Should You Treat Them or Should You Eat Them? How to Improve Mastitis Treatments

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Take Home Messages

- Most cases of clinical mastitis have similar mild or moderate symptoms even though they may be caused by different types of bacteria.
- Cure rates for mastitis are highly associated with the type of bacteria that has caused the infection and farmers should routinely culture cases to guide or adjust treatment decisions.
- Cows with a history of previous clinical or subclinical mastitis, cows in early lactation, cows that are in >3rd lactation and cows with other existing diseases may not respond as well to routine mastitis treatments as compared to cows without those characteristics.
- Extended duration intramammary therapy (more than 2-3 days of treatment) should not be used for all cases of mastitis but should be reserved for cases caused by pathogens that infect deep in the udder tissue.

Introduction

Control of mastitis caused by *Streptococcus agalactiae* and *Staphylococcus aureus* has resulted in reductions in bulk tank somatic cell count (SCC) but many herds continue to struggle with treatment of clinical mastitis caused by environmental pathogens. Common environmental mastitis pathogens include both Gram negative bacteria (such as *E. coli* and *Klebsiella spp*.) and Gram positive bacteria (such as *Streptococcus uberis* and *Streptococcus dysgalactiae*). The duration of infection is associated with the degree of host adaptation of the pathogen. Some environmental pathogens (such as most *E. coli*), are truly opportunistic and the immune response successfully eliminates them after a brief period of mild clinical disease. Other environmental pathogens (such as *Streptococci spp*) have become more host adapted and may present as mild clinical cases that erroneously appear to resolve when the case has actually returned to a subclinical state. Both of

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these scenarios make it very difficult to determine if a treatment has been successful. Research demonstrates that the majority of clinical mastitis cases are mild to moderate in severity. The purpose of this paper is to review research based principles that can help improve treatment of mild and moderate cases of clinical mastitis.

■ Determining Relevant Outcomes of Mastitis Therapy

The practical goal of most mastitis treatments is to rapidly produce a reduction in clinical symptoms, eventually reduce SCC, prevent recurrence of additional clinical cases and maintain expected milk yield. Interpretation of treatment outcomes can be confusing because most cases of mastitis caused by mastitis pathogens present with mild or moderate clinical signs (Table 1). When cows present with mild cases of mastitis, clinical signs will normally abate within 4-6 days, regardless of treatment. However, disappearance of clinical signs does not always indicate that the infection has been successfully treated. While the milk may appear visually normal, many of these cases may have simply regressed to a subclinical state and maintain increased SCC. This occurrence is especially true for Gram positive pathogens.

Table 1. Summary of recent studies on distribution of pathogens causing clinical mastitis

Study	Number of Cases	*Strep ag* or *Staph aureus*	CNS	Env. Strep	Coliform	Other	No growth
Oliveira & Ruegg, 2011[a]	788 cases; 151 herds	4%	7%	13%	30%	16%	31%
Pinzon-Sanchez & Ruegg, 2011	207 cases; 4 herds	2%	3%	18%	26%	9%	42%
Olde Riekerink, 2008 (Canada)	2850 cases; 106 herds	11%	6%	16%	14%	7%	46%
Lago et al., 2011a & b	421 cases; 8 herds	6%	10%	16%	25%	10%	32%

[a]not yet published

Bacteriological cure rates are generally used in research studies as the primary indicator of treatment efficacy but few farmers evaluate bacterial clearance of pathogens from affected glands. The ability to achieve a bacteriological cure depends on the pathogen, case severity, variation in immune response among cows, efficacy of the treatment protocol and the promptness of initiating treatment. In one study, bacteriological cure was 7 times more likely for first cases of mastitis as compared to recurrent cases (Pinzon-Sanchez et al., 2011). Laboratory issues such as the frequency of sampling, the volume of milk that is inoculated, the time period after therapy until sampling and time between collection of consecutive samples all contribute to the wide variation in bacteriological cure rates noted in the literature (Ruegg, 2010). Therefore, assessment of bacteriological cure is not routinely used as an indicator of success in the field.

On a practical basis, clinical success is often based on indicators such as recurrence of clinical mastitis, reduction in SCC, return of milk yield to normal, retention of the cow within the herd and number of days milk is discarded. Recurrence of another case of clinical mastitis is one of the least desirable outcomes after treatment and is much more likely for cases that are early in lactation as compared to cases that occur later (Figure 1; Pinzon-Sanchez and Ruegg, 2011). This may indicate the need for more aggressive treatment protocols (for example, longer duration therapy) for cows experiencing mastitis in early lactation as compared to treatments for cases that occur later.

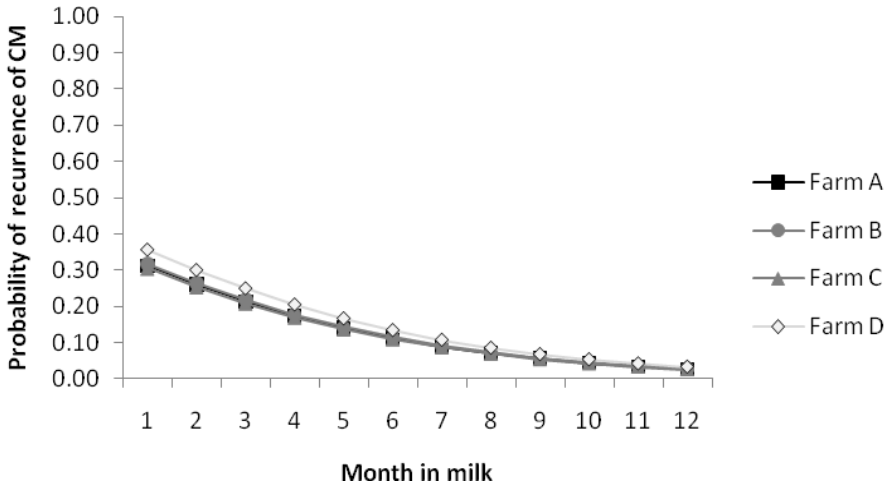

Figure 1. Recurrence of clinical mastitis (CM) by stage of lactation

Somatic cell reduction below 200,000 cells / mL is another desired outcome after treating mild and moderate cases of clinical mastitis but occurs slowly

and this outcome is highly influenced by pathogen. Pinzon-Sanchez and Ruegg (2011) reported that 63% of cases caused by Gram-negative pathogens or no growth resulted in somatic cell reductions to less than 200,000 cell/mL within 21-55 days after treatment in contrast to only 44% of cases caused by Gram-positive bacteria. While long-term SCC reductions should occur after successful therapy, short-term changes in SCC should not be used to determine when to stop therapy nor to determine if therapy has been effective.

■ Cow Factors Influencing Treatment Outcomes.

Age of Cow

Older cattle have a greater risk of developing clinical mastitis and several studies have indicated that older cattle have poorer responses to treatment as compared to younger cattle. Deluyker et al., (1999) used a rigorous definition of clinical cure (normal milk by 5 d and no relapse within 3 weeks post-treatment) and reported a reduction in combined "clinical & bacteriological cure rates" from 39% (lactation 1) to 26-30% for older cattle. Other researchers have also reported that bacteriological cure after mastitis therapy was less likely for older cows (Sol et al., 2000; McDougall et al., 2007a, b). Age has also been associated with reduced clinical responses to therapy. Hektoen et al. (2004) measured responses to treatment by comparing scores for both acute and chronic symptoms obtained before treatment and at various periods post-treatment. While number of lactations (cow age) was not associated with differences in acute symptoms, the reduction in chronic symptoms (changes in the milk, gland or inflammatory response) was markedly greater in first lactation as compared to older cattle. The effect of number of lactations should be considered before beginning mastitis treatments. For example, extended duration therapy may be appropriate for treatment of some mastitis cases occurring in older cows. Likewise, older cows (>3 lactation) may not be considered as good candidates for withholding treatment if that option is used for managing some types of mastitis on particular farms.

Differences among Pathogens

It is well known that mastitis is caused by a diverse group of bacteria (Table 1) and the probability of cure is highly influenced by characteristics of the pathogen. Cure rates for several mastitis pathogens (Serratia, yeasts, pseudomonas, mycoplasma, prototheca etc.) are essentially zero, regardless of treatment. Combining data from 2 equally efficacious treatments, McDougall et al. (2007a or b?) noted the following typical differences in bacteriological cure based on type of pathogen: *Strep uberis* (89%, n = 488

cases); *Strep dysgalactiae* (69%, n = 32 cases), *Staph aureus* (33%, n = 40 cases), and CNS (85%, n = 71).

On farms that have controlled contagious mastitis, approximately 25-40% of clinical cases are microbiologically negative before treatment (Table 1). Clinical and spontaneous cure rates for these "no-growth" samples are often very high with or without treatment (Guterbock et al., 1993; Morin et al., 1998). For example, Hektoen et al. (2004) noted that both acute symptoms and long term responses were significantly improved for mastitis cases which were microbiologically negative as compared to cases from which *Staph aureus* or other bacteria were isolated. In contrast, mastitis caused by environmental Streptococci typically responds well to intramammary (IMM) antimicrobial therapy but has a low spontaneous cure rate and a high rate of recurrence when antimicrobials are not administered (Morin et al., 1998). These differences among pathogens demonstrate that identification of pathogen considerably improves mastitis treatment protocols. With current laboratory methods, it is not feasible for all farms to culture all milk samples before beginning therapy but guiding treatment by use of on-farm culture systems has been shown to be economically beneficial (Lago et al., 2011a, b). Even if a diagnosis is not immediately available, farmers can submit milk samples to laboratories for rapid provisional diagnosis and then readjust therapy when the pathogen is diagnosed 24-48 hours after beginning treatment. In the future, it is likely that rapid methods will become available to guide treatments and consistent and accurate identification of pathogens before initiating therapy should result in improved therapeutic responses.

Treatment of Mastitis caused by *Staphylococcus aureus*

As compared to other mastitis pathogens, there is a much larger body of evidence upon which to base treatment decisions for *Staph aureus*. Expectations for spontaneous bacteriological cure of subclinical and clinical mastitis caused by *Staph aureus* are essentially zero (Oliver et al., 2004a&b). Most of the evidence agrees that treatment of clinical mastitis caused by chronic infections with *Staph aureus* is not rewarding and many of these cows will have periodic episodes of mild or moderate clinical mastitis. It is not considered cost-effective to treat clinical mastitis in cows that are chronically infected with *Staph aureus* because cure rates are typically <35% and in most instances, when the clinical symptoms disappear, the infection has simply returned to a subclinical state. Somewhat effective cure of cows infected with *Staph aureus* has been shown to be strongly related to duration of subclinical infection. In one study, bacteriological cure rates for chronic (> 4-weeks duration) *Staph aureus* infections were only 35% compared to 70% for newly acquired (< 2-weeks duration) infections (Owens et al., 1997) but it is important to note that these infections were induced using laboratory strains of bacteria. Treatment protocols designed for farms where *Staph aureus* infections are common should not prescribe the use of antimicrobials to treat

mild clinical cases occurring in chronically infected cows. In these instances it is more cost effective to simply isolate the cow or affected quarter, discard the milk until it returns to normal and then make a decision about culling or retaining and isolating the cow. An excellent review of factors influencing therapeutic success of mastitis caused by *Staphylococcus aureus* notes that treatment outcomes can be influenced by cow factors (age, duration of infection, SCC, etc.), pathogen factors (different strains, inherent resistance to penicillin as indicated by presence of β-lactamase) and treatment factors (duration or therapy) (Barkema, et al., 2006). Cure rates for subclinical 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 (Sol et al., 1997). Similar results have been demonstrated for clinical mastitis and bacteriological cure rates have been shown to be significantly greater if the pathogen is β-lactamase negative as compared to positive. The use of extended duration therapy has been shown to increase cure of clinical mastitis caused by *Staph aureus* and at least 5 days of therapy is recommended (Sol et al., 2000). Extended duration IMM treatment of clinical cases of *Staph aureus* may be successful for young cows in early lactation with recent single quarter infections but should not be attempted for chronically infected cows. It is also important to note, that in the best of circumstances, only about 30-50% of cows infected with *Staph aureus* will be expected to cure, thus expectations of the farmers should be appropriately lowered and preventive programs initiated to limit spread of the infection.

Duration of Therapy

Discarded milk is the greatest proportion of expense associated with treatment of clinical mastitis. In general, duration of antibiotic treatment is kept as short as possible to minimize the economic losses associated with milk discard. The appropriate duration of antibiotic treatment for clinical mastitis has not been well-defined and varies depending on the causative pathogen. There is considerable evidence that extended administration of antibiotics increases cure rates for pathogens that have the ability to invade deep into udder tissue. For example, bacteriological cure for subclinical mastitis caused by *Staph aureus* treated with IMM ceftiofur were 0 % (no treatment), 7% (2 days), 17% (5 days) and 36% (8 days; Oliver et al., 2004b). Cure rates reported for clinical mastitis caused by β-lactamase negative *Staph aureus* were significantly greater when extended duration therapy was used (50%) versus administration of 3 treatments over 36 hours (38%; Sol et al., 2000). Likewise, bacteriological cure rates for experimentally induced *Strep uberis* infections increased from 58% (2-d treatment) to 69-80% for treatments of 5 or 8 days (Oliver et al., 2003). Therefore, for mastitis caused by potentially invasive pathogens, the duration of therapy should be 5 to 8 days. However, research to support the use of extended duration therapy to

treat pathogens that infect superficial tissues (for example coagulase negative staphylococci or most *E. coli*) has not been published and the use of extended duration therapy to treat these pathogens increases costs without improving treatment outcomes (Pinzón-Sánchez et al., 2011).

■ Research about Use of Alternative Treatments for Clinical Mastitis

In the U.S., cows used for production of organic milk may not receive any antimicrobials and producers use a variety of herbal and homeopathic remedies for treatment of mastitis. Many alternative therapies have some theoretical basis for efficacy but there are almost no peer reviewed studies that demonstrate clinical efficacy. One recent review of veterinary usage of botanical and herbal remedies stated that "With few exceptions, controlled studies on the clinical effects of herbal or botanical preparations in veterinary medicine appear to be essentially nonexistent" (Ramey, 2007). While theoretical basis for efficacy may exist, no credible evidence has been published that demonstrates effectiveness of herbal compounds currently used as alternatives to antimicrobials.

Homeopathic remedies were first introduced in Germany in the era before microorganisms were identified and a few articles have specifically evaluated veterinary homeopathy. Of three published studies investigating the effect of homeopathic nosodes on mastitis outcomes, none have demonstrated efficacy (Egan, 1998; Hektoen et al., 2004; Holmes et al., 2005). Evidence that demonstrates efficacy of veterinary homeopathy is completely lacking and practitioners seeking to apply concepts of evidence-based veterinary medicine (EBVM) will not be able to support the use of these products.

■ Conclusion

Veterinarians should continue to increase their involvement in developing and implementing mastitis treatment protocols and should actively monitor outcomes of treatments that farm personnel administer. Research evidence is available to help guide mastitis treatment decisions and to better select animals that will benefit from specific treatments. There is sufficient research evidence to help practitioners develop mastitis treatment protocols that vary depending on animal characteristics and the history of subclinical disease. Research can also be used to guide decisions about duration of therapy, determine if cows affected with *Staph aureus* should be treated or culled and to make rational decisions about the use of alternative and ancillary treatments.

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