J. Dairy Sci. 100:1–12
https://doi.org/10.3168/jds.2016-11614

Clinical outcome comparison of immediate blanket treatment versus a delayed pathogen-based treatment protocol for clinical mastitis in a New York dairy herd

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ABSTRACT

The purpose was to compare immediate intramammary antimicrobial treatment of all cases of clinical mastitis with a selective treatment protocol based on 24-h culture results. The study was conducted at a 3,500-cow commercial farm in New York. Using a randomized design, mild to moderate clinical mastitis cases were assigned to either the blanket therapy or pathogen-based therapy group. Cows in the blanket therapy group received immediate on-label intramammary treatment with ceftiofur hydrochloride for 5 d. Upon receipt of 24 h culture results, cows in the pathogen-based group followed a protocol automatically assigned via Dairy Comp 305 (Valley Agricultural Software, Tulare, CA): *Staphylococcus* spp., *Streptococcus* spp., or *Enterococcus* spp. were administered on-label intramammary treatment with cephapirin sodium for 1 d. Others, including cows with no-growth or gram-negative results, received no treatment. A total of 725 cases of clinical mastitis were observed; 114 cows were not enrolled due to severity. An additional 122 cases did not meet inclusion criteria. Distribution of treatments for the 489 qualifying events was equal between groups (pathogen-based, n = 246; blanket, n = 243). The proportions of cases assigned to the blanket and pathogen-based groups that received intramammary therapy were 100 and 32%, respectively. No significant differences existed between blanket therapy and pathogen-based therapy in days to clinical cure; means were 4.8 and 4.5 d, respectively. The difference in post-event milk production between groups was not statistically significant (blanket therapy = 34.7 kg; pathogen-based = 35.4 kg). No differences were observed in test-day linear scores between groups; least squares means of linear scores was 4.3 for pathogen-based cows and 4.2 for blanket therapy cows. Odds of survival 30 d postenrollment was similar between groups (odds ratio of pathogen-based = 1.6; 95% confidence interval: 0.7–3.7) as was odds of survival to 60 d (odds ratio = 1.4; 95% confidence interval: 0.7–2.6). The one significant difference found for the effect of treatment was in hospital days; pathogen-based cows experienced, on average, 3 fewer days than blanket therapy cows. A majority (68.5%) of moderate and mild clinical cases would not have been treated if all cows on this trial were enrolled in a pathogen-based protocol. The use of a strategic treatment protocol based on 24-h postmastitis pathogen results has potential to efficiently reduce antimicrobial use.
Key words: clinical mastitis, cephapirin, ceftiofur, no treatment

INTRODUCTION

Clinical mastitis (**CM**) is defined by visible signs of inflammation in an affected mammary gland such as redness, swelling, pain, or heat, and alterations such as clots, flakes, discoloration, or abnormal consistency of secretions. Clinical mastitis has a high incidence on North American dairy farms, ranging from 20 to 51% of cows (Sargeant et al., 1998; Olde Riekerink et al., 2008). This disease can create severe economic losses due to discarded milk, reduced production, decreased conception, premature culling, transmission to other cattle, and treatment costs (Fetrow, 2000; Hertl et al., 2014). The current practice on many farms is treatment of all CM cases or "blanket treatment" with intramammary (**IMM**) antimicrobials. In a previous Wisconsin study, 80% of all antimicrobial drugs used on dairies were used for treatment or prevention of mastitis (Pol and Ruegg, 2007a). Problems attributed to the use of antimicrobials in animals include potential drug residues in the food supply, possible development of antimicrobial resistance, and monetary losses associated with treatment and discarded milk (Owens et al., 1997; Barton, 2000).

Received June 14, 2016.
Accepted December 7, 2016.
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A recent economic deterministic approach estimated financial losses for CM during the first 30 d of lactation at $444 per case, accounting for diagnostics, antimicrobial costs, nonsalable milk, veterinary costs, milk and reproductive losses, and replacement costs (Rollin et al., 2015). Pathogen-specific treatment may be preferential in an economic model as it has the ability to decrease the use of antimicrobials, leading to reduced risks of residues and lower treatment and milk-discard costs (Schukken et al., 2011; MacDonald et al., 2011).

Targeted therapy of CM using on-farm culture results or other accurate diagnostic tools can replace the routine use of broad-spectrum antimicrobials, replacing the dated practice of treating without diagnosis (Hogeveen et al., 2011). Selective treatment of CM is defined as the use of antimicrobials only for cases that may benefit from them; outcomes regarding antimicrobial usage in specific pathogen groups have been studied in depth. Differences in cure rates between etiological bacteria may be attributed to the targeting of components of bacterial cell walls (Pyörälä et al., 1994). This proves difficult in gram-negative bacteria due to their complex additional lipopolysaccharide layer, likely reflected in the failure of efficacy for antimicrobial products in induced coliform mastitis trials (Lago et al., 2014). Where antimicrobials are not used, 85% spontaneous bacteriological cure rates for experimentally induced gram-negative *Escherichia coli* have been observed by d 7 (Leininger et al., 2003). Furthermore, 30% or greater of CM cases exhibit culture-negative outcomes when sampled, for which the use of antimicrobials can be difficult to justify (Lago et al., 2011a; Oliveira and Ruegg, 2014).

Contrary to gram-negative CM, many IMM products are labeled for the treatment of gram-positive bacteria. Aggressive IMM treatment of clinical and subclinical cows infected with CNS and experimentally induced cases of environmental *Streptococcus uberis*, for example, is often successful with some cure rates exceeding 90% (Hillerton and Kliem, 2002; Oliver et al., 2004). Alternatively, the spontaneous cure rate for CM caused by environmental *Streptococcus* spp. may exceed 50%, but these cows can suffer frequent relapses (Morin et al., 1998).

Subsequent to the publication of studies analyzing "gram-specific" treatment response, farms gravitated toward a "treat or no-treat" system: gram-positive environmental pathogens were treated with IMM antimicrobials and gram-negative and no-growth culture cows remained untreated. No significant differences were seen in probability of bacteriological cure of a culture-based system versus blanket therapy when such a protocol was employed (Keefe et al., 2010). Likewise, Lago et al. (2011a,b) showed no significant differences between blanket treatment and selective treatment groups in CM recurrence, days to clinical cure, bacteriological cure risk, treatment failure risk, SCC, culling, or milk production when 24-h culture results were used to make treatment decisions on 8 commercial farms.

Antimicrobial products currently available for IMM use not only have varying label claims that include effectiveness against gram-negative organisms, but also have diverse durations of use, formulations, and withdrawal periods, making it difficult to determine whether a treat or no-treat regimen is beneficial. Cephapirin sodium, a first generation cephalosporin, was recently described as noninferior to ceftiofur hydrochloride, a third generation cephalosporin, when considering bacteriological cure of gram-positive etiologies and clinical cure of all CM cases (Schukken et al., 2013). Results of this study led to speculation of how cephapirin would perform in a treat or no-treat pathogen-based system, as treatment time would result in 3 less antimicrobial treatments and 4 less treatment days per cow as compared with the more widely used ceftiofur: a Wisconsin survey of 51 dairies found of the cows receiving only IMM treatment for CM, 74.9% received ceftiofur and 13.7% received cephapirin (Oliveira and Ruegg, 2014). Economic benefits could be realized with a reduction in treatment time, duration, and product cost. The current trial is not a comparison of 2 different antimicrobials. Our objective, rather, was to determine if a protocol based on culture results, specifically treating gram-positives with cephapirin, offered similar outcomes to treating all cows with ceftiofur. To compare, we investigated differences in days to clinical cure, milk production, linear score (**LS**), risk of culling post-CM event, and hospital days. Our hypothesis is that a pathogen-driven treatment protocol, as used in the current trial, may not only decrease the use of antimicrobials and protect aspects of public health, but also create economic benefits for the farm.

MATERIALS AND METHODS

Study Animals

Clinical mastitis cases were assessed for inclusion at a 3,500 Holstein cow commercial dairy in central New York between December 2014 and April 2015 under Institutional Animal Care and Use Committee approval. This farm was chosen due to its large herd size, a monthly incidence of 5 to 6% CM, availability of reliable health records, consultation opportunity with management and veterinarians, and access to microbiological diagnosis of milk samples within 24 h of collection. This farm used DHIA services, which included monthly SCC and milk weights. Health records included treatment,