment. These cows do not appear in any of the above figures.

The leucocyte count of the blended herd milk in the bulk tank on the date of pre-treatment sampling

Table 4
Treatment Results - Group II: 48 Cows

Organism	Pre-Treatment		Post-Treatment		Cure Rate Qtrs. %
	Cows	Qtrs.	Cows	Qtrs.	
Str. Agalactiae	36	85	0	0	100
Hemolytic Staph	26	37	6	6	84
Streps - Other species	20	28	5	6	79
Negative	5		24		

Table 5
Treatment Results - Total Herd: 90 Cows

Organism	Pre-Treatment		Post-Treatment		Cure Rate Qtrs. %
	Cows	Qtrs.	Cows	Qtrs.	
Str. Agalactiae	63	145	0	0	100
Hemolytic Staph	39	55	9	9	83.6
Streps - Other species	28	37	7	8	78.4
Negative	10		53		

6/26/73 was 1,277,040/ml. At the time of post treatment sampling of Group II, 8/7/73, the leucocyte count was 805,292/ml, using the direct microscopic somatic cell count.

Leucocyte counts were done on all quarters pre-treatment and post-treatment using the direct microscopic cell count, and recorded as CMT reaction. The decrease in average CMT reaction/quarter was from 1.80 pre-treatment to 0.61 (trace) post-treatment.

On 6/15/74 all quarters of a 23 cow dairy were treated with sodium cephalosporin twice at 12-hour intervals following a routine mastitis survey revealing a high infection rate and high leucocyte count.

Table 6
Treatment Results - Reid Herd: 23 Cows

Organism	Quarters	Quarters	Cure Rate
	Pre-Treatment	Post-Treatment	
Str. Agalactiae	41	0	100%
Hemolytic Staph	14	1	93%
Streps - Other species	8	1	88%
Negative Cows	1	16	
Leucocytes	1,842,912/ml	373,248/ml	

Discussion

The opportunity to blitz treat a dairy of 96 cows heavily infected with chronic streptococcus and staphylococcus mastitis pathogens with two intramammary infusions of 200 mgm. of sodium cephalosporin at 12-hour intervals resulted in cure rates of 100% for *Streptococcus agalactiae* infected quarters, 83.6% for hemolytic staphylococcus, and 78.4% for other streptococcus species. Cures were determined by disappearance of the pathogen, apparent return of milk to normal, and decrease in leucocyte counts. The study was closely controlled, no concomitant treatment was administered to any cows during this period. No evidence of drug induced irritation was observed by the clinical investigator or the dairyman. All quarters treated would be considered sub-clinical, chronic, or an acute flare-up of a chronic infection. No acute or peracute mastitis was observed at treatment time.

Considering the frequency with which dairies with similar mastitis problems are encountered, and the results noted following therapy with intramammary sodium cephalosporin, the drug would appear to be a useful, safe and highly effective preparation.

Additional information produced by this study using the Kirby-Bauer sensitivity test indicates penicillin resistant hemolytic staphylococcus infected quarters had a recovery rate of 18 of 21 quarters, or 85.7%, penicillin sensitive hemolytic staphylococci had recovery rate of 29 of 33 quarters, or 87.9%, when treated with sodium cephalosporin.

It is of interest to note that these data also indicate an incidence of penicillin-resistant hemolytic staphylococci of 38.8%.

Summary

A new broad spectrum antibiotic in an intramammary infusion was used in commercial dairy herds in New York State with a history of chronic clinical and subclinical mastitis. Laboratory facilities were used to furnish pre-treatment and post-treatment bacteriology and leucocyte counts on all quarters of all cows.

The cure rate in cows following intramammary infusion of a cephalosporin is recorded in the return of milk to normal on visual examination, by the disappearance of the pathogen, and the reduction of leucocyte counts in milk from infected quarters and the herd bulk milk sample.

The rate of cure was impressively high in these heavily infected herds.