J. Dairy Sci. 104:12164–12172
https://doi.org/10.3168/jds.2021-20593

Treatment practices after calving-related events on 45 dairy farms in California

N. Silva-del-Río,[1,2]* A. Valldecabres,[1,2] A. Espadamala,[1] A. García-Muñoz,[3] P. Pallares,[1] A. Lago,[4] F. S. Lima,[2] and R. V. Pereira[2]

[1]Veterinary Medicine Teaching and Research Center, 18830 Road 112, Tulare, CA 93274
[2]Department of Population Health and Reproduction, School of Veterinary Medicine, University of California–Davis, One Shields Avenue, Davis 95616
[3]Facultad de Veterinaria, Universidad CEU Cardenal Herrera, Valencia 46115, Spain
[4]DairyExperts Inc., Tulare, CA 93274

ABSTRACT

Retained fetal membranes (RFM), dystocia, and twinning are common postpartum events that increase the risk of metritis, impair reproductive performance, and contribute to antimicrobial use on dairies. The overall objective of this study was to describe treatment decisions after RFM, severe dystocia (cesarean section and fetotomy), nonsevere dystocia (nonmechanical and mechanical assistance to extract the calf), and twinning. A total of 44 dairies from California's San Joaquin Valley (39 Holstein and 6 Jersey or crossbreed herds) with 450 to 9,500 lactating cows were enrolled in this study. Researchers visited each dairy once to observe cow-side fresh cow health evaluations and to interview health evaluators and maternity workers, using a standardized survey tool. The survey included questions about antimicrobial (class, dose, and duration) and nonantimicrobial therapies for calving-related events. Antimicrobial therapy was used in all 44 dairies to treat RFM at 24 (n = 23), 48 (n = 10), or 72 h (n = 5) after calving, or when puerperal metritis signs were observed (n = 6). Antimicrobial therapy was used after all severe dystocia cases, and after nonsevere dystocia (n = 27) and twinning (n = 15). Ceftiofur products were the most common antimicrobial class; they were used to treat RFM cases (n = 29), nonsevere dystocia (n = 13), and twinning (n = 10). Supportive therapy for calving-related events included nonantimicrobial intrauterine treatments, nonsteroidal antiinflammatory drugs, oxytocin, i.v. calcium, or oral drenches. Our study highlights opportunities to reduce extra-label use of antimicrobials in postpartum cows affected with RFM, and the need for education and outreach efforts on judicious use of antimicrobials. Furthermore, antimicrobial treatment choices differed largely across dairies, indicating a need to reach consensus and promote standardized practices within the industry.

Key words: antimicrobial, dairy cow, calving-related events

INTRODUCTION

Calving-related events are common in US dairy farms; retained fetal membranes (**RFM**), dystocia, and twins can affect 3.4 to 5.3%, 3.6 to 5.9%, and 4.2 to 8.7% of the cows in a herd, respectively (Silva-del-Río et al., 2007; USDA-NAHMS, 2014; Schambow et al., 2021). Cows undergoing RFM, dystocia, or twinning are at higher risk of developing uterine disease (McDougall, 2001; Sheldon and Dobson 2004; Giuliodori et al., 2013). Furthermore, calving-related events increase the risk of culling, and negatively affect the reproductive and productive performance of affected cows (Oltenacu et al., 1990; Potter et al., 2010). The cost associated with calving-related events has been estimated at $298 per case of RFM (Gohary and LeBlanc, 2018), $155 to 556 per case of dystocia (McGuirk et al., 2007), and over $100 per twin calving (Eddy et al., 1991; Cabrera and Fricke, 2021). To mitigate the negative consequences of calving-related events, antimicrobial strategies have been studied to prevent uterine diseases (McDougall, 2001; Dubuc et al., 2011; McLaughlin et al., 2013; Bartolome et al., 2014).

Over the past decades antimicrobial resistance has become a worldwide health concern. It is believed that the misuse and overuse of antimicrobials, both in humans and animals, contributed to this health concern (Jensen et al., 2008). Several strategies have been proposed to mitigate the progression of the antimicrobial resistance trend, including judicious use of antimicrobials in livestock production systems (Chatterjee et al., 2018). To support this strategy, the World Health Organization has generated a list with critically impor-

Received April 11, 2021.
Accepted June 30, 2021.
*Corresponding author: nsilvadelrio@ucdavis.edu

tant drugs that should be judiciously used both in human and veterinary medicine (WHO AGISAR, 2017). Within critically important drugs, the highest priority category includes cephalosporins (third, fourth, and fifth generations), glycopeptides, macrolides, polymyxins, and quinolones. The United States Food and Drug Administration's Center for Veterinary Medicine (21 CFR Part 530) regulates the extra-label use of critically important drugs by not allowing (i.e., glycopeptides) or restricting (i.e., ceftiofur products) their use (FDA, 2020). The State of California (2015) has implemented Senate Bill 27, "Livestock: Use of antimicrobial drugs" (SB-27; 2015; effective January 1, 2018), which outlines more stringent laws than federal legislation for use of medically important antibiotics in livestock, and supports the implementation of antimicrobial educational stewardship efforts and surveillance of antimicrobial resistance in livestock through state-supported efforts. Under CA Senate Bill 27, all injectable antimicrobial drugs administered to livestock, including those previously available over the counter such as tetracycline or penicillin procaine, require a veterinary prescription through a veterinary-client-patient relationship.

Veterinary treatment practices for calving-related events have been described in Europe (Heuwieser et al., 2010; Eppe et al., 2021), revealing the need for outreach and education in the judicious use of antimicrobials. In large California dairies identification and treatment of sick animals are mostly performed by dairy employees (Espadamala et al., 2016, 2018). Therefore, the description of how calving-related events are treated by dairy employees can contribute to designing relevant antimicrobial use stewardship programs in California. The objective of the present study was to describe treatment practices after calving-related events (RFM, dystocia, and twining) in 45 California dairies.

MATERIALS AND METHODS

The University of California Davis Institutional Review Board exemption was acquired before field visits were conducted. This study includes a convenience sample of 45 dairy herds that were visited from February to August 2015. General herd information and description of data collection process has been previously reported in Espadamala et al. (2016, 2018). Enrolled dairies were identified with the assistance of California county extension advisors, dairy veterinarians, and consultants from California's San Joaquin Valley. At the time of the study, the San Joaquin Valley housed 89% of the cows in California (CDFA, 2016).

A survey tool was designed to collect information on postpartum treatment decisions for RFM, dystocia, and twinning (Table 1). Two researchers (A. E. and P. P.) visited all enrolled herds one time to complete the survey tool. They observed fresh cow evaluators while performing RFM treatments during health evaluations, and later they interviewed them to ensure completion of the standardized survey tool. Researchers also visited the maternity pen in 44 dairies and interviewed dairy workers to document treatment practices after severe dystocia (dystocia resolved by cesarean section and fetotomy), nonsevere dystocia (nonmechanical or mechanical assistance to extract the calf; score 2 and 3 from Schuenemann et al., 2011), and twinning. The survey tool was initially beta-tested on 5 dairies and subsequently modified; this served to expand the scope of the survey tool and to train both observers on data collection. To increase data accuracy, questions were asked at least twice at different times during the herd visit.

Each day upon returning from the field visit, data collection sheets were compared between the 2 researchers performing field visits. Discrepancies were discussed, and if agreement was not reached, the cow evaluators were consulted by phone. A report was written, and data were entered into spreadsheets for descriptive statistical analysis (Excel 2010, Microsoft Corp.). Responses to open-ended questions were categorized before data analysis. Reported percentages were rounded to the nearest whole percentage point. Antimicrobial active ingredients are reported as ceftiofur products [ceftiofur hydrochloride (**CHCl**), ceftiofur crystalline-free acid, and ceftiofur sodium] and penicillin products (penicillin procaine and ampicillin).

Multiple correspondence analysis was performed using JMP 15 PRO (SAS Institute Inc.) to identify associations between dairy size (<2,000 or ≥2,000 cows), RFM treatment practices [time to RFM treatment (24 h, 48 h, 72 h, or puerperal metritis signs) and antimicrobial treatment choice for RFM (ceftiofur products, penicillin products, or tetracycline)], and the use of antimicrobials to treat dystocia (yes or no) or twinning (yes or no).

RESULTS

Retained Fetal Membranes

Researchers documented treatment decisions for cows with RFM based on observations and open-ended questions (n = 25) or only on open-ended questions (n = 20).

Time to Treat Retained Fetal Membranes. Most enrolled dairies defined the time to treat RFM based on visual observation of nonexpelled fetal membranes, either at 24 h (n = 23), 48 h (n = 10), or 72 h (n = 5). On 6 dairies, cows with nonexpelled fetal membranes were treated when showing signs of puerperal metritis (i.e., abnormal vaginal discharge, fever, or systemic signs of disease).

Antimicrobial Treatments. The class, dose, and length of antimicrobial treatments are described in Table 2. One dairy did not use antimicrobials for RFM treatment. Ceftiofur (n = 29) and penicillin (n = 14) products were the most common systemic antimicrobials used. Some dairies selected the antimicrobial treatment based on parity (n = 2) or on the extent of vaginal damage (n = 2). Only 6 dairies restricted the antimicrobial treatment to those cows showing signs of puerperal metritis (i.e., abnormal vaginal discharge, fever, or systemic signs of disease). Six dairies used intrauterine infusions of tetracycline to treat cows affected with RFM [alone (n = 2), combined with systemic penicillin products (n = 3), or combined with systemic penicillin products in primiparous and ceftiofur products in multiparous (n = 1)].

Nonantimicrobial Treatments. Some dairies used nonantimicrobial intrauterine treatments [urea pills (n = 5), chlorhexidine solution (n = 1), or essential oils (n = 1)], nonsteroidal antiinflammatory drugs [acetylsalicylic acid oral pills (n = 5) or flunixin meglumine i.m. (n = 2)], oxytocin (n = 5), i.v. calcium (n = 2), or oral drenches (mixture of energy sources, minerals, and probiotics; n = 5) as a supportive treatment to RFM cows. Nonantimicrobial intrauterine treatments were used combined with systemic antimicrobials (n = 2), infused as a first treatment option on dairies delaying systemic antimicrobials to 48 h postpartum (n = 3), or used only when the cow showed systemic signs of disease (n = 2).

Manual Removal of Fetal Membranes. Removal of the fetal membranes by manual force was a practice performed on 15 dairies (33%). On most dairies, placenta removal was attempted at 24 h after calving (n = 9), but some dairies delayed it after the first antimicrobial treatment was completed (n = 5) or waited 48 h after calving (n = 1).

Dystocia

The class, dose, and length of antimicrobial therapy after dystocia cases is described in Table 3. Dystocia cases resolved with advance obstetrics or surgical procedures, such as fetotomy or cesarean section, were treated with systemic antimicrobials, penicillin products (n = 32), ceftiofur products (n = 7), and tetracycline (n = 2). Three dairies reported that no cesarean sections or fetotomies were performed at their premises. Dystocic calvings that required nonmechanical or mechanical assistance to extract the calf were treated with antimicrobials (60%), ceftiofur products (n = 13), penicillin products (n = 12), or tetracyclines (n = 2). Supportive therapy was also provided in some

Table 1. Survey tool used to collect information on treatment decisions after calving-related events [retained fetal membranes (RFM), dystocia, and twinning] in 45 dairies in California

Event
Retained fetal membranes
1. Do you administer antimicrobial treatment to cows with RFM? If yes,
1.a. When do you start antimicrobial treatment?
1.b. What drug do you use?
1.c. What dose do you use?
1.d. How long do you treat?
2. Do you administer nonantimicrobial treatments to cows with RFM? If yes,
2.a. What type of nonantimicrobial treatments do you use?
3. Do you remove the fetal membranes manually?
Dystocia
4. Do you administer antimicrobial treatment to cows with dystocia? If yes,
4.a. Do you treat cows with nonsevere (nonmechanical and mechanical assistance to extract the calf) or severe (cesarean sections, fetotomy) dystocia?
4.b. When do you start antimicrobial treatment?
4.c. What drug do you use?
4.d. What dose do you use?
4.e. How long do you treat?
5. Do you administer nonantimicrobial treatments to cows with dystocia? If yes,
5.a. What type of nonantimicrobial treatments do you use?
Twinning
6. Do you administer antimicrobial treatment to cows with twins? If yes,
6.a. When do you start antimicrobial treatment?
6.b. What drug do you use?
6.c. What dose do you use?
6.d. How long do you treat?
7. Do you administer nonantimicrobial treatments to cows with twins? If yes,
7.a. What type of nonantimicrobial treatments do you use?

Table 2. Class, daily dose, and duration of antimicrobial therapy in 45 California dairies after retained fetal membranes (RFM)

Item	Drug[1]	Dose/d	Duration (d)	Number of dairies[2]
At 24 h after calving	i.m. CHCl	750 to 1,500 mg	3 to 5	8 [#3[V]]
		1,000 mg	Until RFM is expelled	3
	s.c. CCFA	4,000 mg	Single dose	1 [#3[V]]
		4,000 mg	Second dose at 72 h	3
	i.m. pen	(9 to 15) × 10[6] IU	3 to 6	5 [#3[V], #30[P]]
		9 × 10[6] IU	Until RFM is expelled	1
	i.m. amp	6,250 to 7,500 mg	4 to 6	2 [#30[M]]
	i.u. tet	No documented	Second dose at 72 h	3 [3 dairies][3]
At 48 h after calving	i.m. CHCl	1,000 to 1,500 mg	3 to 5	7 [#27[M,] #45[V]]
	i.m. pen	(12 to 18) × 10[6] IU	3 to 6	2 [#27[P], #45[V]]
	i.m. amp	6,250 to 7,500 mg	3 to 6	1
	i.u. tet	No documented	Second dose at 72 h	2 [1 dairy][3]
At 72 h after calving	i.m. CHCl	1,000 to 1,250 mg	3 to 5	2
	i.m. pen	12 × 10[6] IU	3	1
	i.m. amp	6,250 to 7,500 mg	3	1
	i.u. tet	No documented	Second dose at 72 h	1
Based on signs of metritis	i.m. CHCl	1,750 mg	3	1
	s.c. CCFA	4,000 mg	1	1
	i.m. CNa	750 to 1,500 mg	3 to 5	2
	i.m. pen	6 × 10[6] IU	5	1
	i.m. amp	8,750 mg	6	1

[1]Ceftiofur hydrochloride (CHCl), ceftiofur crystalline-free acid (CCFA), ceftiofur sodium (CNa), penicillin procaine (pen), ampicillin (amp), and tetracycline (tet). One dairy did not use antimicrobials. i.u. = intrauterine.

[2]Numbers in brackets refer to a dairy (# assigned in study) that treats multiparous (M) and primiparous (P) cows differently or treats differently based on vaginal damage (V).

[3]Number of dairies that combine i.u. tet with systemic antimicrobials.

dairies: calcium supplementation (i.v., n = 7; oral, n = 3), flumixin meglumine (n = 3), dextrose (i.v., n = 2), dexamethasone (n = 1), and oxytocin (n = 1).

Twinning

The class, dose, and the length of antimicrobial therapy after twinning is described in Table 3. Systemic antimicrobials were administered to dams after calving twins in 31% of the enrolled dairies. On 3 dairies dams of twins only received antimicrobial treatment if they required calving assistance. The antimicrobial class of choice were ceftiofur products (n = 10) or penicillin products (n = 5). On some dairies, after twining dams were treated with calcium supplementation (i.v., n = 1; oral, n = 6), flunixin meglumine (n = 3), dextrose (i.v., n = 2), dexamethasone (n = 1), or oxytocin (n = 1).

Multiple Correspondence Analysis

Map of multiple correspondence analysis is presented in Figure 1. The first 2 dimensions of the analysis ac-

Table 3. Class, daily dose, and duration of antimicrobial therapy used after nonsevere dystocia (nonmechanical and mechanical assistance to extract the calf) and twin calving in 44 California dairies

Drug[1]	Dose/d	Duration (d)	Number of dairies[2]
Nonsevere dystocia			
i.m. CHCl	750 to 1,500 mg	3 to 5	8
i.m. CNa	1,500 mg	5	1
s.c. CCFA	4,000 mg	Single dose	4
i.m. pen	(6 to 18) × 10[6] IU	4	10 [#30[P]]
i.m. amp	7,500 mg	4	3 [#30[M]]
i.v. tet	12,000 mg	3 to 6	2
i.m. CHCl	750 to 1,500 mg	3 to 5	8
i.m. CNa	1,500 mg	5	1
s.c. CCFA	4,000 mg	Single dose	1
i.m. pen	(12 to 18) × 10[6] IU	4 to 6	4 [#30[P]]
i.m. amp	6,250 to 7,500 mg	3 to 4	2 [#30[M]]

[1]Ceftiofur hydrochloride (CHCl), ceftiofur crystalline-free acid (CCFA), ceftiofur sodium (CNa), penicillin procaine (pen), ampicillin (amp), and tetracycline (tet).

[2]Numbers in brackets refer to the dairy (# assigned in study) that treats multiparous (M) and primiparous (P) cows differently.

counted for 60% of the total inertia (dimension 1: 35.6%; dimension 2: 24.3%). Associations were observed among dairy size >2,000 cows, the use of ceftiofur products to treat RFM, and starting the RFM antimicrobial treatment at 48 and 72 h (top-right quadrant). Dairy size ≤2,000 cows and starting RFM antimicrobial treat-

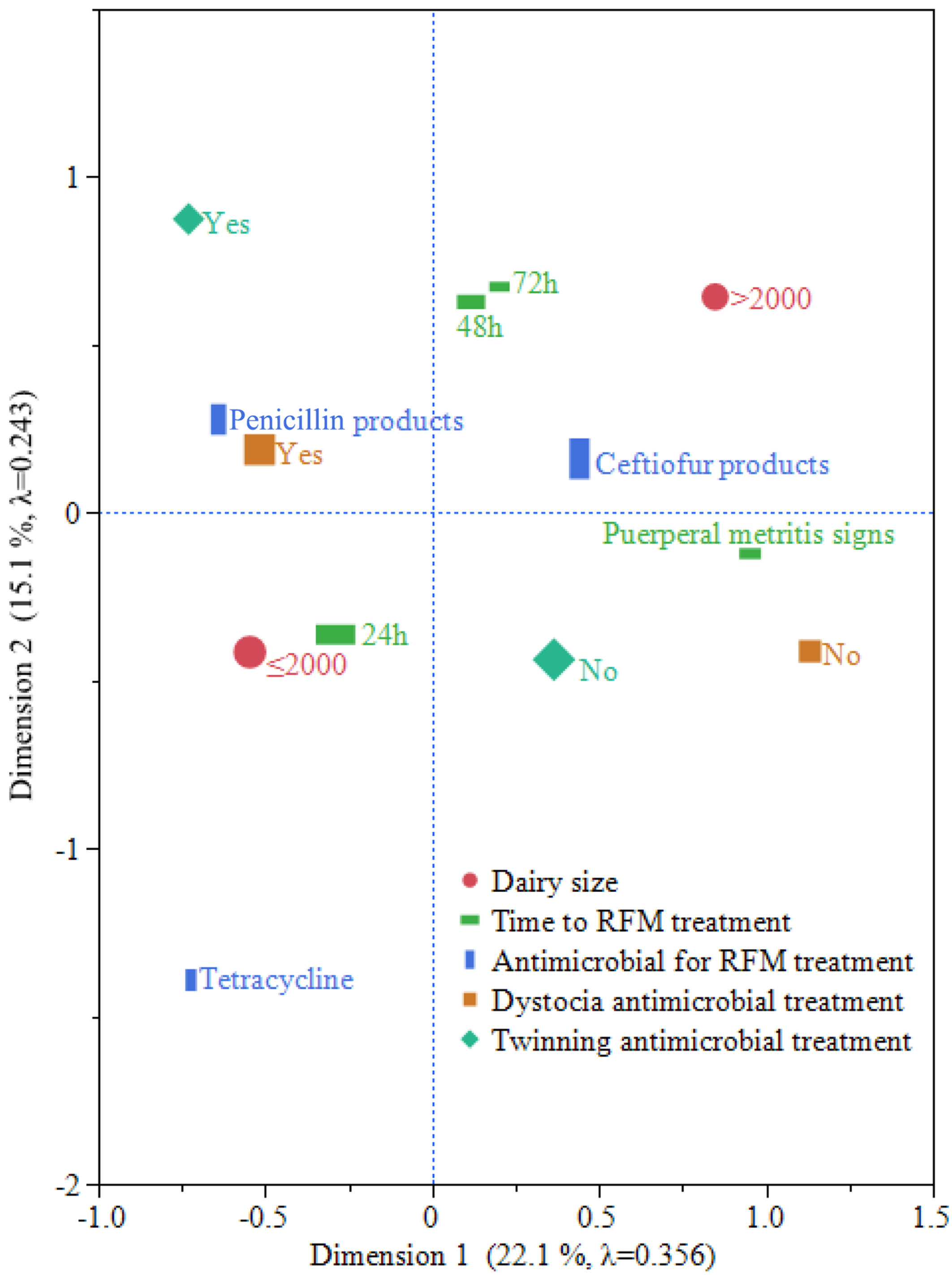

Figure 1. Map of multiple correspondence analysis evaluating the associations between dairy size (<2,000 or ≥2,000 cows), retained fetal membrane (RFM) treatment practices [time to RFM treatment (24 h, 48 h, 72 h, or puerperal metritis signs) and antimicrobial treatment choice for RFM (ceftiofur products, penicillin products, or tetracycline)], and the use of antimicrobials to treat dystocia (yes or no) or twinning (yes or no). The size of each symbol in the plot is proportional to the number of observations for each variable represented. For each dimension, the proportion of inertia and the inertia (ʎ) is presented.

ment at 24 h postpartum were associated (bottom-left quadrant). Dairies that delayed RFM treatment until observing signs of puerperal metritis were associated with dairies that did not use antimicrobials to treat nonsevere dystocia or twinning (bottom-right quadrant). Using antimicrobials to treat dystocia was associated with using antimicrobials to treat twinning and having penicillin products as the antimicrobial of choice for RFM treatment (top-left quadrant).

DISCUSSION

The present study evaluated antimicrobial use practices for the treatment of cows undergoing calving-related events (RFM, dystocia, or twinning). A convenience sample of 44 California dairy farms was enrolled in the study. Our study documented that antimicrobial treatments were often administered after calving-related events, with ceftiofur products being the drug class most commonly selected for treatment.

Systemic and intrauterine antimicrobials are commonly used to treat cows undergoing calving-related events (Peters and Laven, 1996; Heuwieser et al., 2010; Eppe et al., 2021); however, there is conflicting evidence in literature regarding antimicrobial effectiveness in these cases. Previous studies have indicated that cows at risk for puerperal metritis (dystocia, twins, RFM, hypocalcemia, or stillbirths) treated with ceftiofur products had lower incidence of puerperal metritis than untreated cows (Dubuc et al., 2011; McLaughlin et al., 2013); whereas outcomes from these studies support an improvement in the well-being of treated cows, no differences on reproductive performance or milk yield have been observed, bringing into question the cost-effectiveness of this practice (Dubuc et al., 2011; McLaughlin et al., 2013).

Furthermore, Bartolome et al. (2014) reported that blanket administration of CHCl to cows at risk for metritis (dystocia, twins, RFM, hypocalcemia, or stillbirth) had no effect on puerperal metritis incidence when evaluated 4 to 10 d postpartum. Accordingly, Drillich et al. (2006b) proved that cows with RFM assigned to blanket systemic antimicrobial treatment (CHCl; 1 mg/kg of BW, s.c. for 3 to 5 d postpartum) or selective treatment (if fever $\geq$39.5°C) had similar outcomes regarding fever and reproductive performance. Likewise, the effectiveness of intrauterine antimicrobial infusions for the treatment of cows with RFM remains questionable (Drillich et al., 2006a; Goshen and Shpigel, 2006), and poses potential detrimental effects if oxytetracyclines are used (inhibition of metalloproteinases; Arnoczky et al., 2004). Thus, based on the lack of consistent scientific evidence supporting antimicrobial use to treat cows at risk of metritis, Constable et al. (2008) and LeBlanc (2008) proposed an approach to limit antimicrobial therapy to cows with clinical signs of puerperal metritis (i.e., fetid vaginal discharge or abnormal nonfetid vaginal discharge with fever or signs of systemic illness). However, our findings agree with results from other recent European studies (Hehenberger et al., 2015; Eppe et al., 2021), suggesting a lack of agreement on the combination of clinical signs that should lead to antimicrobial treatment decisions. Thus, the aforementioned guidelines have yet to be widely adopted by dairy producers and veterinarians.

In California dairies, the most common antimicrobial class of choice for cows with RFM were ceftiofur products, used on 66% of the dairies. Similarly, ceftiofur products were used for nonsevere dystocia (30%) and twinning (23%). These results are in agreement with the USDA-NAHMS (2014) report which describes cephalosporin as the primary antimicrobial class used for reproductive disease in dairy farms in the United States, followed by penicillin and tetracycline. However, Zwald et al. (2004) reported that dairies in the Midwest and Northeast chose with similar frequency ceftiofur products (41.4%) or penicillin (43.4%) to treat metritis and RFM, suggesting regional preference of one drug class over another. In Belgium, most veterinarians treated RFM with penicillin products (benzylpenicillin, amoxicillin, and ampicillin), with few choosing cephalosporins (Eppe et al., 2021). Ceftiofur products do not require a milk-withdrawal period, which makes them very attractive therapeutic options in California dairy operations. However, the extra-label use of ceftiofur products, including its use for disease prevention, is prohibited. Thus, our results emphasize the need for outreach efforts to ensure stakeholders are informed about the efficacy and regulatory mandates for critically important drugs such as ceftiofur products.

Our study showed that there was partial agreement across dairies on time to commence treatment for cows with RFM. Most dairies treated cows at first health check, but some dairy operations (36%) chose to delay treatment 48 to 72 h postpartum. Delaying treatment may reduce the number of cows receiving treatment, as fetal membranes will be expelled either spontaneously (32%) or after light manual traction (50%; Eiler and Fecteau, 2007) by 2 to 4 d postpartum. Even though most fresh cow evaluators reported length of antimicrobials treatment according with label indications, 4 dairies reported to treat with antimicrobials until fetal membranes were expelled. Thus, the diverse treatment regimens for cows with RFM (antimicrobial class, dose, and time to initiation and duration of treatment) suggest a need to reach a greater agreement across dairy farms on treatment protocols. Currently no antimicrobial has a label approval for the treatment of RFM;

thus, all antimicrobial treatments are extra-label. However, if other diseases are concurrently occurring (i.e., metritis), antimicrobials can be prescribed following label recommendations.

The most used nonantimicrobial intrauterine treatment identified in our study was urea; however, although urea-based commercial products claim antiseptic and proteolytic activity, there is a lack of randomized control studies that prove its efficacy for intrauterine disease treatment. The possibility to treat cows with drugs other than antimicrobials may appeal to some dairy producers; if effective, those treatments could potentially improve odor and color of vaginal discharge, without the hazard of antimicrobial residues in meat or bulk tank milk. However, only treatments that are scientifically validated are prudent.

Manual removal of RFM is less common in California (33%) than in herds in the United Kingdom, Germany, or Belgium, where nearly 90% of dairy operations or veterinary practitioners reported adopting this practice (Peters and Laven, 1996; Heuwieser et al., 2010; Eppe et al., 2021). The combination of endometrial damage, bacterial invasion, suppression of uterine leukocytic phagocytosis, and the increased risk of uterine disease makes manual removal of the fetal membranes a strategy that is not recommended (Bolinder et al., 1988). Furthermore, manual removal of RFM was associated with delayed resumption of postpartum ovarian cyclicity and increased risks and severity of postpartum uterine infections (Bolinder et al., 1988). Thus, our observation illustrates the perpetuation of a practice, shown to be detrimental several decades earlier.

Cows enduring severe dystocia require surgery or invasive obstetric procedures. Based on a 1970s survey (Sloss, 1974a), Australian veterinarians had to often resort to cesarean section (3.8%) or fetotomy (13.1%) to resolve dystocia cases in dairy cows. In US dairy operations, dystocia cases ranged from 3.6 to 5.9%, and approximately 0.1% of the total calvings required cesarean section (USDA-NAHMS, 2014). Broad-spectrum systemic antimicrobials should be given after cesarean sections or fetotomies to prevent postintervention infections (Mijten, 1998). However, our study reported discrepancies in the antimicrobial of choice after these procedures. Ceftiofur products were used on some farms, but this practice should be re-evaluated to favor antimicrobials that are not critically important. In our study 3 dairies systematically culled all cows enduring severe dystocia that required surgery or invasive obstetric procedures. This approach might be the best course of action in severe dystocia cases, especially after considering cow's likelihood of survival, welfare, and economic value (Sloss, 1974b; Huxley and Whay, 2006).

It is well document that dystocia and twining increase the risk of RFM and postpartum metritis and have detrimental effects on reproductive performance (Erb et al., 1985; Eddy et al., 1991; Dubuc et al., 2010). As an attempt to mitigate the negative effects on uterine health associated with dystocia or twinning, prophylactic therapy seems to be a common practice adopted by dairy producers in California. However, as previously discussed, there is limited evidence supporting antimicrobial treatments after calving-related events to prevent uterine disease (Dubuc et al., 2011; McLaughlin et al., 2013; Bartolome et al., 2014). Systemic antimicrobial therapy may be adequate in dystocia cases where cervical, vaginal, or vulvar lacerations occur, especially if these lacerations become infected. Human intervention during nonsevere dystocia cases can increase the risk of uterine contamination, even when only a gentle pull is applied. Thus, limiting calving assistance to those cows that require it may reduce antimicrobial use postpartum. Also, performing obstetric practices that minimize uterine tract lacerations during dystocia resolution may decrease the need for antimicrobials postpartum. Our results highlight the importance of conducting educational efforts on antimicrobial decisions after dystocia cases and desirable calving management practices that may reduce the need for calving assistance and lacerations (Schuenemann et al., 2013).

Overall, the associations observed in the multiple correspondence analysis suggested that treatment practices differ with dairy size; thus, when conducting outreach efforts a slightly different emphasis might be needed when addressing small versus large dairies. It was also notable that dairies following a conservative approach to antimicrobial treatment did it across all the calving-related events evaluated in the present study. This is encouraging, as it seems to suggest that if dairy farmers favor rational use of antimicrobials, they will do it across different disorders.

Finally, when interpreting our results, it should be considered that our data were based on fresh cow evaluators' responses to open-ended questions and researchers' observations during RFM treatments on 55.6% of the dairies. However, the responses and behaviors of fresh cow evaluators might have been influenced by the presence of the 2 researchers. It is plausible that our results depict treatment practices that, to some degree, deviate from the usual practices implemented at the dairy. Furthermore, our data were collected 3 yr after the US Food and Drug Administration's Center for Veterinary Medicine (21 CFR Part 530) regulated the extra-label use of critically important drugs, and 3 yr prior to CA Senate Bill 27 (regulating over-the-counter antimicrobials; in effect in 2018). Thus, it is possible that treatment practices on CA dairies have evolved during the last few years.

CONCLUSIONS

Opportunities to reduce extra-label use of antimicrobials in postpartum cows affected with RFM, dystocia, and twinning were identified, as well as the need to reach consensus and promote standardized practices for antimicrobial use within the dairy industry. The present study highlights the need for antimicrobial use stewardship programs for calving-related events on dairies; all relevant stakeholders should be educated on the state of the art of antimicrobial efficacy (and lack thereof), especially of the most critically important molecules in human health, for the treatment of common postpartum ailments.

ACKNOWLEDGMENTS

This project was supported by University of California–Davis Innovative development award. The authors appreciate the collaboration of the participant dairies. We gratefully acknowledge the support of the following veterinarians and dairy consultants to enroll dairies in this project: John Champagne, DVM [Veterinary Medicine Teaching and Research Center (VMTRC), Tulare, CA]; Douglas Giovani, DVM; Lori Lenihan, DVM (Lander Veterinary Clinic, Turlock, CA); and Cesar Narciso, DVM (Sequoia Veterinary Services and IVF Lab Inc., Visalia, CA). Additional project support in data collection was received from Marc Pineda, DVM, and Sonia Rodríguez, DVM (VMTRC). The authors have not stated any conflicts of interest.

REFERENCES

Arnoczky, S. P., M. Lavagnino, K. L. Gardner, T. Tian, Z. M. Vaupel, and J. A. Stick. 2004. In vitro effects of oxytetracycline on matrix metalloproteinase-1 mRNA expression and on collagen gel contraction by cultured myofibroblasts obtained from the accessory ligament of foals. Am. J. Vet. Res. 65:491–496. https://doi.org/10.2460/ajvr.2004.65.491.

Bartolome, J. A., P. Khalloub, R. L. de la Sota, M. Drillich, and P. G. Melendez. 2014. Strategies for the treatment of dairy cows at high risk for postpartum metritis and for the treatment of clinical endometritis in Argentina. Trop. Anim. Health Prod. 46:79–85. https://doi.org/10.1007/s11250-013-0450-z.

Bolinder, A., B. Seguin, H. Kindahl, D. Bouley, and D. Otterby. 1988. Retained fetal membranes in cows: Manual removal versus nonremoval and its effect on reproductive performance. Theriogenology 30:45–56. https://doi.org/10.1016/0093-691X(88)90262-2.

Cabrera, V. E., and P. M. Fricke. 2021. Economics of twin pregnancies in dairy cattle. Animals (Basel) 11:552. https://doi.org/10.3390/ani11020552.

CDFA (California Department of Food and Agriculture). 2016. California Agricultural Statistics Review, 2015–2016. Accessed Jan. 20, 2021. https://www.cdfa.ca.gov/statistics/pdfs/2016report.pdf.

Chatterjee, A., M. Modarai, N. R. Naylor, S. E. Boyd, R. Atun, J. Barlow, A. H. Holmes, A. Johnson, and J. V. Robotham. 2018. Quantifying drivers of antibiotic resistance in humans: A systematic review. Lancet Infect. Dis. 18:e368–e378. https://doi.org/10.1016/S1473-3099(18)30296-2.

Constable, P. D., S. Pyörälä, and G. W. Smith. 2008. Guidelines for antimicrobial use in cattle. Pages 143–160 in Guide to Antimicrobial Use in Animals. L. Guardabassi, L. B. Jensen, and H. Kruse, ed. Blackwell.

Drillich, M., M. Mahlstedt, U. Reichert, B. A. Tenhagen, and W. Heuwieser. 2006a. Strategies to improve the therapy of retained fetal membranes in dairy cows. J. Dairy Sci. 89:627–635. https://doi.org/10.3168/jds.S0022-0302(06)72126-9.

Drillich, M., U. Reichert, M. Mahlstedt, and W. Heuwieser. 2006b. Comparison of two strategies for systemic antibiotic treatment of dairy cows with retained fetal membranes: Preventive vs. selective treatment. J. Dairy Sci. 89:1502–1508. https://doi.org/10.3168/jds.S0022-0302(06)72217-2.

Dubuc, J., T. F. Duffield, K. E. Leslie, J. S. Walton, and S. J. LeBlanc. 2010. Risk factors for postpartum uterine diseases in dairy cows. J. Dairy Sci. 93:5764–5771. https://doi.org/10.3168/jds.2010-3429.

Dubuc, J., T. F. Duffield, K. E. Leslie, J. S. Walton, and S. J. LeBlanc. 2011. Randomized clinical trial of antibiotic and Prostaglandin treatments for uterine health and reproductive performance in dairy cows. J. Dairy Sci. 94:1325–1338. https://doi.org/10.3168/jds.2010-3757.

Eddy, R. G., O. Davis, and C. David. 1991. An economic assessment of twin births in British dairy herds. Vet. Rec. 129:526–529.

Eiler, H., and K. A. Fecteau. 2007. Retained placenta. Pages 345–354 in Current Therapy in Large Animal Theriogenology, 2nd ed. R. S. Younquist and W. R. Threlfal, ed. W.B. Saunders. https://doi.org/10.1016/B978-072169323-1.50048-9

Eppe, J., T. Lowie, G. Opsomer, G. Hanley-Cook, M. Meesters, and P. Bossaert. 2021. Treatment protocols and management of retained fetal membranes in cattle by rural practitioners in Belgium. Prev. Vet. Med. 188:105267. https://doi.org/10.1016/j.prevetmed.2021.105267.

Erb, H. N., R. D. Smith, P. A. Oltenacu, C. L. Guard, R. B. Hillman, P. A. Powers, M. C. Smith, and M. E. White. 1985. Path model of reproductive disorders and performance, milk fever, mastitis, milk yield, and culling in Holstein cows. J. Dairy Sci. 68:3337–3349. https://doi.org/10.3168/jds.S0022-0302(85)81244-3.

Espadamala, A., P. Pallarés, A. Lago, and N. Silva-Del-Río. 2016. Fresh-cow handling practices and methods for identification of health disorders on 45 dairy farms in California. J. Dairy Sci. 99:9319–9333. https://doi.org/10.3168/jds.2016-11178.

Espadamala, A., R. Pereira, P. Pallarés, A. Lago, and N. Silva-Del-Río. 2018. Metritis diagnosis and treatment practices in 45 dairy farms in California. J. Dairy Sci. 101:9608–9616. https://doi.org/10.3168/jds.2017-14296.

FDA (U.S. Food and Drug Administration). 2020. Extralabel drug use in animals. In Electronic Code of Federal Regulations, 21 CFR Part 530.41. Accessed Jan. 20, 2021. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=530&showFR=1.

Giuliodori, M. J., R. P. Magnasco, D. Becu-Villalobos, I. M. Lacau-Mengido, C. A. Risco, and R. L. de la Sota. 2013. Metritis in dairy cows: risk factors and reproductive performance. J. Dairy Sci. 96:3621–3631. https://doi.org/10.3168/jds.2012-5922.

Gohary, K., and S. J. LeBlanc. 2018. Cost of retained fetal membranes for dairy herds in the United States. J. Am. Vet. Med. Assoc. 252:1485–1489. https://doi.org/10.2460/javma.252.12.1485.

Goshen, T., and N. Y. Shpigel. 2006. Evaluation of intrauterine antibiotic treatment of clinical metritis and retained fetal membranes in dairy cows. Theriogenology 66:2210–2218. https://doi.org/10.1016/j.theriogenology.2006.07.017.

Hehenberger, E. M., M. G. Doherr, M. Bodmer, A. Steiner, and G. Hirsbrunner. 2015. Diagnosis and therapy of retained fetal membranes, puerperal metritis and clinical endometritis in cattle: Results of the Online-survey among Swiss practitioners. Schweiz. Arch. Tierheilkd. 157:497–502. https://doi.org/10.17236/sat00032.

Heuwieser, W., M. Iwersen, J. Gossellin, and M. Drillich. 2010. Survey of fresh cow management practices of dairy cattle on small and large commercial farms. J. Dairy Sci. 93:1065–1068. https://doi.org/10.3168/jds.2009-2783.

Huxley, J. N., and H. R. Whay. 2006. Current attitudes of cattle practitioners to pain and the use of analgesics in cattle. Vet. Rec. 159:662–668. https://doi.org/10.1136/vr.159.20.662.

Jensen, L. B., F. J. Angulo, K. Mølbak, and H. C. Wegener. 2008 Human health risks associated with antimicrobial use in animals. Pages 13–26 in Guide to Antimicrobial Use in Animals. L. Guardabassi, L. B. Jensen, and H. Kruse, ed. Blackwell.

LeBlanc, S. J. 2008. Postpartum uterine disease and dairy herd reproductive performance – A review. Vet. J. 176:102–114. https://doi.org/10.1016/j.tvjl.2007.12.019.

McDougall, S. 2001. Effect of intrauterine antibiotic treatment on reproductive performance of dairy cows following periparturient disease. N. Z. Vet. J. 49:150–158. https://doi.org/10.1080/00480169.2001.36223.

McGuirk, B. J., R. Forsyth, and H. Dobson. 2007. Economic cost of difficult calvings in the United Kingdom dairy herd. Vet. Rec. 161:685–687. https://doi.org/10.1136/vr.161.20.685.

McLaughlin, C. L., E. P. Stanisiewski, C. A. Risco, J. E. P. Santos, G. E. Dahl, R. C. Chebel, C. LaGrow, C. Daugherty, L. Bryson, D. Weigel, J. Hallberg, and M. J. Lucas. 2013. Evaluation of ceftiofur crystalline free acid sterile suspension for control of metritis in high-risk lactating dairy cows. Theriogenology 79:725–734. https://doi.org/10.1016/j.theriogenology.2012.11.029.

Mijten, P. 1998. Puerperal complications after cesarean section in dairy cows and in double-muscled cows. Reprod. Domest. Anim. 33:175–179. https://doi.org/10.1111/j.1439-0531.1998.tb01339.x.

Oltenacu, P. A., A. Frick, and B. Lindhé. 1990. Epidemiological study of several clinical diseases, reproductive performance and culling in primiparous Swedish cattle. Prev. Vet. Med. 9:59–74. https://doi.org/10.1016/0167-5877(90)90042-G.

Peters, A. R., and R. A. Laven. 1996. Treatment of bovine retained placenta and its effects. Vet. Rec. 139:535–539. https://doi.org/10.1136/vr.139.22.535.

Potter, T. J., J. Guitian, J. Fishwick, P. J. Gordon, and I. M. Sheldon. 2010. Risk factors for clinical endometritis in postpartum dairy cattle. Theriogenology 74:127–134. https://doi.org/10.1016/j.theriogenology.2010.01.023.

Schambow, R. A., T. B. Bennett, D. Döpfer, and J. P. N. Martins. 2021. Retrospective study investigating the association of parity, breed, calving month and year, and previous parity milk yield and calving interval with twin births in US dairy cows. J. Dairy Sci. 104:5047–5055. https://doi.org/10.3168/jds.2020-19421.

Schuenemann, G. M., S. Bas, E. Gordon, and J. D. Workman. 2013. Dairy calving management: Description and assessment of a training program for dairy personnel. J. Dairy Sci. 96:2671–2680. https://doi.org/10.3168/jds.2012-5976.

Schuenemann, G. M., I. Nieto, S. Bas, K. N. Galvão, and J. Workman. 2011. Assessment of calving progress and reference times for obstetric intervention during dystocia in Holstein dairy cows. J. Dairy Sci. 94:5494–5501. https://doi.org/10.3168/jds.2011-4436.

Sheldon, I. M., and H. Dobson. 2004. Postpartum uterine health in cattle. Anim. Reprod. Sci. 82–83:295–306. https://doi.org/10.1016/j.anireprosci.2004.04.006.

Silva del Río, N., S. Stewart, P. Rapnicki, Y. M. Chang, and P. M. Fricke. 2007. An observational analysis of twin births, calf sex ratio, and calf mortality in Holstein dairy cattle. J. Dairy Sci. 90:1255–1264. https://doi.org/10.3168/jds.S0022-0302(07)71614-4.

Sloss, V. 1974a. A clinical study of dystocia in cattle 1. Treatment. Aust. Vet. J. 50:290–293. https://doi.org/10.1111/j.1751-0813.1974.tb05314.x.

Sloss, V. 1974b. A clinical study of dystocia in cattle 2. Complications. Aust. Vet. J. 50:294–297. https://doi.org/10.1111/j.1751-0813.1974.tb05315.x.

State of California. 2015. Senate Bill 27. Livestock: Use of antimicrobial drugs. Chapter 758, An act to add Chapter 4.5 (commencing with Section 14400) to Division 7 of the Food and Agriculture Code, relating to livestock. Accessed Nov. 17, 2017. https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=201520160SB27.

USDA-NAHMS. 2014. National Animal Health Monitoring System (NAHMS). Health and Management Practices on U.S. Dairy Operations.

World Health Organization (WHO), Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). 2017. Complete list of antimicrobials for human and veterinary use, categorized as Critically Important, Highly Important and Important. Pages 21–36 in Critically Important Antimicrobials for Human Medicine, 5th rev. WHO.

Zwald, A. G., P. L. Ruegg, J. B. Kaneene, L. D. Warnick, S. J. Wells, C. Fossler, and L. W. Halbert. 2004. Management practices and reported antimicrobial usage on conventional and organic dairy farms. J. Dairy Sci. 87:191–201. https://doi.org/10.3168/jds.S0022-0302(04)73158-6.

ORCIDS

N. Silva-del-Río https://orcid.org/0000-0002-2826-6797
A. Valldecabres https://orcid.org/0000-0002-3235-2487
A. García-Muñoz https://orcid.org/0000-0003-1545-7890
A. Lago https://orcid.org/0000-0003-0380-0292
F. S. Lima https://orcid.org/0000-0001-8377-6469
R. V. Pereira https://orcid.org/0000-0003-2028-8761