Pathogen-based treatment programs for milk quality: dry cows and clinical mastitis

Daryl V. Nydam,[1] DVM, PhD; **Amy K. Vasquez,** DVM, PhD; **Steve W. Eicker,** DVM, MS; **Paul D. Virkler,** DVM; **Rob Lynch,** DVM; **Matthias Wieland,** DVM; **Michael B. Capel,**[2] DVM
[1] Cornell University, College of Veterinary Medicine, Ithaca, NY 14853
[2] Perry Veterinary Clinic, Perry, NY 14530
Corresponding author: Dr. D. V. Nydam, dvn2@cornell.edu

Abstract

Blanket dry-cow therapy has been recommended for decades. For a variety of reasons, this recommendation is being reconsidered. The alternative is selective treatment. Diagnostics and dry-cow therapy treatment decisions can be performed at the quarter or cow level. Selective antimicrobial use at dry-off creates an opportunity to practice good drug stewardship. In many situations, it has been shown to offer economic benefits. Research indicates that success of a selective dry-cow therapy (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.

Key words: blanket dry cow therapy, selective dry cow therapy, drug stewardship

Résumé

La thérapie systématique pour vaches taries est recommandée depuis des décennies. Pour plusieurs raisons, cette recommandation est remise en question. L'alternative est le traitement sélectif. Le diagnostic et les choix de traitement pour la thérapie des vaches taries peuvent être faits au niveau du quartier ou de la vache. L'utilisation sélective d'antimicrobiens au tarissement donne l'occasion de faire une bonne intendance des drogues. Dans plusieurs situations, l'approche sélective génère des retombées économiques. Les travaux montrent que le succès d'un programme de thérapie sélective pour vaches taries varie d'une ferme à l'autre. Les vétérinaires devraient se tenir au courant des résultats des recherches en cours et considérer la gestion de la ferme et la présence de pathogènes lorsqu'ils travaillent avec les producteurs afin de développer la meilleure stratégie pour le programme de thérapie sélective pour vaches taries.

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,[11] 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.[4,11,43] 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.[8,28,34] The prevalence of contagious pathogens, such as *Streptococcus agalactiae* and *Staphylococcus aureus*, and reduction of bulk-tank somatic cell counts (BTSCC) from 295,000 cells/mL in 1997 to 193,000 cells/mL in 2014 also suggests that BDCT is not currently a necessity in all herds.[9,35,45] Additionally, only 11.1% of overall test days were greater than 400,000 cells/mL in 2016; this compares to 30.3% of test days in 1998.[23,24]

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 United States, according to a survey by the National Animal Health Monitoring System in 2014.[46] 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;[9] 3) the introduction of an applicator into the teat end is not risk-free;[20] 4) alternative/adjunct products to antibiotics including teat sealants are reported to have success decreasing the risk of new infections;[10,33] 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 somatic cell count (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 regard 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 (IMI) in cows/quarters not receiving treatment. For example, Hogan et al[15] performed a study on 4 US herds with BTSCC <250,000/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.[15] However, statistical comparisons between groups that did not receive PAI were not provided. Schukken[40] performed a study on 1 Dutch herd with a BTCC of 140,000/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.[40] 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; 240,000/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 (≤500,000/mL) SCC groups.[2] Scherpenzeel[37] 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 <150,000 cell/mL and multiparous animals with SCC <250,000/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 days-in-milk (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[5] in an Australian field trial including 1,044 cows from 12 herds. Culture-negative cows were randomly allocated to receive blanket therapy or no treatment, whereas 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 vs blanket treated culture-positive cows.[5] 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.[26] Cows were randomly allocated into a placebo group, control group, or 1 of 2 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% fewer 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[29] 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.[29]

Cow Records Only: SCC and/or Mastitis Events

Though not presented as a SDCT trial, Huxley[17] evaluated the use of a teat sealant in cows with routine composite SCC below 200,000/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.[17] Another trial evaluating internal teat sealant in the United Kingdom used a split-udder design with the same cow-level criteria. However, in this trial,[3] 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[21] assigned cows (~900 cows from 6 New Zealand herds) with SCC ≤150,000 cells/mL 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.[21] A study performed in the United States by Rajala-Schultz[34] on 4 herds (~400 cows) also used computer records and mastitis events to determine which cows to enroll. Cows had to have a SCC ≤200,000 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 <100,000/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.[34] 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 1 clinical mastitis event, a mean of the last 3 test-days ≤200,000 cells/mL, a last-test SCC of ≤200,000 cells/mL, and a projected dry period of <100 days. 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, first test milk production, first test linear score, 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 coagulase-negative staphs (CNS).[47]

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.[10,14,32]

Combination of Culture and Cow-level Data

A teat sealant study on 482 low SCC (<200,000/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.[48] 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 results were found for new IMIs at calving.

A BTSCC requirement of <250,000 cells/ml (4 herds) was combined with individual culture data at dry-off to evaluate new infection and clinical mastitis risks.[1] 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 vs 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.[1]

Cameron[6,7] 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 <200,000 cells/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 180 days, clinical mastitis risk

within 120 days, 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 >250,000 cells/mL.

In an effort to generate an overall outcome for trials that evaluated treatment protocols at dry-off, 2 groups performed meta-analysis on previously published research. One analysis by Halasa[12] was performed on 4 SDCT trials (SDCT protocol vs BDCT protocol) and 13 BDCT trials (BDCT vs 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 vs SDCT in the 2 meta-analyses.[13,36] 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.[13] In the Robert[36] 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 regard to sample size, study design, and statistical evaluations. These include Scherpenzeel (Netherlands),[36] Cameron (Canada),[6,7] (US).[29,34,47] 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.[22] More recently, stochastic modeling was used to evaluate the economics of SDCT by Huijps and Hogeveen.[16] 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 have 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.[16] 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.[29] This accounted for the cost of labor and supplies to segregate, sample, and culture all cows at the quarter level.[29] As cure and infection risks were similar between groups, the authors did not account for additional cases of mastitis experienced by 1 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[38] 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 use 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 first-lactation and higher animals, and 2) using 150,000 cells/mL for first-lactation animals and 50,000 cells/mL for greater than first lactation animals.[36] Subsequent to this analysis, the same group[39] 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% to 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.[39]

Application

According to Ekman and Østerås,[9] and Cameron,[7] herds with a bulk tank SCC ≤250,000 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.[27,35]

Cow-side or record-based tests, such as CMT, clinical mastitis history, and DHIA SCC, offer the convenience of readily accessible data. 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.[21,34,44] 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.

Pathogen-based Treatment Decision for Clinical Mastitis

Clinical mastitis is the main reason lactating dairy cows are administered antibiotics.[31,42] 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.[25] 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 3 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% to 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 4 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 15 to 20 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 similarly. For example, 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 2 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.[18,19] With excellent training and retraining 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 retrain 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 of 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 desorption ionization – time of flight mass spectrometry), which can very accurately and inexpensively identify pathogens within minutes, 12 to 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 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 3,500-cow commercial dairy in central New York between December 2014 and April 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 (<15 days), or impending sale. Samples were collected using sterile technique and retrieved daily by the QMPS courier service. Results were available after 24 hours by direct electronic upload onto farm computers in DairyComp 305 (DC305). Standard culture technique was performed by QMPS according to National Mastitis Council guidelines for identification of aerobic organisms and *Mycoplasma* spp.

Cows in the BDCT group received 1 tube of ceftiofur hydrochloride (Spectramast®) into the affected quarter for 5 days, according to label. Cows assigned to the culture group (CBT) received no treatment for the first 24 hours. 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 12 hours 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 to 45 days post-treatment, and test day milk (8 to 45 days post-treatment). Binary data included removal from the herd at <30 days or <60 days post-CM. A cow was followed until she was culled, the end of her lactation, or 60 days 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 2-by-2 tables, Pearson's Chi-squared tests, and logistic regression.

A partial budget analysis was used to compare the differences in the 2 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 blanket therapy (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 lb (27 kg) per day production for mastitis cows and a $20.00/hundredweight milk price. Herd-level cost estimates were based on 5% monthly incidence of mastitis per 1,000 lactating cows.

Results

A total of 489 CM events were enrolled, with 247 cows assigned to the culture group and 242 cows to the blanket therapy group. A total of 164 cows in the culture group (33.5% of total) received no treatment, while 83 (17%) received IMM cephapirin sodium. A total of 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=77.0 lb [35.0 kg]; blanket: n=222, mean=74.7 lb [33.9 kg]; 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

Conclusions

More than 60% 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 more $30,000 per 1,000 cows. The directionality, relative magnitude, and similar treatment protocols are in agreement with some previous models assessing economic decision making for treating clinical mastitis.[30,41]

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.

The veterinarian of record/ herd veterinarian has many opportunities to decide what methods of decision making will be best for dry cows for each 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 while maintaining the economic sustainability of dairy production.

Acknowledgements

The authors declare no conflict of interest.

Research was partially funded by USDA-NIFA, NY Farm Viability Institute, Atkinson Center for Sustainability, Boehringer Ingelheim, Engaged Cornell.

The contribution farms, farm management, and farm employees as well as Rachel Murphy, German Granados, Anja Sipka, and Valeria Alanis are greatly appreciated.

References

1. Berry EA, Hillerton JE. The effect of selective dry cow treatment on new intramammary infections. *J Dairy Sci* 2002; 85:112.
2. Berry SL, Maas J, Kirk JH, Reynolds JP, Gardner IA, Abmadi A. Effects of antimicrobial treatment at the end of lactation on milk yield, somatic cell count, and incidence of clinical mastitis during the subsequent lactation in dairy herds with a low prevalence of contagious mastitis. *J Am Vet Med Assoc* 1997; 211:207.
3. Bradley AJ, Green JE, Payne B, Williams P, Green MJ. The use of a cephalonium containing dry cow therapy and an internal teat sealant, both alone and in combination. *J Dairy Sci* 2010; 93:1566.
4. Bradley AJ, Green MJ. A study of the incidence and significance of intramammary Enterobacterial infections acquired during the dry period. *J Dairy Sci* 2000; 83:1957.
5. Browning JW, Mein GA, Barton M, Nicholls TJ, Brightling P. Effects of antibiotic therapy at drying off on mastitis in the dry period and early lactation. *Aust Vet J* 1990; 67:440.
6. Cameron M, Keefe GP, Roy JP, Dohoo IR, Macdonald KA, McKenna SL. Evaluation of a 3M Petrifilm on-farm culture system for the detection of intramammary infection at the end of lactation. *Prev Vet Med* 2013; 111:1.
7. Cameron M, McKenna SL, MacDonald KA, Dohoo IR, Roy JP, Keefe GP. Evaluation of selective dry cow treatment following on-farm culture: Risk of postcalving intramammary infection and clinical mastitis in the subsequent lactation. *J Dairy Sci* 2014; 97:270.
8. du Preez J H, Greeff AS. Comparison of the effect of antibiotic dry cow teat canal and intramammary dry cow therapy of dairy cows on the prevalence of teat canal and intramammary infections at calving. *J S Afr Vet Assoc* 1985; 56:191.
9. Ekman T, Østerås O. Mastitis control and dry cow therapy in the Nordic countries, in *Proceedings*. National Mastitis Council 2003; 18-30.
10. Godden S M, Royster E, Timmerman J, Rapnicki P, Green H. Evaluation of an automated milk leukocyte differential test and the California Mastitis Test for detecting intramammary infection in early- and late-lactation quarters and cows. *J Dairy Sci* 2017; 100:6527.
11. Green MJ, Green LE, Medley GF, Schukken YH, Bradley AJ. Influence of dry period bacterial intramammary infection on clinical mastitis in dairy cows. *J Dairy Sci* 2002; 85:2589.
12. Halasa T, Østerås O, Hogeveen H, van Werven T, Nielen M. Meta-analysis of dry cow management for dairy cattle. Part 2. Cure of existing intramammary infections. *J Dairy Sci* 2009; 92:3150.
13. Halasa T, Østerås O, Hogeveen H, van Werven T, Nielen M. Meta-analysis of dry cow management for dairy cattle. Part 1. Protection against new intramammary infections. *J Dairy Sci* 2009; 92:3134.
14. Hockett M, Payne M, Rodriguez R. Milk leucocyte differential diagnosis as a tool to guide quarter-level, selective dry cow therapy, in *Proceedings*. Regional Meeting of National Mastitis Council, Ghent, Belgium. National Mastitis Council 2014.
15. Hogan JS, Smith KL, Todhunter DA, Schoenberger PS. Efficacy of dry cow therapy and a *Propionibacterium acnes* product in herds with low somatic cell count. *J Dairy Sci* 1994; 77:3331.
16. Huijps K, Hogeveen H. Stochastic modeling to determine the economic effects of blanket, selective, and no dry cow therapy. *J Dairy Sci* 2007; 90:1225.
17. Huxley JN, Green MJ, Green LE, Bradley AJ. Evaluation of the efficacy of an internal teat sealer during the dry period. *J Dairy Sci* 2002; 85:551.
18. Lago A, Godden SM, Bey R, Ruegg PL, Leslie K. The selective treatment of clinical mastitis based on on-farm culture results: II. Effects on lactation performance, including clinical mastitis recurrence, somatic cell count, milk production, and cow survival. *J Dairy Sci* 2011; 94:4457-4467.
19. Lago A, Godden SM, Bey R, Ruegg PL, Leslie K. The selective treatment of clinical mastitis based on on-farm culture results: I. Effects on antibiotic use, milk withholding time, and short-term clinical and bacteriological outcomes. *J Dairy Sci* 2011; 94:4441-4456.
20. Leelahapongsathon K, Piroon T, Chaisi W, Suriyasathaporn W. Factors in dry period associated with intramammary infection and subsequent clinical mastitis in early postpartum cows. *Asian-Australas J Anim Sci* 2016; 29:580.
21. McDougall S. A randomised, non-inferiority trial of a new cephalonium dry-cow therapy. *NZ Vet J* 2010; 58:45.
22. McNab W, Meek AH. A benefit cost analysis of dry-cow mastitis therapy in dairy cattle in Ontario. *Can Vet J* 1991; 32:347.
23. Miller RH, Norman HD. Somatic cell counts of milk from 1998 Dairy Herd Improvement herds. Council on Dairy Cattle Breeding Research Reports, SCC1(12-99), 1999.
24. Norman HD, Walton LM, Durr J. Somatic cell counts of milk from Dairy Herd Improvement herds during 2016. Council on Dairy Cattle Breeding Research Reports, SCC18 (2-17), 2017.
25. Oliveira L, Hulland C, Ruegg PL. Characterization of clinical mastitis occurring in cows on 50 large dairy herds in Wisconsin. *J Dairy Sci* 2013; 96:7538-7549.
26. Østerås O, Sandvik L. Effects of selective dry-cow therapy on culling rate, clinical mastitis, milk yield and cow somatic cell count. A randomized clinical field study in cows. *Zentralbl Veterinarmed B* 1996; 43:555.
27. Paixão MG, Abreu LR, Richert R, Ruegg PL. Milk composition and health status from mammary gland quarters adjacent to glands affected with naturally occurring clinical mastitis. *J Dairy Sci* 2017; 100:7522.
28. Pantoja JC, Hulland C, Ruegg PL. Dynamics of somatic cell counts and intramammary infections across the dry period. *Prev Vet Med* 2009; 90:43.

29. Patel K, Godden SM, Royster EE, Timmerman JA, Crooker BA, McDonald N. Pilot Study: Impact of using a culture-guided selective dry cow therapy program targeting quarter-level treatment on udder health and antibiotic use. *Bov Pract* 2017; 51:48.
30. Pinzón-Sánchez CL, Cabrera VE, Ruegg PL. Decision tree analysis of treatment strategies for mild and moderate cases of clinical mastitis occurring in early lactation. *J Dairy Sci* 2011; 94:1873-1892.
31. Pol M, Ruegg PL. Relationship between antimicrobial drug usage and antimicrobial susceptibility of gram-positive mastitis pathogens. *J Dairy Sci* 2007; 90:262-273.
32. Poutrel B, Rainard P. 1981. California mastitis test guide of selective dry cow therapy. *J Dairy Sci* 1981; 64:241.
33. Rabiee AR, Lean IJ. The effect of internal teat sealant products (Teatseal and Orbeseal) on intramammary infection, clinical mastitis, and somatic cell counts in lactating dairy cows: A meta-analysis. *J Dairy Sci* 2013; 96:6915.
34. Rajala-Schultz PJ, Torres AH, DeGraves FJ. Milk yield and somatic cell count during the following lactation after selective treatment of cows at dry-off. *J Dairy Res* 2011; 78:489.
35. Robert A, Bareille N, Roussel P, Poutrel B, Heuchel V, Seegers H. Interdependence of udder quarters for new intramammary infection during the dry period in cows submitted to selective antibiotic therapy. *J Dairy Res* 2006; 73:345.
36. Robert A, Seegers H, Bareille N. Incidence of intramammary infections during the dry period without or with antibiotic treatment in dairy cows – a quantitative analysis of published data. *Vet Res* 2006; 37:25.
37. Scherpenzeel CG, den Uijl IE, van Schaik G, Olde Riekerink RG, Keurentjes JM, Lam TJ. Evaluation of the use of dry cow antibiotics in low somatic cell count cows. *J Dairy Sci* 2014; 97:3606.
38. Scherpenzeel CG, den Uijl IEM, van Schaik G, Olde Riekerink RGM, Hogeveen H, Lam TJGM. Effect of different scenarios for selective dry-cow therapy on udder health, antimicrobial usage, and economics. *J Dairy Sci* 2016; 99:3753.
39. Scherpenzeel CG, Hogeveen H, Maas L, Lam TJGM. Economic optimization of selective dry cow treatment. *J Dairy Sci* 2018; 101:1.
40. Schukken YH, Vanvliet J, Vandegeer D, Grommers FJ. A randomized blind trial on dry cow antibiotic infusion in a low somatic cell count herd. *J Dairy Sci* 1993; 76:2925.
41. Steeneveld W, van Werven T, Barkema HW, Hogeveen H. Cow-specific treatment of clinical mastitis: An economic approach. *J Dairy Sci* 2011; 94:174-188.
42. Sundlof SF, Kaneene JB, Miller R. National survey of veterinarian-initiated drug use in lactating dairy cows. *J Am Vet Med Assoc* 1995; 207:347-352.
43. Todhunter DA, Smith KL, Hogan JS, Schoenberger PS. Gram-negative bacterial infections of the mammary gland in cows. *Am J Vet Res* 1991; 52:184.
44. Torres AH, Rajala-Schultz PF, Degraves FJ, Hoblet KH. Using dairy herd improvement records and clinical mastitis history to identify subclinical mastitis at dry-off. *J Dairy Res* 2008; 75:240.
45. U.S. Department of Agriculture, Plant and Animal Health Inspection Service. Dairy 2014, Milk Quality, Milking Procedures, and Mastitis in the United States, 2014. USDA-APHIS-VS-CEAH-NAHMS. Fort Collins, CO. 2016; 704.0916.
46. U.S. Department of Agriculture, Plant and Animal Health Inspection Service. Dairy 2014, Dairy Cattle Management Practices in the United States, 2014. USDA-APHIS-VS-CEAH-NAHMS. Fort Collins, CO. 2016; 704.0916.
47. Vasquez A, Nydam DV, Capel MB, Eicker S, Virkler PD. Clinical outcome comparison of immediate blanket treatment versus a delayed pathogen-based treatment protocol for clinical mastitis in a New York dairy herd. *J Dairy Sci* 2017; 100:2992-3003.
48. Woolford MW, Williamson JH, Day AM, Copeman PJA. The prophylactic effect of a teat sealer on bovine mastitis during the dry period and the following lactation. *NZ Vet J* 1998; 46:12.