Economically Prudent Use of Antibiotics in Dairy Production: Selective Dry Cow Therapy and Pathogen-Based Treatment of Clinical Mastitis

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Introduction

Dry-cow intramammary (IMM) antimicrobials were developed in the 1950s; their use was recommended in the 1960s as part of the National Institute for Research into Dairying's 5-point plan (United Kingdom). Blanket dry cow therapy (BDCT), or the treatment of every quarter of every cow with a long-acting antimicrobial at dry-off, was instituted to combat the high rate of clinical mastitis observed within the 2-weeks post-calving (Green et al., 2002) as well as to cure existing infections at dry-off. Research groups have demonstrated that a majority of clinical mastitis cases during this time are contributed by organisms that were present at dry off or newly acquired over the dry period (Todhunter et al., 1991; Bradley and Green, 2000; Green et al., 2002). However, management and control of mastitis pathogens during the dry and lactating periods has been widely successful as indicated by the increase in negative quarter-level culture results at dry-off from 44% in 1985 to between 73% and 95% of quarters within the last decade (du Preez and Greeff, 1985; Pantoja et al., 2009; Rajala-Schultz et al., 2011). The prevalence of contagious pathogens such as *Streptococcus agalactiae* and *Staphylococcus aureus* and reduction of bulk tank somatic cell counts (BTSCC) from 295k cells/mL in 1997 to 193k cells/mL in 2014 also suggests that BDCT is not currently a necessity in all herds (Ekman and Østerås, 2003; Robert et al., 2006, USDA NAHMS, 2016a). Additionally, only 11.1% of overall test days were greater than 400k cells/mL in 2016; this compares to 30.3% of test days in 1998 (Miller and Normal, 1999; Norman et al., 2017).

Regardless of these improvements since the implementation of BDCT, over 90% of cows are treated and 90% of operations use antimicrobial products at dry-off in the USA according to a survey by the National Animal Health Monitoring System in 2014 (USDA NAHMS, 2016b). There are several reasons why a producer/management might elect to not use IMM antibiotics at dry-off: 1) economic returns via decreased labor and dry-tube costs; 2) public or government policy: for example, Nordic countries have adopted restrictions that permit only selective use of antimicrobials, leading to reductions of approximately 80% and 40% for dry-cow and clinical mastitis treatments, respectively (Ekman and Østerås, 2003); 3) the introduction of an applicator into the teat end is not risk-free (Leelahopongsathon et al., 2016); 4) alternative/adjunct products to antibiotics including teat sealants are reported to have success decreasing the risk of new infections (Godden et al., 2003; Rabiee and Lean, 2013); and 5) consequences related to public health such as accidental residues in the bulk tank or the development of antimicrobial resistance. For these reasons, selective treatment of cows at dry-off is an opportunity that is being considered by producers and veterinarians.

Selective dry cow therapy (SDCT) is the identification and treatment of only cows/quarters having an infection at dry-off or at high risk for acquiring an infection during the dry period. The clinical, health, and microbiological outcomes resulting from the use of specific strategies have been explored by research groups over the past few decades. Most practitioners and researchers wish to address the following question: "Are cows in selective treatment protocols, or cows that are not treated with dry-cow antimicrobials at higher risk for experiencing negative outcomes?" This question has been interrogated using field trials and subsequent statistical models to compare treatment groups when evaluating outcomes such as risk of clinical mastitis, bacteriological cure, new infection risk, early lactation milk production, early lactation SCC/linear score, and risk of culling.

Current Strategies

Identification of the cows or quarters that would benefit from antimicrobial treatment is the cornerstone of SDCT protocols and can be performed in several manners. The diagnostics elected for use can be performed at the quarter or cow level, and treatment decisions in regards to dry cow therapy can be made similarly. Accuracy, costs, labor, and ease of use/implementation should be considered when selecting tools to identify cows/quarters to be treated within SDCT programs. The following paragraphs describe strategies for SDCT and the respective results of field trials. The selected trials considered all mastitis pathogens in their microbiological and statistical analysis; all were published after 1990.

Use of a bulk tank SCC or single composite SCC prior to dry-off. The first studies on decreased IMM antibiotics at dry-off were performed in herds with low bulk tank somatic cell counts (BTSCC). These studies randomly assigned cows or quarters to either blanket-treatment or to no treatment; cows/quarters were not separated based on risk or infection status. This often resulted in an increased incidence rate of clinical mastitis or risk of new intramammary infections (IMIs) in cows/quarters not receiving treatment. For example, Hogan et al. (1995) performed a study on 4 US herds with BTSCC < 250k cells/mL where cows were randomized into 4 groups: antibiotic dry cow therapy, antibiotic dry cow therapy and *Propionibacterium acnes* injections (PAI), PAI only, or no treatments. A statistically higher percentage of cured quarters and lower percentage of new IMIs were found in cows that received IMM antibiotic versus those that had not (Hogan et al., 1995). However, statistical comparisons between groups that did not receive PAI were not provided. Schukken et al. (1993) performed a study on one Dutch herd with a BTCC of 140k cells/ml (50 cows) in which 2 quarters were treated and 2 quarters remained untreated within each cow. This resulted in a 10-fold increased risk of clinical mastitis, or 10 cases of clinical mastitis in uninfused quarters versus 1 case in a quarter that was infused with dry-cow antibiotics (Schukken et al., 1993). In the same trial, no statistical differences were found between groups for new infection risk or bacteriologic cure of major pathogens. Minor pathogens were reduced in quarters that were treated with antimicrobials. When treatment was performed on the cow level in a California herd (233 cows; 240k cells/mL) with a low prevalence of contagious mastitis pathogens, no statistical differences were found between groups for culling, clinical mastitis risk, or SCC in the first 120 days of the subsequent lactation, even when cows were stratified into high and low (≤500k cells/mL) SCC groups (Berry et al., 1997). Scherpenzeel et al. (2014) used a split udder design and evaluated use of an individual-cow SCC threshold rather than use of a bulk-tank threshold. Primiparous animals with SCC <150k cell/mL and multiparous animals with SCC <250k cells/mL were included; 1,657 cows had 2 quarters that were treated and 2 that were not. In the trial, the incidence of clinical mastitis was 1.7 times higher in quarters dried without antimicrobials (95% CI: 1.4-2.1). SCC was higher in

non-treated quarters and a higher percentage of the quarters were culture positive at calving and at 14 DIM.

Culture only method. The current gold standard for diagnosing an IMI is aerobic culture. However, the time, labor, and materials associated with culturing cows can be an added cost, and this diagnostic tool, when used in a SDCT protocol can identify infected cows/quarters, but will not determine cows at higher risk for acquiring infections during the dry period. The effects of culture-driven antibiotic use at dry-off were determined by Browning et al. (1990) in an Australian field trial including 1044 cows from 12 herds. Culture-negative cows were randomly allocated to receive blanket therapy or no treatment while culture-positive cows were randomly allocated to receive blanket therapy or treatment of only infected quarters. No statistical differences were detected in clinical mastitis risks between the groups within the first 5 months of lactation. No differences were found for new infection risk in the cows that were culture-negative at dry-off; however, new infection risk was 4 times higher in selectively treated culture-positive cows versus blanket treated culture-positive cows (Browning et al., 1990). Only cows infected with a major pathogen (n=608) were enrolled in a Norwegian study that assessed the effects of SDCT on culling, mastitis, milk yield and SCC (Østerås and Sandvik, 1996). Cows were randomly allocated into a placebo group, control group, or one of two IMM antibiotic treatments. Cows within the antibiotic groups only received treatments in quarters experiencing IMIs. It should be noted that quarters known to have an IMI in the placebo and control groups were not treated with antibiotics. There were 21% less cases of mastitis in antibiotic treated quarters ($P = 0.09$). Treated quarters also had lower SCC and a higher lactational milk yield. There was no effect of therapy on culling rate. Patel et al. (2017) used quarter-level treatment of culture-positive quarters in addition to internal teat sealant (1 herd, 56 cows) and described no statistical differences between BDCT and selective quarter treatment when assessing bacteriological cure and new infection risks (Patel et al., 2017).

Cow records only: SCC and/or mastitis events. Though not presented as a SDCT trial, Huxley et al. (2002) evaluated the use of a teat sealant in cows with routine composite SCC below 200k cells/mL with no previous cases of mastitis and a projected dry period of >51d. Comparisons were made between cows only receiving internal teat sealant and cows receiving only blanket antibiotic therapy. No statistical differences were found for clinical mastitis cases, new infections with minor pathogens, nor overall bacteriologic cure. While new infection risk for major pathogens was lower in antibiotic-treated cows, bacteriologic cure rates were only higher for the minor pathogens *Corynebacterium* spp. in antibiotic-treated cows (Huxley et al, 2002). Another trial evaluating internal teat sealant in the UK used a split-udder design with the same cow-level criteria. However, in this trial (Bradley et al., 2010) all quarters received the internal teat sealant product, even those treated with antibiotics. No statistical differences were described between groups of quarters for bacteriologic cure and new infection risks and no differences were found in clinical mastitis risk.

In a non-inferiority study comparison, McDougall (2010) assigned cows (~900 cows from 6 New Zealand herds) with SCC ≤ 150k and no history of clinical mastitis in the current lactation to no treatment, a novel antibiotic, or a reference antibiotic at dry-off. When analysis was performed on the quarter level, there were fewer IMIs characterized by any pathogen at freshening in antibiotic treated groups; when analysis was performed on the cow level, there was only a difference seen for major pathogens. SCC was lower in treated groups, and there was a lower hazard of clinical mastitis during the dry period and in early lactation for treated groups (McDougall, 2010). A study performed in the US by Rajala-Schultz et al. (2011) on 4 herds (~400 cows) also used computer records and mastitis events to determine which cows to enroll. Cows had to have a SCC ≤ 200k

cells/mL over the last 3 tests with no cases of mastitis in the current lactation. If the cow met the criteria but there was 1 case of mastitis, the cow had to maintain a SCC < 100k cells/mL until dry-off. Cows were then randomly assigned to receive IMM antibiotics or no treatment. No statistical differences were described for new infection risk or early lactation milk production. Overall, there was a lower SCC in the treated cows; however, when evaluated on the herd level, only 1 herd had a statistical difference between groups for this outcome (Rajala-Schultz et al., 2011). Most recently, our group used only on farm data from DHIA tests and on-farm computer record keeping systems, performed/employed by 72.8% and 98% of large dairies, respectively, to guide SDCT. In our study, a computer algorithm identified "low risk" cows as having no more than one clinical mastitis event, a mean of the last 3 test-days ≤ 200k cells/mL, a last-test SCC of ≤ 200k cells/mL, and a projected dry period of <100d. Low risk cows were randomized to receive dry-cow antibiotics and external teat sealant or external teat sealant only. When comparisons were made between antibiotic-treated and teat-sealant only low risk cows, no statistical differences were found for new infection risks, 1st test milk production, 1st test LS, daily milk production in the first 30 DIM, clinical mastitis risks, and culling risks. Bacteriologic cure was different between groups. Of the 20 quarters that did not cure, 13 were in quarters not treated with antibiotics; 19 were contributed by the minor pathogens CNS (Vasquez et al., 2017).

Cowside tests only. Though no randomized field trials have assessed the performance of only rapid cow-side tests such as California Mastitis Test (CMT) and milk leukocyte differential (MLD) tests in a SDCT protocol, they have been evaluated to determine the infection status of a cow at dry-off. CMT and MLD have fair to good sensitivities and specificities for late lactation animals, but are dependent upon cut-point and interpretation (Poutrel and Rainard, 1981; Hockett et al., 2014; Godden et al., 2017).

Combination of culture and cow-level data. A teat-sealant study on 482 low SCC (< 200k cells/mL), culture-negative cows was performed using a randomized quarter-level study design and 4 different treatments: control (no treatments), IMM antibiotic, IMM antibiotic and internal teat sealant, and teat sealant only (Woolford et al., 1998). The number of clinical IMIs during the dry period was higher in the control quarters than the infused quarters, but not different between the teat sealant only and control quarters. The same findings were found for new IMIs at calving.

A BTSCC requirement of < 250k cells/ml (4 herds) was combined with individual culture data at dry-off to evaluate new infection and clinical mastitis risks (Berry and Hillerton, 2002). The group found a 9% difference in cases of clinical mastitis between the untreated and treated cows (P = 0.001). However, cows randomized into treatment groups were those with negative, CNS-positive, or *Corynebacterium*-positive culture results 1 week prior to dry-off. The overall new IMI risk was statistically higher in the untreated versus treated cows; the greatest contribution to this finding was for major pathogens (*S. uberis)* in quarters already infected with minor pathogens. No statistical differences were found in the prevalence of CNS post-calving between treated and untreated groups (Berry and Hillerton, 2002).

Cameron et al. (2013, 2014) used culture in addition to several other screening tools on 16 Canadian herds: cow level inclusion criteria in the study consisted of a dry period between 30 and 90 days, 3 serial SCC < 200k cell/mL prior to dry-off, no clinical mastitis in the 90 days prior to dry-off, and a CMT score of < 2 on the day prior to dry-off. Cows were then randomized to BDCT or SDCT. While cows within the BDCT were all treated with antimicrobials, only culture-positive cows within the SDCT group were treated. All cows also received internal teat sealant. No statistical

differences were found for bacteriological cure and new infection risks at calving, ln(SCC) over the first 180d, clinical mastitis risk within 120 d, or test day milk production between SDCT and BDCT cows.

Making sense of discrepant data. In trials that did not use a combination of tools, cows at risk due to historically higher SCC or multiple mastitis events, and currently infected cows (if culture was not used) were among the cows included in the non-treated group. Dissimilarities between findings could also be due to the presence of higher levels of major pathogens on the included dairies, the lack of teat sealant use, or the inclusion of herds with BTSCC >250k cells/mL.

In an effort to generate an overall outcome for trials that evaluated treatment protocols at dry-off, two groups performed meta-analysis on previously published research. One analysis by Halasa et al. (2009a) was performed on 4 SDCT trials (SDCT protocol versus BDCT protocol) and 13 BDCT trials (BDCT versus no-treatment). In it, the meta-analytic pooled relative risks for bacteriological cure were 1.76 and 1.78, respectively. For new infection, pooled relative risks of 0.58 and 0.55 were described for BDCT versus SDCT in the 2 meta-analyses (Robert et al., 2006a; Halasa et al., 2009b). While statistical differences in relative risk were seen for protection against new quarter IMI, no statistical differences were calculated when the selection unit was the cow (Halasa et al. 2009b). In the Robert et al. (2006a) meta-analysis, pooled differences in new IMI risk were statistically significant for streptococcal and *Staphylococcus aureus* IMIs and not for IMIs caused by CNS or coliforms. Statistically different findings for BDCT versus SDCT in 15 of the 25 studies could be due to the fact that contributions of streptococcal species and *Staphylococcus aureus* represented more than 35% of IMIs in 50% of the studies included.

Readers will note that the main objective of many of the studies described here was not to compare a selectively treated or untreated group of cows/quarters to a blanket-treated group of cows or quarters, rather the SDCT data comparing these groups could be extracted from the results presented in each manuscript. Overall, there are limited studies that adequately capture the best comparisons in regards to sample size, study design and statistical evaluations. These include Sharpenzeel et al., 2016 (Netherlands), Cameron et al., 2013 and 2014 (Canada), and Rajala-Schultz et al., 2007, Patel et al. 2017 and Vasquez et al. 2017 (US). The differing findings in each of these trials dictate the need for more research on the subject. However, we do know that selection of farms for SDCT should be dependent on pathogen prevalence.

Economics of SDCT

An economic analysis comparing BDCT to no dry-cow therapy of all cows within a herd concluded that dry-cow therapy was advantageous. However, the modeled costs of not using dry cow antibiotics always included lower milk production and higher SCC for these cows, with values retrieved from regression analyses with suboptimal R^2 values (McNab and Meek, 1991). More recently, stochastic modeling was used to evaluate the economics of SDCT by Huijps and Hogeveen (2007). The economic parameters associated with the greatest influence on costs were antibiotics, milk losses, and the hourly rate for labor. The infection parameters that produced the most influence on costs were clinical mastitis, the probability of culling, and infection rate over the dry period. When infection rate and antibiotic costs are low, no DCT might be best, but variation is high; in scenarios where selection criteria has high sensitivity, there will be lower average costs. Default values of the input variables and probabilities in this Dutch model showed that SDCT economically is the best option (Huijps and Hogeveen, 2007). In studies where “economic” outcomes were similar

between groups (milk production, infection risk, clinical mastitis risks, and culling risks) partial budget analysis can easily be performed. A net benefit of $2.62 per cow was calculated for the pilot study performed at the University of Minnesota by Patel et al., (2014). This accounted for the cost of labor and supplies to segregate, sample, and culture all cows at the quarter-level (Patel, 2014). As cure and infection risks were similar between groups, the authors did not account for additional cases of mastitis experienced by one group over another. Eliminating the costs of culture by using only computer data, our group found a net benefit of $6.87 per cow when 35% of cows were allocated to the "high risk" group and subsequently treated with dry-cow antibiotics. The economic analysis performed by Scherpenzeel et al. (2016) used computer modeling to predict economic outcomes using 7 different SDCT scenarios. These models assumed higher subclinical and clinical mastitis prevalence and decreasing total antimicrobial usage for each scenario of decreasing sequential SCC thresholds. Two of 7 programs produced an economic advantage of SDCT over BDCT: 1. using 50,000cells/mL for 1st lactation and higher animals and 2. using 150,000cells/mL for first lactation animals and 50,000cells/mL for >1st lactation animals (Sherpenzeel et al., 2016). Subsequent to this analysis, the same group (Sherpenzeel et al., 2018) used mathematical modeling to determine the effect of individual-farm BTSCC and clinical mastitis incidences on economic values (costs associated with clinical mastitis or subclinical mastitis in early lactation). BDCT was compared to a sliding scale of SDCT (100% -0% antibiotic use) on farms with permutations of low, high, and average BTSCC and low, high and average clinical mastitis incidences. The authors concluded that for all evaluated BTSCC levels, SDCT was more economically beneficial than BDCT, with greater profits occurring in herds with lower incidences of clinical mastitis; all types of herds can reduce dry-cow antimicrobial use without negative economic consequences (Sherpenzeel et al., 2018).

Application

According to Ekman and Østerås, 2003; and Cameron et al., 2014 herds with a bulk tank SCC ≤250k cells/mL, hygienic dry-off procedures, and very low prevalence of contagious pathogens could be considered for SDCT. Treatments should be on the cow level: some groups have also shown that due to interdependence of quarters, split-udder or quarter-level treatment design might contribute to negative outcomes, and quarters do not act independently when considering infection risk (Robert et al., 2006b; Paixão et al., 2017).

Cow side or record-based tests such as CMT, clinical mastitis history, and DHIA SCC offer the convenience of readily accessible data, but if using microbiological culture as a reference gold-standard, these methods will result in more misclassifications. High sensitivity will minimize the potential risk of not treating a cow that might benefit from treatment. Sensitivity can be increased by using lower SCC thresholds to define "at risk" cows. With a more sensitive test, more cows will be treated. Regardless, lower thresholds will result in more prudent use of antimicrobials than in a BDCT system. Sensitivities and specificities of using monthly SCC and clinical mastitis events as treatment criteria for SDCT range from 58.4% to 69.4% and 62.7% to 71.5%, respectively (Torres et al., 2008; McDougall, 2010; Rajala-Schultz et al., 2011). As described by the referenced field trials, aerobic culture can be used on all cows or a subpopulation of cows (e.g. cows with SCC below a certain threshold) to screen cows or quarters for treatment. This generates additional costs and the need for reliable and conscientious sampling as well as trained personnel or external laboratory staff to define an infected quarter. Additionally, cows need to be segregated for sampling at least 1 day prior to dry-off and again when animals to be treated are identified.

Conclusion

BDCT has been an effective method to reduce new IMI and increase bacteriologic cure in subclinical and clinically infected cows at and during dry-off; however, selective use of IMM antibiotics for those cows that will likely benefit can produce similar results when applied in appropriate herds. Selective antimicrobial use at dry-off creates an opportunity to practice good drug stewardship and in many situations SDCT has been shown to offer economic benefits. Research indicates that success of a SDCT program is farm specific. Veterinarians should remain abreast of current research findings and consider farm management and pathogen presence as they work with producers to develop a best SDCT strategy.

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Pathogen Based Treatment Decisions for Clinical Mastitis

Introduction

Clinical mastitis is the main reason lactating dairy cows are administered antibiotics (Sundlof et al., 1995; Pol and Ruegg, 2007). Prudent use of antimicrobials is based on informed decision making. Using a pathogen based approach to help select which cows to treat and what to treat with will help achieve prudent use of antibiotics in the dairy industry. Judicious use of antibiotics will help preserve the public's trust in the quality and safety of dairy products as well potentially reducing the risk of antimicrobial resistance. Culture based decision making is also profitable for individual dairies because they will be able to save money on intramammary antibiotics and labor as well as have less discarded milk while cows are waiting for the withholding times to expire such that there are no antibiotic residues entering the food supply.

Approximately 25 to 35% of clinical mastitis cases result in no bacterial growth via conventional culture techniques and therefore do not likely have antibiotic responsive bacteria associated with the event. (Oliveira et al., 2013). Further, there are certain organisms that either do not respond favorably to antibiotic treatment (e.g. *Pseudomonas*) or have spontaneous clinical cure rates similar to treatment (e.g. *E. coli*). While in these three instances using antibiotics likely does not help increase cure rates, it does cost money, decreases the amount of saleable milk, and perhaps increases the risk for antimicrobial resistance. In addition, approximately 85% of all clinical cases are classified as mild (only abnormal milk) or moderate (abnormal milk and inflammation of the udder) and only 15% of the cases are severe (abnormal milk, inflammation of the udder, and systemic illness such as dehydration, fever, etc.). Certainly some pathogens are more likely to be associated with severe cases such as *E coli* or *Klebsiella*, but even these organisms typically don't cause severe mastitis in more than 25-30% of the cases. Unfortunately, one cannot tell which organism is associated with a case of mastitis based on clinical signs alone which necessitates making a diagnosis from a milk sample.

There are four main ways of reacting to and treating clinical mastitis on dairy farms. The first is to not treat any of the mild and moderate cases and provide supportive care (e.g. fluids, systemic antibiotics, anti-inflammatory drugs) to only cows with severe cases. This was in style approximately fifteen to twenty years ago and on many dairies led to increased chronic cases, especially with *Streptococcal* infections, and thereafter increasing bulk milk SCC. The second could be to treat all clinical cases the similarly, e.g. use intramammary antibiotics in all cows with abnormal milk. As described above this is likely not the most profitable choice, especially for larger dairies. Depending on the ecology of pathogens on a particular dairy farm this leads to overtreatment of more than 50% of mild and moderate cases.

The next two ways are reliant on obtaining a milk sample from a cow with mastitis and making a decision based on the results of a diagnostic test. Subsequently a third way could be to culture the milk on-farm and make a treatment decision approximately 24 hours after detection of mastitis (Lago et al., 2011 a, b). With excellent training and re-training of on-farm personnel, proficiency training and monitoring by a reference laboratory, good maintenance of supplies, and dedication to data recording this method can be accurate enough when determining which cows have a pathogen at all (i.e. growth or no-growth of bacteria on culture media) and the difference between Gram

positive bacteria and Gram negative bacteria. This is especially true when culture media that selects for growth of particular kinds of organisms is used. With this method a dairy could, for example, decide to treat only those cows with mild or moderate mastitis that had Gram positive growth and not treat those with no growth or Gram negative growth. Another dairy may decide not to treat only those with no growth. This method should not be relied upon for making culling decisions for *Staph aureus* or finding cows, for example, with *Mycoplasma* or *Prototheca*.

The fourth way would be to have an outside service culture the milk and then make treatment decisions approximately 24 hours after detection of mastitis. One benefit of this method is alleviating the need to train and re-train on-farm personnel because dedicated microbiologists are performing the work. Also, almost all pathogens can be identified in a good laboratory which allows not only for accurate treatment decisions but also for surveillance for contagious pathogens such as *Mycoplasma, Streptococcus agalactiae, Prototheca*, and *Staphylococcus aureus*. New diagnostic technologies being employed in some laboratories will facilitate rapid and economical identification of mastitis pathogens. One example is MALDI-TOF (matrix-assisted laser desorbtion ionization – time of flight mass spectrometry) which can very accurately and inexpensively identify pathogens within minutes 12-18 hours post culture.

Data from a number of research trials has shown that for organisms that respond to antibiotics delaying treatment for approximately 24 hours after detection of clinical signs does not diminish treatment efficacy. We conducted a field trial on a commercial dairy farm close to Quality Milk Production Services (QMPS), Ithaca, NY to compare blanket intramammary (IMM) antibiotic therapy (i.e. treating all clinical cases concurrent with detection of signs) to a pathogen-based treatment protocol.

Materials and Methods

All clinical mastitis (CM) cases were assessed for inclusion at a 3500 cow commercial dairy in central New York between Dec 2014 and Apr 2015. Using a randomized design, cows with clinical scores (CS) of 1 or 2 were assigned to either the blanket or culture-based therapy group. Cows were excluded with a CS of 3 (i.e. systemically ill), prior treatment with antibiotics (<15d), or impending sale. Samples were collected using sterile technique and retrieved daily by the QMPS courier service. Results were available after 24h by direct electronic upload onto farm computers in DC305. Standard culture technique was performed by QMPS according to NMC guidelines for identification of aerobic organisms and *Mycoplasma spp.*

Cows in the blanket therapy (BT) group received 1 tube of ceftiofur hydrochloride (Spectramast®) into the affected quarter for 5d according to label. Cows assigned to the culture group (CBT) received no treatment for the first 24h. Upon upload of results, the following protocol was automatically assigned via DC305: *Staph spp., Strep spp., or Enterococcus* were administered an IMM tube of cephapirin sodium (Today®) once every 12h for 2 treatments. Cows positive for other organisms or no growth received no treatment. Any cow with positive cultures for *Prototheca, Mycoplasma, Staph aureus, or Strep ag.* was culled.

Pen moves and dates milk became clinically normal were recorded daily. Continuous variables offered to multivariable model building included days to return to visibly normal milk, days out of the tank, linear score (LS) 8-45d post treatment, and test day milk (8-45d post treatment). Binary data included removal from the herd at <30d or <60d post CM. A cow was followed until she was

culled, the end of her lactation, or 60d after CM. Continuous outcome variables following CM were analyzed by ANOVA in JMP® Pro 11.0.0 (SAS Institute, 2013). Distribution of binary response variables were analyzed for treatment effect using two-by-two tables, Pearson's Chi-squared tests, and logistic regression.

A partial budget analysis was used to compare the differences in the two approaches relative to cost of therapy, time spent in the hospital pen, and milk discarded using measured outcomes from the on-farm clinical trial. IMM tube cost was $3.80 x 5 tubes Spectramast for BT and $3.10 x 2 tubes Today for CBT. Labor cost was $15/hour (5 minutes per cow). Culture cost was based on $6.00 per culture. Milk discard value was based on 60 lbs per day production for mastitis cows and a $20.00/cwt milk price. Herd level cost estimates were based on 5% monthly incidence of mastitis per 1000 lactating cows.

Results

A total of 489 CM events were enrolled. 247 cows were assigned to the culture group, and 242 cows to the blanket therapy group. 164 cows in the culture group (33.5% of total) received no treatment, while 83 (17%) received IMM cephapirin sodium. 113 cows were not enrolled due to the severity of their CM (13% of CM). No statistically significant differences existed between blanket therapy and culture-based therapy cows in days to clinical cure (culture: n=163, mean=5.2d; blanket: n=235, mean=5.1d; p=0.42). No statistical differences were observed in next test day milk production between groups (culture: n=218, mean=77.0lb; blanket: n=222, mean=74.7lb; p=0.31). Average LS on the next test day was for the culture group was 4.3 (n=214) and 4.2 for the blanket group (n=210) (p=0.36). Risk of culling before 30 days post-enrollment was statistically the same for both groups (OR=0.80; p=0.54), as was risk of culling prior to 60 days (OR=0.99; p=0.96). Days out of the bulk tank was significantly higher for the blanket therapy group than the culture group (culture: n=184, mean=6.9d; blanket: n=240, mean=8.9d; p<0.001).

Costs associated with clinical mastitis treatment group were as follows:
Material/Culture/Labor- BT $25.25 / CBT- IMM therapy $15.95, no IMM therapy $7.25;
Value of Milk Discard- BT $106.80 / CBT IMM therapy $84.00, no IMM therapy $60.00;
Cost per Treatment Protocol: BT $132.05 / CBT- IMM therapy $99.95, no IMM therapy $67.25;
Total Cost by Treatment Group: BT $132.05 / CBT $78.24 (difference of $53.81 per case)
Economic Impact- Cost of Mastitis Treatment / 1000 Cows: BT $79,230 / CBT $46,943; Savings per 1000 Cows: $32,287

Conclusion

More than 60 percent of moderate and mild CM cases would not have been treated if all cows on this trial were enrolled in a protocol based on pathogen results. This strategic method of treatment decreased milk withholding time by 2 days for those cows that are treated, with no difference in days to clinical cure, milk yields, and LS post-mastitis event; nor additional risk of culling in the days following. The increased milk sales and decrease in antibiotic costs resulted in an increased cash flow of over $30,000 per 1000 cows. The directionality, relative magnitude, and similar treatment protocols are in agreement with some previous models assessing economic decision making for treating clinical mastitis (Pinzon-Sanchez, et al., 2011; Steeneveld, et al., 2011)

Work with your regular herd veterinarian to decide what methods of decision making will be best for your dairy farm and also to establish appropriate treatment protocols for cows with mastitis. Doing so will preserve the public's trust in the safe, nutritious, and affordable dairy foods we help to produce.

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