Article

A survey of antimicrobial use during bovine abdominal surgery by western Canadian veterinarians

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Abstract — Members of the Western Canadian Association of Bovine Practitioners were surveyed regarding their use of antimicrobials in bovine abdominal surgery. Perioperative antimicrobials were used in 100% of abdominal surgeries by 96 of 98 respondents. Although postoperative administration was the most common perioperative period for antimicrobial use, intraoperative intraperitoneal use was reported by more than half of the veterinarians surveyed. Procaine penicillin G and oxytetracycline were the most commonly administered perioperative antimicrobials.

Résumé — Enquête sur l'utilisation des antimicrobiens lors de chirurgies abdominales chez les bovins par des vétérinaires de l'ouest du Canada. Un sondage a été mené auprès des membres de l'association des praticiens bovins de l'ouest du Canada sur leur utilisation des antimicrobiens lors de chirurgies abdominales. En période périopératoire, les antimicrobiens ont été utilisés dans 100 % des chirurgies abdominales par 96 des 98 répondants. Même si la période postopératoire était la période périopératoire où l'utilisation d'antimicrobiens était la plus fréquente, l'utilisation intra-opératoire intrapéritonéale (IP) était rapportée par plus de la moitie des vétérinaires sondés. La pénicilline G procaïnique et l'oxytétracycline étaient les antimicrobiens périopératoires les plus fréquemment administrés.

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Introduction

The Canadian global food animal residue avoidance databank (CgFARAD) has received many requests for meat and milk withdrawal recommendations after perioperative extralabel use of antimicrobials, including the intraperitoneal (IP) or intra-abdominal infusion of antimicrobials. Due to the unhygienic operating conditions often encountered during ambulatory surgeries, many veterinarians choose to administer perioperative antimicrobials. Gram positive staphylococci, gram negative enteric bacteria, and anaerobes are all potential contaminants during ambulatory bovine surgery. In human medicine, current guidelines call for prophylactic antimicrobials to be selected, based on predicted efficacy against probable pathogens, and administered before microbial contamination occurs (1,2). The success of preoperative antimicrobial prophylaxis has also been demonstrated in bovine surgery (3). However, due to the withdrawal times required for most antimicrobials used in cattle, presurgical antimicrobials may be withheld, if the prognosis is uncertain and the animal is to be salvaged for slaughter. Following successful corrective surgery, practitioners may opt to administer antimicrobials directly into the abdomen.

The IP route is employed in human abdominal surgery and peritoneal dialysis, with cephalosporins and aminoglycosides commonly being used (4–6). All reports cite antimicrobial formulations suitable for intravenous (IV) use that are thoroughly diluted in appropriate lavage/dialysis solutions. The efficacy of IP antimicrobials in reducing infections after human abdominal surgery has not been proven decisively. The kinetics of IP antimicrobials in humans are variable, with maximum plasma concentrations occurring from 15 min to 5 h after administration for various antimicrobials (4,5,7). Intraperitoneal antimicrobials are also used in animal species, including dogs, rabbits, and fish (8–11). One trial in rabbits found that an abdominal lavage containing saline and a cephalosporin was more efficacious than one containing saline alone for treating peritonitis, but only if the bacterial contamination was severe and the antimicrobial was administered promptly after contamination (10). Experimental trials in cows have used IP infusions of oxytetracycline in saline and ampicillin/cloxicillin and kanamycin/penicillin preparations designed for intramammary use (12–14). One retrospective study showed a lower rate of postsurgical infection in cows after IP administration of antimicrobials compared with cows not given antimicrobials (14). However, comparisons involving

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the use of preoperative intravenous (IV) prophylaxis are lacking.

Although the IP route is generally considered nonirritating and safe in human medicine, the formulation of the antimicrobial may play an important role. There is evidence of peritonitis in cows after IP infusions of an ampicillin anhydrate formulation, but not of sodium ampicillin (15). Other antimicrobials and formulations have not been evaluated for peritoneal inflammation or safety. Another issue that has not been addressed in cattle is withdrawal times after IP administration. Because this practice is extralabel, practitioners have contacted CgFARAD for advice regarding meat and milk withdrawal times. Unfortunately, insufficient data is available in the literature to develop an informed withdrawal interval estimate. The CgFARAD has received anecdotal reports of cows with penicillin-positive milk samples for weeks after perioperative IP use, though cows given ampicillin by IP infusion had positive milk tests for only 24 to 96 h, depending on the formulation (15). Tissue residue depletion kinetics in cows are not available, but a 1955 study found residues in muscle, kidney, and liver in bulls given IP oxytetracycline 1 h before slaughter (16). As well, in trials involving IP injections of oxytetracycline and macrolides in salmon, detectable drug residues were found in various tissues up to 8 wk later (8,9).

The frequency of IP antimicrobial administration during bovine surgery has not been reported. Before pursuing a kinetic trial to evaluate this practice, we surveyed members of the Western Canadian Association of Bovine Practitioners (WCABP) on their use of antimicrobials during bovine abdominal surgery. The objective was to establish the occurrence and describe the use of perioperative antimicrobials by bovine veterinarians, with special emphasis on IP administration

Materials and methods

Survey design

In June of 2005, surveys were mailed to all 240 members of the WCABP, a voluntary membership organization representing mixed and large animal veterinarians practising beef and/or dairy medicine in the 4 western Canadian provinces. Surveys were mailed, along with prepaid return envelopes, as part of the WCABP quarterly newsletter. The survey was designed by 2 of the authors (AC, PD). It was not pretested, but it was reviewed by a bovine practitioner at the Western College of Veterinary Medicine, whose comments were incorporated into the final survey design. Respondents were asked to record the percentage of cattle undergoing abdominal surgery that they treated with antimicrobials at each of 3 surgical time periods (preoperative, postoperative, and IP). Although data regarding IP use was the primary motivation for the survey, questions about preoperative and postoperative antimicrobial use questions were included to give perspective on IP use compared with preoperative and postoperative use. Veterinarians were also asked to list which drug(s) and what dose and route of administration they commonly used at each surgical time period. Trade or generic names of antimicrobials were accepted. Because IP antimicrobial use is extralabel, veterinarians were also asked for the meat and milk withdrawal intervals (WDI) they recommended after IP use.

Statistical analysis

The percentages of abdominal surgeries in which antimicrobials were administered at the 3 perioperative time periods were compared. Individual practitioner reported percentage of surgeries receiving antimicrobials in the 3 perioperative periods was not correlated (a practitioner who reported using preoperative antimicrobials in a high percentage of surgeries did not necessarily report using IP antimicrobials in a low percentage of surgeries, etc.), so, for analysis, all practitioner reported percentages were grouped in 3 levels of the perioperative time period for analysis. As the data were not normally distributed, a Kruskal-Wallis one-way analysis of variance was used to test for differences between reported percentages of surgeries receiving antimicrobials for each perioperative time period ($\alpha = 0.05$). Post-hoc comparisons were performed with the Wilcoxon rank-sum test and Bonferroni's correction. Data were analyzed by using a commercial software package (Statistix Version 8; Analytical Software, Tallahassee, Florida, USA).

Results

Response rate and data tabulation

Survey responses were received for 6 wk after mailout. The survey response rate was 40.8% (98/240). As responses were anonymous, no specific follow-up with either nonrespondents or respondents was possible. A general follow-up to all survey recipients was not performed. Drugs were categorized according to their generic formulation, regardless of brand. Percentages of antimicrobial administration were combined into the following categories: Never (0%), Rarely (1% to 24%), Sometimes (25% to 74%), and Often (75% to 100%). Since there were few respondents that identified use as either 25% to 50% or 50% to 74% these responses were combined for inclusion in the "Sometimes" category.

Perioperative antimicrobial use

Of the 98 respondents, 96 treated all cattle with some type of perioperative antimicrobial. Seventy-nine of 98 respondents administered postoperative antimicrobials to at least 75% of their surgical patients. Intraoperative antimicrobial use, at least some of the time, was reported by 54 of 98 respondents, and often by 30 of 98 respondents. Forty-four of 98 respondents never utilized IP antimicrobials. Those using IP antimicrobials reported a percentage of administration ranging from 1% to 100% of surgeries. Preoperative antimicrobials were administered often by 18/98 respondents, but never by (52/98) of respondents. Overall, the Kruskal-Wallis ANOVA detected a significant difference ($P < 0.001$) in the reported percentages of antimicrobial use among the 3 perioperative time periods of administration; post-hoc analysis revealed that the distribution of reported percentages for postpoperative administration was higher than for both preoperative and IP administration. No significant difference between the reported percentages for preoperative and IP administration was observed.

Types and doses of antimicrobials used

The antimicrobials predominantly used perioperatively by the survey respondents are shown in Figure 1. Overall, penicillin and oxytetracycline were the most commonly used antimicrobial

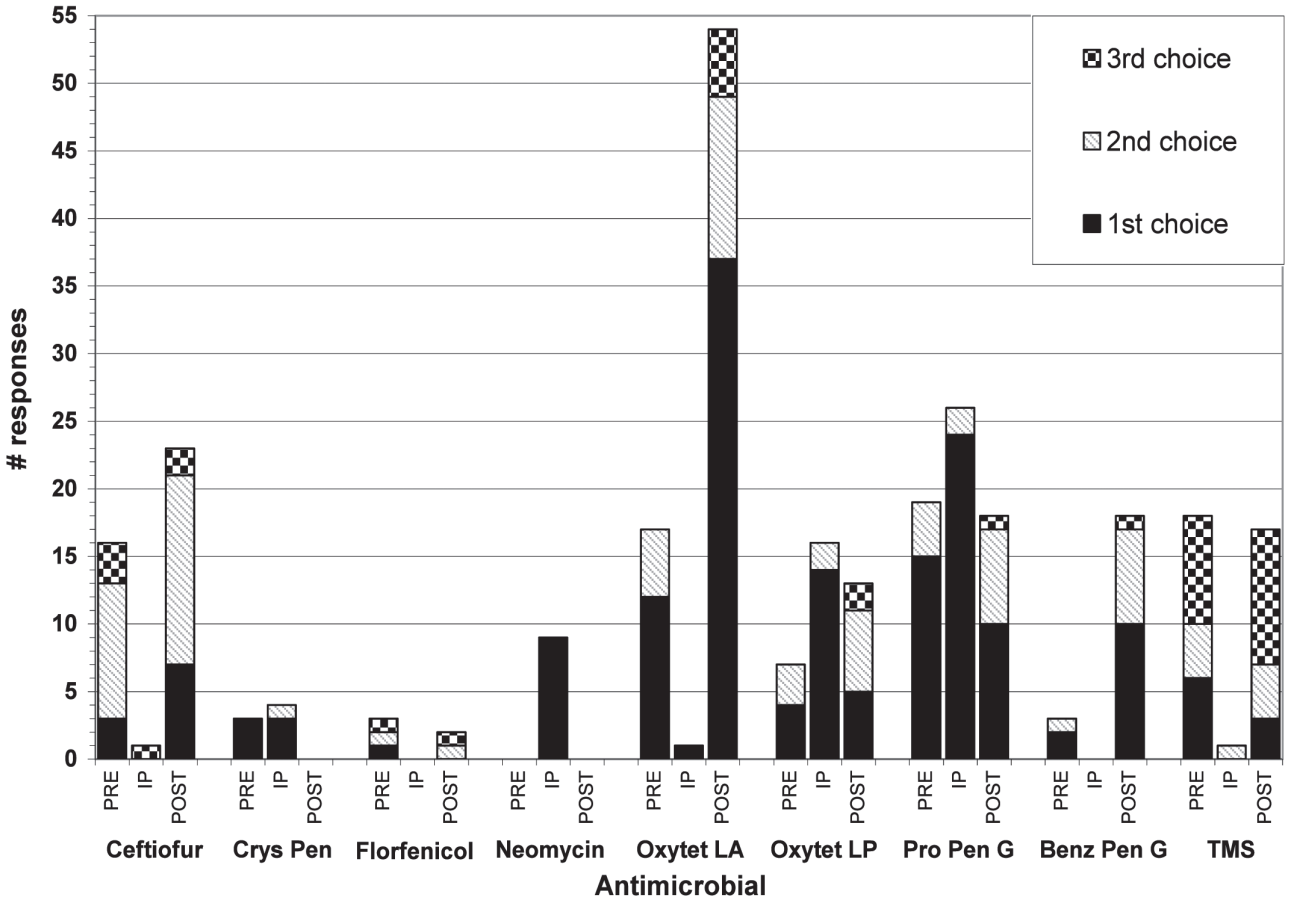

Figure 1. Frequency of perioperative antimicrobial administration by type of antimicrobial and time of administration

PRE – preoperative, IP – intraperitoneal, POST – postoperative
Crys Pen – crystalline penicillin G
Oxytet LA – oxytetracycline (long-acting formulation)
Oxytet LP – oxytetracycline (short-acting formulation)
Pro Pen G – procaine penicillin G (short-acting)
Benz Pen G – benzathine + procaine pencillin G (long-acting)
TMS – trimethoprim/sulfonamide combination

at each perioperative period. Other antimicrobials used included chlorhexidine (IP; $n = 1$), nitrofurazone (IP; $n = 1$), and sulfamethazine (IP; $n = 1$; postoperative, $n = 1$). Doses of preoperative and postoperative antimicrobials closely followed the manufacturer's label recommendations. Predominantly, the doses of the IP antimicrobials used were similar to the label IM/SC dose ($n = 28$), with 8 respondents using more and 3 using less than the label dose.

IP meat and milk withdrawal intervals

Withdrawal intervals recommended by respondents after IP administration of various antimicrobials are shown in Figure 2. The WDIs ranged from 3 to 14 d ($n = 14$) for procaine penicillin G (PPG) in milk, 3 to 60 d ($n = 5$) for oxytetracycline LP in milk, and 5 to 120 d ($n = 51$) for various antimicrobials in meat. Thirteen of 14 respondents recommended a milk WDI of 96 h or more after using IP procaine penicillin G, and 5/5 recommended 72 h or more after IP oxytetracycline LP use. Recommended meat WDIs were ≥ 10 d for 23/25 respondents who used IP procaine penicillin G, and ≥ 18 d for 9/11 respondents after IP oxytetracycline LP use.

Discussion

The purpose of this survey was to develop a better understanding of the current perioperative antimicrobial practices of bovine veterinarians in western Canada, with specific emphasis on IP use. Members of the Western Canadian Association of Bovine Practitioners (WCABP) were chosen to receive this survey as they were deemed representative of bovine practitioners in western Canada even though only approximately 27% of veterinarians in western Canada performing bovine work are members of the WCABP. Few veterinary clinics have more than 1 WCABP member, so clustering of responses by clinic would be minimized in this study. Potential biases may be present in the survey results. Antimicrobial usage by WCABP members may not mirror that of non-WCABP bovine practitioners, or that of the WCABP members who did not respond to the survey. A lack of central information on other veterinarians practising bovine medicine in western Canada precluded sending surveys to non-WCABP members.

Interpretation of survey results was also limited by other factors. Veterinarians who routinely use perioperative antimicrobials

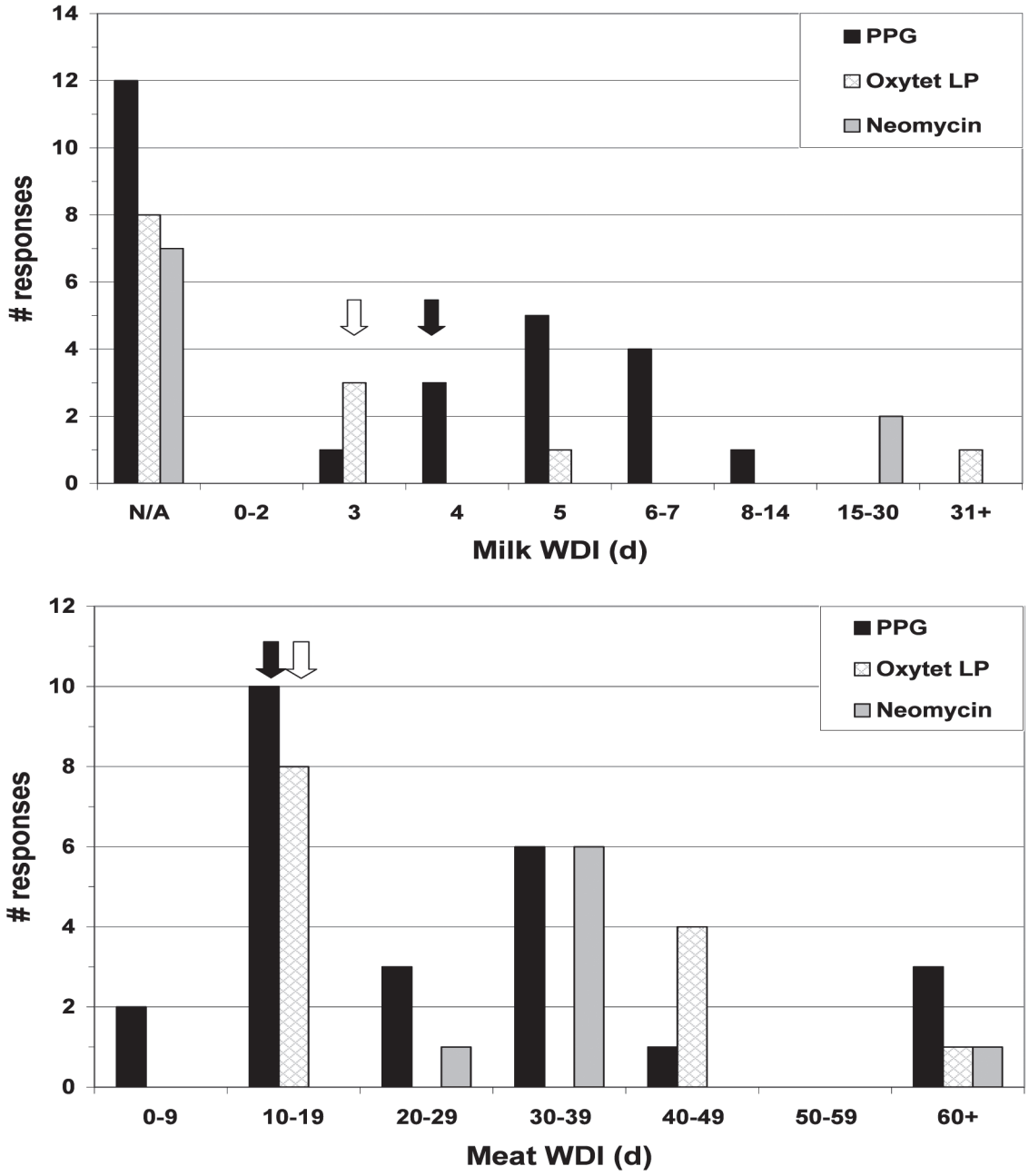

Figure 2. Milk and meat withdrawal intervals (WDIs) recommended by veterinarians after IP use of primary antimicrobials

PPG – procaine penicillin G
Oxytet LP – oxytetracycline LP (short-acting)
Vertical arrows indicate manufacturer's label withdrawal time (WDT) after intramuscular administration. Empty arrow – oxytetracycline LP: WDT, 3 d (milk), 18 d (meat). Solid arrow – procaine penicillin G: WDT, 4 d (milk), 10 d (meat). Neomycin is not labeled for parenteral use in cattle and does not have an established milk or meat withdrawal time. N/A – not applicable (no milk WDI given for beef cattle).

may have been more likely to respond than nonusers. The percentage of surgeries receiving antimicrobial treatment was likely a "best guess" and may have been under- or over-estimated. As respondents were instructed to write their specific antimicrobial choices and dose regimens, answers were sometimes ambiguous. To maintain survey brevity and confidentiality, respondents were not asked for information on personal and practice details that might affect antimicrobial usage, such as veterinary school attended, year of graduation, or how their perioperative regimen was established. However, despite these difficulties, a number of observations can be made from the data.

Perioperative antimicrobial use is routine during bovine abdominal surgery, as nearly all respondents treated all of their bovine abdominal surgery patients with an antimicrobial. The most common surgical period for antimicrobial administration in this group of respondents was postoperatively, despite limited evidence for its efficacy compared with preoperative administration (3). It is unknown why practitioners continue to favor this

practice when other alternatives appear more effective. Perhaps the evidence of limited efficacy has not reached practitioners or their empirical surgical success leads them to believe postoperative therapy is beneficial. The relatively low use of preoperative antimicrobial administration is also surprising, given the importance of adequate systemic drug concentrations when surgery is initiated (1,2). As well, some drugs used preoperatively in this survey are long-acting formulations (such as oxytetracycline LA or benzylpenicillin) that do not achieve therapeutic plasma concentrations by the time surgery is underway (17,18). One possible reason for the hesitancy of practitioners to use preoperative antimicrobials is an unwillingness to incur a long withdrawal time, if the prognosis following surgery is poor and the animal will be sent to slaughter (15). This reason is not valid, as the use of lidocaine before surgery will result in a 5-day meat withdrawal time. Likewise, if prolonged withdrawal times are a concern for the producer, an antimicrobial can be chosen that has no milk or meat withdrawal time (ceftiofur sodium).

Intraperitoneal antimicrobial use also occurred during bovine abdominal surgery. The small survey size does not allow for a precise determination of the frequency of IP use in individual animal surgeries. However, a sufficient number of respondents indicated that they commonly administer antimicrobials IP (30/98 respondents $\geq$ 75% of their surgeries) to conclude that this practice is not an isolated occurrence. Possible rationales for IP use include ease of administration, perceived quicker absorption than with intramuscular or subcutaneous injections, and a perceived local antimicrobial effect. However, IP kinetic data is limited, and a local (peritoneal) antimicrobial effect has not been proven.

The majority of WDIs recommended after IP antimicrobial administration were longer than the manufacturer's label withdrawal time (WDT) after intramuscular use of the same drug. Respondents were not specifically asked whether on-farm drug residue milk tests were used, or if CgFARAD was contacted for a withdrawal recommendation. A large number of "not applicable" responses were given for milk withdrawal recommendations, presumably because the surgeries were performed on beef cattle.

Procaine penicillin G and oxytetracycline were the most commonly administered perioperative antimicrobials. However, some clearly inappropriate drugs were administered perioperatively as well. These include the IP use of neomycin (inappropriate spectrum of activity, chemical irritation, and prolonged residues due to renal accumulation), nitrofurazone (banned in food producing animals), and chlorhexidine (chemical irritation).

Perioperative antimicrobial use was practised by the majority of WCABP members who responded to this survey. Postoperative administration was the most common perioperative period for antimicrobial use, but IP use was reported to occur in at least some surgeries by more than half of the respondents. Information on IP antimicrobial use provided by this survey has guided the specific direction of the authors' ongoing IP antimicrobial pharmacokinetic trials.

Authors' contributions

Dr. Chicoine performed the literature review, drafted the survey, compiled the survey results and statistics, and wrote the initial manuscript. Dr. Dowling provided the initial ideas behind this project, drafted the survey, and interpreted results. Dr. Boison offered input during survey design and analysis. Dr. Parker was instrumental in statistical analysis and helped write the manuscript discussion. All authors were involved in editing the manuscript.

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