

TREATMENT OF SUBCLINICAL MASTITIS

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INTRODUCTION

Mastitis can occur in both a clinical and subclinical form. Clinical mastitis is readily apparent and easily detected by abnormalities in milk or the udder or the occurrence of secondary clinical signs. Treatment decisions for clinical mastitis are generally motivated by a desire to return milk to a saleable state. Detection of subclinical mastitis is more difficult because clinical signs are not apparent and use of indirect tests (such as enumeration of somatic cells or bacteriological analysis of milk samples) is required for detection. Consequently, subclinical mastitis is often undetected and has the greatest economic consequences because of long term effects on milk yields. With the exception of infections caused by *Streptococcus agalactiae*, treatment of cows diagnosed with subclinical mastitis is usually discouraged because discard of saleable milk results in financial loss. However, presence of cows with subclinical mastitis within the herd has some potentially negative unintended consequences. Cows infected with subclinical mastitis have greater somatic cell counts (SCC) and the farmer may be paid less for the milk. Approximately 25-30% of cows with chronic cases of subclinical mastitis may exhibit clinical symptoms that require antibiotic treatments and withholding of milk (Barlow et al., 2009). The failure to treat subclinical mastitis may result in chronic infections that are unlikely to respond to antibiotic therapy. Cows with subclinical mastitis maintain a reservoir of infection within the herd and increase exposure of healthy cows to contagious pathogens. Finally, cows with subclinical mastitis infections are known to produce less milk (Hortet and Seegers, 1998). Cows that maintain subclinical mastitis across the dry period (SCC > 200,000 cells/ml at the last test of the completed lactation and first test of the subsequent lactation) have been shown to produce 9.1 kgs (20 lbs) less milk at their first test (Pantoja, 2008). In spite of these potentially negative effects, few mastitis experts advocate treatment of subclinical mastitis during lactation. The objective of this paper is to review recent research examining the efficacy and cost effectiveness of treatment of subclinical mastitis during lactation.

IDENTIFICATION AND DIAGNOSIS OF SUBCLINICAL MASTITIS

Identification of infected quarters and a provisional diagnosis of the most common pathogens is the first step toward making a treatment decision. When control has not been successful, contagious pathogens (*Staph aureus* & *Strep ag*) are usually most prevalent but many other pathogens such as Streptococci and some Gram-negative organisms such as *Klebsiella* spp. can cause subclinical mastitis. When herds have controlled *Staph aureus* and *Strep ag*, most subclinical mastitis is caused by host adapted, Gram-positive opportunistic pathogens that initiate a moderate to severe inflammatory response. However, the SCC responses of quarters subclinically infected with Gram-negative pathogens can be similar to SCC responses of quarters infected with *Staph aureus* or *Strep* spp..

By definition, milk from subclinically infected quarters appears normal, even when millions of somatic cells are present. Detection of subclinical mastitis is dependent on use of screening tests (such as the CMT) or monthly SCC testing. The ability of these tests to predict the recovery of bacteria from milk samples is fair at best. A quarter SCC threshold of >200,000 cells/ml is generally considered to be evidence of subclinical mastitis. In herds that have not controlled *Staph aureus* or *Strep ag*, about 10-25% of quarters above that threshold will be bacteriologically negative and about the same proportion of quarters below the threshold may be bacteriologically positive (Schepers et al., 1997). When contagious pathogens have been controlled, the rate of "false negatives" (inability to recover bacteria from quarters that exceed the threshold) is even greater. In data obtained from the University of Wisconsin dairy herd, the rate of false negatives increased from 14-70% as the threshold SCC increased from 50,000 to 300,000 cells/ml (Pantoja, 2008). When using monthly SCC data to identify potentially infected cows, it is important to recognize that the positive predictive value (PPV) of that data is relatively poor for most modern dairy herds that have moderate prevalence of subclinical infections. In recent research, the PPV (defined as the probability of recovering mastitis pathogens from milk samples when the first test SCC was > 200,000 cells/ml) was only 41% (Pantoja, 2008). In contrast, the negative predictive value (NPV; defined as the probability of NOT recovering mastitis pathogens from milk samples when the first test SCC was < 200,000 cells/ml) was 85%. This indicates the need to educate clients that most milk samples used to determine mastitis pathogens (or results of treatments) are likely to be negative and results of single milk samples should not be overinterpreted relative to infection status nor treatment efficacy. When initiating a

treatment program for subclinical mastitis, it is important to perform culturing of enough quarter milk samples to arrive at a diagnosis of the likely pathogen and also to select a well defined detection plan for identification of quarters that are candidates for treatment.

EFFICACY OF INTRAMAMMARY TREATMENTS

The use of intramammary antibiotics to treat cows subclinically infected with *Strep agalactiae* is usually successful and results in increased production and dramatic decreases in bulk tank SCC. In contrast, it is not considered cost-effective to treat most cows that are chronically infected with *Staph aureus* because cure rates during lactation are generally quite poor. The difference in these therapeutic outcomes is thought to be related to differences in the site of infection. Some pathogens (*Strep ag*, CNS, *E.coli* etc.) infect superficial surfaces (such as the epithelial surface of the ducts). Other pathogens (*Staph aureus*, *Strep uberis* etc.) are invasive and it is more difficult to achieve a therapeutic concentration of antimicrobial at the site of infection. The spontaneous cure rates for many mastitis pathogens that cause superficial infection are quite acceptable. In a clinical trial for subclinical infections caused by CNS, we observed bacteriological cure rates of 66% for untreated control quarters (n =71) versus 71% for quarters that received 2 intramammary treatments using pirlimycin (n = 59 quarters) (Apparao et al, 2009). Bacteriological cure rates after antimicrobial treatment are often monitored and may appear acceptable but other clinical outcomes such as recurrence, SCC response, retention within the herd and milk production may be much more relevant (Pínzon-Sánchez, C., and P.L. Ruegg. 2011). A randomized, controlled clinical trial examined short and long term effects of intramammary therapy of subclinical mastitis (Sandgren et al., 2007). Milk samples were obtained from cows with monthly SCC values of >300,000 cells/ml and cows from which *S. aureus* (n = 48), *Str. dysgalactiae* (n = 43) or *Str. Uberis* (n = 35) were isolated were enrolled in the study. Bacteriological cure rates were determined using milk samples collected at 42-52 days after treatment and SCC, milk yield, occurrence of a clinical case and culling were monitored for 10 months after treatment. Bacteriological cure rates were 25%, 74% and 60% for infections caused by *Staph aureus*, *Strep dysgalactiae* and *Strep uberis*, respectively. While treatment with antimicrobial compounds initially appeared to improve outcomes, the effect of treatment disappeared as the lactation progressed. As previously reported (Deluyker et al., 2005, Pínzon-Sánchez, C., and P.L. Ruegg. 2011), the impact of treatment was significantly affected by a number of cow related risk factors. Cure rates were less for older cows, infections caused by *Staph aureus* and for cows with greater SCC before treatment. Overall, the authors concluded that beneficial long-term effects of antimicrobial treatment during lactation were not observed for these pathogens. Treatment of subclinical infections also increases the pool of quarters that are susceptible to reinfection (Barlow et al., 2009). It is important to recognize that after treatment for mastitis, the recovered quarters have greater susceptibility as compared to naïve quarters (Zadoks, et al., 2001; Pantoja et al., 2009).

COST EFFECTIVENESS OF TREATMENT

The cost effectiveness of treatment during lactation is driven by the interaction between the value of discarded milk and the potential benefits of treatment. If there is a positive production response to treatment then potential benefits of treatment are more evident. Except for *Strep ag*, very little data that documents significant production responses after lactational therapy of subclinical mastitis is available. A recent study modeled the economic benefits of treatment (3 or 8 days) of subclinical mastitis caused by *Staph aureus* (Swinkels et al., 2005). The researchers created a partial budget that included reduced costs for prevention of clinical mastitis, prevention of new subclinical infections and prevention of culling. Reduced revenues included discarded milk and extra costs associated with treatment and milk cultures. No additional revenue from milk was included. Results were presented for 2 herd scenarios: 1) low probability of contagious transmission (each infected cow infected 0.3 other cows) or 2) high probability of transmission (each infected cow infected 5 other cows). When the probability of transmission was high, the net profit was about \$140 and \$210 USD for 3 day and 8 day treatments, respectively. When the probability of transmission was low, treatment resulted in net losses of \$30-\$85. Importantly, the authors identified that economic benefits of treatment of subclinical mastitis are dependent on the cost of discarded milk and host, pathogen and management factors that influence the probability of cure.

In low transmission herds, when the probability of cure was high (about 60%), 3 days of treatment was barely profitable. As reported by Sol et al.(1997) cure rates for mastitis caused by *Staph aureus* have been shown to decrease with age (from 81 % for cows \leq 48 months of age to 55% for cows \geq 96 months),

the number of infected quarters (from 73% for 1 infected quarter to 56% for 4 infected quarters) and increasing SCC. In herds with low transmission, only treatment of 1st or 2nd parity cows in early lactation (<100 days in milk) with SCC < 1,000,000 cells/ml and single quarter infections were found to be profitable. The authors concluded that treatment of subclinical mastitis may be justified during lactation depending on factors specific to the herd, the cows and the particular strain of Staph aureus. It is also important to note that this research reinforces the importance of emphasizing management practices that reduce transmission among cows.

A second study by the same group was conducted to evaluate economic effects of treatment of chronic subclinical mastitis caused by Strep uberis (Steenefeld et al., 2007). This study examined the impact of the probability of cure, probability of becoming clinical, transmission to other cows and various physiological effects of mastitis. Overall, the cost of treatment was about \$180 USD as compared to the costs of about \$160 USD if cases were not treated. However, there were important herd and cow level factors that influenced costs and the authors concluded that treatment decisions should be made on an individual cow basis.

Two other recent simulation models, concluded that treatment of some cases of subclinical mastitis during lactation would be cost effective because of the reduced cost of clinical cases that often occur in cows with chronic subclinical infections (Barlow et al., 2009, van den Borne, et al, 2010). Both of these studies modeled herds with significant prevalences of subclinical infections caused by Staph aureus. Both studies also concluded that treatment of subclinical infections during lactation will not be cost effective unless the herds simultaneously implement effective programs that reduce transmission.

TREATMENT OF SUBCLINICAL INFECTIONS IN THE POST-PARTUM PERIOD

The use of CMT or other screening tools to identify infected quarters post-calving and administer antibiotic treatments has been advocated ("Fresh-start" programs). Initial research efforts have not indicated that the strategy of treating high SCC quarters in the immediate post-partum period results in reduced prevalence of subclinical mastitis nor increased milk yield (Wallace et al., 2004). One recent study evaluated the use of CMT combined with on-farm culture results used at 1-4 days postpartum to identify quarters for treatment using IMM cephalosporin (Lago, et al., 2011). Of 1,885 cows on 14 herds, 717 cows (38%) had at least 1 CMT positive quarter. Of CMT + quarters, 58% were culture negative, 2% were Gram negative and 38% were Gram positive (primarily CNS). Cows with CMT + quarters were randomly assigned to a negative control, treatment based on CMT results or a culture based treatment group whereby only quarters with Gram + results were treated. Outcomes indicated that bacteriological cures were improved by treatment but there was no impact on clinical outcomes such as new IMI, nor incidence of clinical cases, culling or intramammary infection. The failure to demonstrate efficacy of this postpartum treatments is probably related to the high prevalence of infections caused by minor pathogens, the high rate of spontaneous cure that occurs in early lactation and the inability of SCC values to differentiate truly infected quarters before at least day 5 post-calving. The SCC of many healthy quarters are increased during the first week post-calving. In unpublished data, we collected quarter milk samples from cows (n = 200) during the first week post-calving. We performed cultures and CMT tests and determined the SCC of duplicate quarter milk samples. For both healthy and infected quarters, there was a strong correlation between the day of sampling and the results of diagnostic testing for both SCC and bacteria. This and other data suggest that when CMT is used in the postpartum period, only the occurrence of very strongly positive reactions (3+) should be used to identify potentially infected quarters. Our research indicates that quarters that have increased SCC both before and after calving ("chronic") have 3 times the high risk of developing clinical mastitis in the first 120 days of the current lactation (Pantoja et al., 2009). Based on this research, a more effective post-calving strategy may be to record quarter level SCC (or CMT) values before dry off, and again post-calving (day 5-7). While the research has not been performed yet, administration of intramammary antibiotics to quarters that have maintained high SCC across those periods may be a more appropriate & cost effective strategy.

RECOMMENDATIONS

Subclinical mastitis is caused by a variety of mostly Gram-positive bacteria and many of these cases have a high rate of spontaneous cure. Many subclinical pathogens are responsive to intramammary treatments using commercially available antibiotic products but there are important cow & herd factors

that will influence the cost effectiveness of treatment. The decision to treat subclinical mastitis is dependent upon the type of pathogens that are prevalent and diagnostic efforts (milk culturing) must be undertaken before developing a treatment protocol. When *Staph aureus* is prevalent, treatment of subclinical cases is only advised for animals that have a high probability of cure. If environmental streptococci are common, treatments of chronic infections of cows diagnosed before 100 days in milk may be cost effective. In all instances, the value of the discarded milk must be taken into account and treatment of some subclinical cases of mastitis may be cost effective for herds with alternative uses of discarded milk (for example, pasteurizing and feeding to calves). Overall, treatment is an important aspect of mastitis control but implementation of management practices that reduce transmission of subclinical pathogens are always more cost effective.

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