
Cross-sectional study of antibiotic use in caesarean section and left displaced abomasum correction by bovine veterinarians in the Netherlands

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ABSTRACT

Background: Political, scientific and societal concerns about antibiotic resistance resulted in a decrease in antibiotic use in the Dutch dairy sector but no information was available about the use of antibiotics surrounding bovine abdominal surgeries.

Objective: The purpose of this study was to collect data on the antibiotic prophylaxis in caesarean sections (CSs) and left displaced abomasum (LDA) corrections in the Netherlands.

Study design: Cross-sectional questionnaire

Methods: An online questionnaire was sent to 373 members of the specialist-ruminant sub-department of the Royal Dutch Veterinary Association (KNMvD). The questionnaire consisted of questions about demographic details of the respondents, how they performed their latest CS and LDA correction and about the timing, application method, and the used antibiotics around these surgeries.

Results: A total of 113 members of the specialist-ruminant sub-department completed the online survey. All the respondents used antibiotics for their latest performed caesarean section (CS) and 79 respondents for their latest LDA correction. Recent graduated veterinarians (<10 years work experience) used less antibiotics around CSs than older graduates. Antibiotics were overall significantly more often used postoperatively compared to pre- and intra-operative antibiotic administration (odds ratio= 10.29; CI 6.43-17.07). Benzylpenicillin, aminopenicillins and combinations of these antibiotics with aminoglycosides were most frequently used for both surgeries.

Conclusion: More education of veterinarians is needed to improve a more prudent use of prophylactic antibiotics around CSs and LDA corrections in the Netherlands.

INTRODUCTION

Until recently, the livestock industry used increasing amounts of antibiotics to cure and prevent bacterial diseases. In order to limit the selection for antibiotic resistance, the use of antibiotics for growth promotion was banned in Europe in 2006 (Smith, 2015). In 2007, The Netherlands had the highest veterinary antibiotic consumption in a group of ten European countries, whereas

the antibiotic usage in humans in the Netherlands was absolutely low (Grave et al., 2010). This controversy led to heavy political, scientific and societal discussions and finally resulted in the implementation of a national antibiotic reduction policy in the Netherlands in 2008 in order to decrease antibiotic use by 20% in 2011 and up to 70% in 2015 compared to the use in 2009 (D. C. Speksnijder et al., 2015b). The Netherlands Veterinary Medicines Institute (SDa) was

founded as an independent institute to quantify antimicrobial use (AMU) by means of daily defined dosages, to establish standards for AMU per livestock sector for benchmarking and to calculate its reduction. In order to achieve these goals, disease-specific antibiotic guidelines per animal species were developed to assist veterinarians in their decision for specific antibiotics (D. C. Speksnijder et al., 2015b). In these guidelines, special attention was given to the reduction of antibiotics that are of critical importance for human medicine. Furthermore, farmers and veterinarians were benchmarked for their antibiotic use. Together with a few other actions, this strategy resulted in an overall reduction in antibiotic use of 63,4% in 2017 (MARAN, 2018).

It appeared that there were large differences in antibiotic use between different sectors of the livestock industry. The Dutch dairy sector had the lowest antibiotic use and had also limited antibiotic resistance in

comparison to other livestock sectors. Nevertheless, a further reduction was achieved, which was largely due to the introduction of “selective dry cow treatment”, as those treatments were responsible for the majority of the antibiotic treatments in the dairy sector (Lam et al., 2013). Until now, less attention was paid to the prudent use of antibiotics for treatments with a relative low prevalence, such as the use of prophylactic antibiotics around bovine abdominal surgeries. In the ideal situation, the application of prophylactic antibiotics in surgeries is based on the wound classification (Dumas et al., 2016; Zinn, 2012). A widely used wound classification is the classification of the US National Research Council (Mangram et al., 1999) as represented in Table 1. This classification is based on the estimated level of bacterial contamination of human wounds and is also commonly cited in the veterinary literature (Dumas et al., 2016).

Classification	Criteria
Clean	[...]An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria
Clean-contaminated	[...]An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
Contaminated	[...]Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.
Dirty	[...]Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation

Table 1. Surgical wound Classification (Mangram et al., 1999)

Caesarean sections (CSs) are common abdominal surgeries in farm animal practice. As the genital tract is entered during this surgery, the wound is classified as clean-contaminated and this justifies antibiotic prophylaxis. Other abdominal surgeries in cows, such as surgical corrections of left displaced abomasum (LDA) and exploratory laparotomies, should be classified as clean and would not necessarily require antibiotic prophylaxis. The validity of these strategies is recently showed in a clinical trial (Jorritsma et al., 2018).

Restrictive use of antibiotic prophylaxis may be possible, but there is also a certain risk of complications and associated economic loss. We acknowledge that in clinical practice it is difficult to estimate this risk in a given situation. In those circumstances, risk averse behavior of practitioners to avoid complications is understandable but may result in the use prophylactic of antibiotics. The use of prophylactic antibiotics in LDA corrections and CSs in the Netherlands has not been published yet. A better insight into current practices is needed to see if suitable antibiotics are used at the appropriate time and route of administration. The objective of this research was to collect data on the antibiotic prophylaxis in these surgeries.

MATERIALS AND METHODS

SURVEY DESIGN/ SURVEY DISTRIBUTION

In August 2018, a cross sectional questionnaire on prophylactic antibiotic usage around CSs and LDA corrections was compiled. The online questionnaire was, in collaboration with the Royal Dutch Veterinary Association (KNMvD), sent to the target population of 373 members of the specialist-ruminant sub-department. The survey was created online using the software EvaSys V7.0 ("Survey Automation Software - EvaSys and EvaExam,") and consisted of fourteen open and seventeen

multiple choice questions. The survey was announced within the network of the researchers using social media. Non-responders received automatically a reminder after 2 weeks. To avoid a bias towards politically correct answers, the veterinary clinicians were able to submit their answers anonymously and were specifically asked how they performed their latest LDA correction and CS. The questions were divided into three sections. The first section consisted of questions about gender, working experience, working time spent with cattle, time since latest performed LDA correction and CS, and the availability of specific protocols for the usage of antibiotics around abdominal surgeries. Survey sections two and three included questions about the timing, application method, and the used antibiotics around CS and LDA correction respectively. Respondents who did not perform a CS or an LDA correction were excluded from the data analyses.

DATA ANALYSES/STATISTICAL ANALYSES

The data were downloaded into Microsoft Excel (2016) for descriptive statistics. For each surgery type, the use of antibiotics at different administration periods, application methods, operation techniques and years of work experience were compared. A logistic regression model was used to test for significant ($\alpha=0,05$) differences in antibiotic use between gender, administration period and years of work experience as binary independent variables and antibiotic administration as binary dependent variable. Gender (male/female), administration periods (pre, intra-, post) and years of work experience (0-10, 10-20, 20-30, 30>) were used in the models as fixed effects and respondents were assessed as random effects. The Akaike's information criteria was used to reduce the multivariable model and odds ratios were calculated of the remaining variables. The data was analyzed with RStudio version 3.3.1.

RESULTS

SURVEY RESPONSE RATE AND RESPONDENT DEMOGRAPHICS

A total of 113 veterinarians completed the online survey resulting in a response rate of 30% (113/373). Respondent demographics are shown in Table 2. Ninety-two percent of the respondents worked in a clinic with 3 or more veterinarians. Specific protocols on antibiotic use were available for 74% of the respondents for CSs and for 64% for LDA corrections.

PRE, INTRA-, POSTOPERATIVE ANTIBIOTIC USE AROUND BOVINE ABDOMINAL SURGERIES

CAESAREAN SECTIONS

A total of 111 of the 113 respondents reported that they performed CSs. All the respondents reported that they used a certain antibiotic prophylaxis for their latest performed CS. Many respondents (76/111)

used more than one antibiotic strategy and 13 (17%) of these 76 respondents used more than two antibiotic strategies. Fifty-two (47%) of 111 respondents administered antibiotics preoperative and 44 (40%) respondents administered antibiotics intra-operative. An overview of the intra-operative antibiotic use during CSs is shown in Figure 1. In addition, 55 (50%) of 111 respondents used intra-uterine antibiotic tablets and 32 (29%) respondents used antibiotic spray on the wound. After the surgery, 104 (94%) respondents initiated postoperative antibiotic treatment, although 75% of the CSs were performed without complications, 13% with minor complications and 12% with serious complications in aseptic technique. Postoperative antibiotic treatment was continued for longer than 24 hours in 103 cases and for longer than 3 days in 13 cases. Postoperative antibiotic use was the most frequently used administration strategy (odds ratio= 18.18; CI 8.11- 46.91) compared with pre-, and intra-operative administration.

Question	Response	Respondents	
Gender		Number	(%)
	Male	89	78,8%
	Female	24	21,2%
Years of work experience	0-10	21	18,6%
	10-20	28	24,8%
	20-30	35	31,0%
	> 30	29	25,7%
	Percentage of time working with cattle		
	0-25%	2	1,8%
	25-50%	10	8,8%
	50-75%	24	21,2%
	75-100%	77	68,1%
Number of veterinarians in practice	1-3	9	8,0%
	3-5	26	23,0%
	5-8	27	23,9%
	>8	51	45,1%

Table 2. Characteristics of the 113 respondents

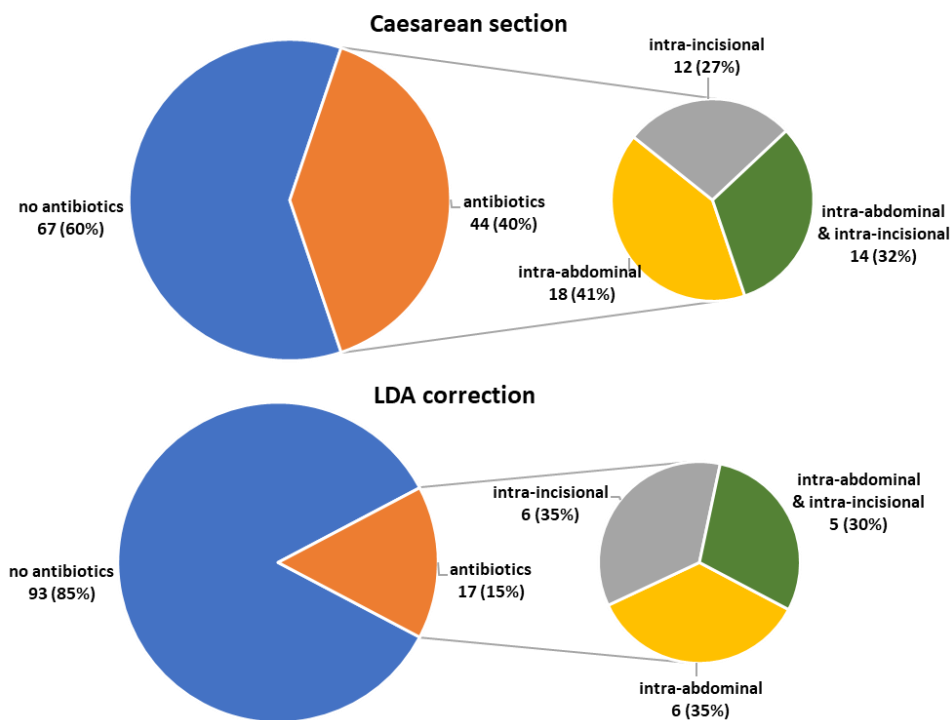


Figure 1. Overview of intra-operative antibiotic use during CS and LDA correction

LDA CORRECTIONS

A total of 110 respondents reported that they performed a LDA correction. Twenty-six (24%) respondents performed laparoscopic abomasopexy, 26 (24%) respondents used left flank laparotomy with ventral omentopexy (Utrecht method), 45 (41%) respondents used right flank laparotomy with pyloro-omentopexy and 13 (12%) respondents used other techniques, such as the Grymer-Sterner toggle technique. The frequencies of antibiotics used for the different correction techniques are shown in Table 3.

Seventy-nine (72%) of 110 respondents used antibiotics for their latest performed LDA correction. Twenty-two of 110 (20%) respondents used preoperative antibiotics and 17 (15%) of 110 respondents used intra-operative antibiotics during LDA corrections. The frequency of different intra-operative antibiotic administration strategies during LDA corrections are shown in Figure 1. After surgery, 39 (35%) of all respondents used antibiotic spray on the wound. Postoperative antibiotics were used by 72 (65%) respondents, although

85% of the LDA corrections were performed without complications, 11% with minor complications and 4% with serious complications in aseptic technique. Postoperative antibiotic treatment was continued for longer than 24 hours in 69 cases and for longer than 3 days in 4 cases. Around LDA corrections, post-operative antibiotic use was also the most frequently used administration strategy (odds ratio= 9.34; CI 4.66-20.83).

Technique	Antibiotics used	No antibiotics used
<i>Laparoscopic abomasopexy</i>	11 (42%)	15 (58%)
<i>Left flank laparotomy</i>	23 (88%)	3 (12%)
<i>Right flank laparotomy</i>	42 (93%)	3 (7%)
<i>Grymer-Sterner toggle</i>	3 (23%)	10 (77%)
Overall	79 (72%)	31 (28%)

Table 3. Antibiotic use for different LDA correction techniques

DIFFERENCE BETWEEN YEARS OF WORK EXPERIENCE AND ANTIBIOTIC ADMINISTRATION.

An overview of the antibiotic use between the different years of work experience is shown in Table 4. The logistic regression model showed more frequent antibiotic use (odds ratio= 2.7 CI 1.2-6.3; 2.7 CI 1.2-5.9; 2.3 CI 1.0-5.2) during CSs by veterinarians with 10-20 years, 20-30 years and more than 30 years of experience compared to veterinarians with 0-10 years of work experience. According to these odds, recent graduated veterinarians (<10 years work experience) used less frequently antibiotics during CSs than older graduates. For LDA corrections, no statistical differences were found between antibiotic use and different years of work experience.

TYPES OF ANTIBIOTICS USED AT DIFFERENT SURGICAL PERIODS

The different antibiotics administered at each occasion related to CS and LDA correction are shown in Figure 2. Overall, benzylpenicillin, aminopenicillins and combinations of these antibiotics with aminoglycosides were most frequently used. Other

administered antibiotics were gentamicin and oxytetracycline. Respondents used significantly ($p < 0.001$) less antibiotics around LDA corrections (odds ratio=0.23; CI 0.15-0.34) compared to CSs. Antibiotics were significantly more often used postoperatively (odds ratio= 10.29; CI 6.43-17.07) compared to pre- and intra-operative antibiotic administration. In both surgeries, Intramuscular (I.M.) administration of prophylactic antibiotics was the most frequently used administration route, even preoperatively (CS=39/52; LDA=14/22) with administration time varying between 0-30 minutes prior to surgery.

DISCUSSION

The objective of this study was to describe and assess the use of antibiotic prophylaxis surrounding bovine abdominal surgeries in the Netherlands. There are a few studies regarding the opinions, attitudes and perceptions of Dutch veterinarians on prescribing antibiotics (Lam et al., 2017; Postma et al., 2016; David C. Speksnijder et al., 2015; D. C. Speksnijder et al., 2015a).

Antibiotic administration at different surgical periods			
<i>Caesarean section</i>			
Years of work experience	Pre	Intra	Post
<i>0-10 year (n=20)</i>	7(35%)	2(10%)	19(95%)
<i>10-20 year(n=27)</i>	12(44%)	13(48%)	27(100%)
<i>20-30 year (n=35)</i>	21(60%)	15(43%)	31(89%)
<i>30 > year (n=29)</i>	12(41%)	14(48%)	27(93%)
Total antibiotic use (n=111)	52(47%)	44(40%)	104(94%)
<i>LDA correction</i>			
Years of work experience	Pre	Intra	Post
<i>0-10 year (n=20)</i>	5(25%)	1(5%)	14(70%)
<i>10-20 year(n=27)</i>	6(22%)	3(11%)	15(56%)
<i>20-30 year (n=35)</i>	7(20%)	4(11%)	22(63%)
<i>30 > year (n=28)</i>	4(14%)	9(32%)	21(75%)
Total antibiotic use (n=110)	22(20%)	17(15%)	72(65%)

Table 4. Reported antibiotic use in CS and LDA correction for different years of work experience

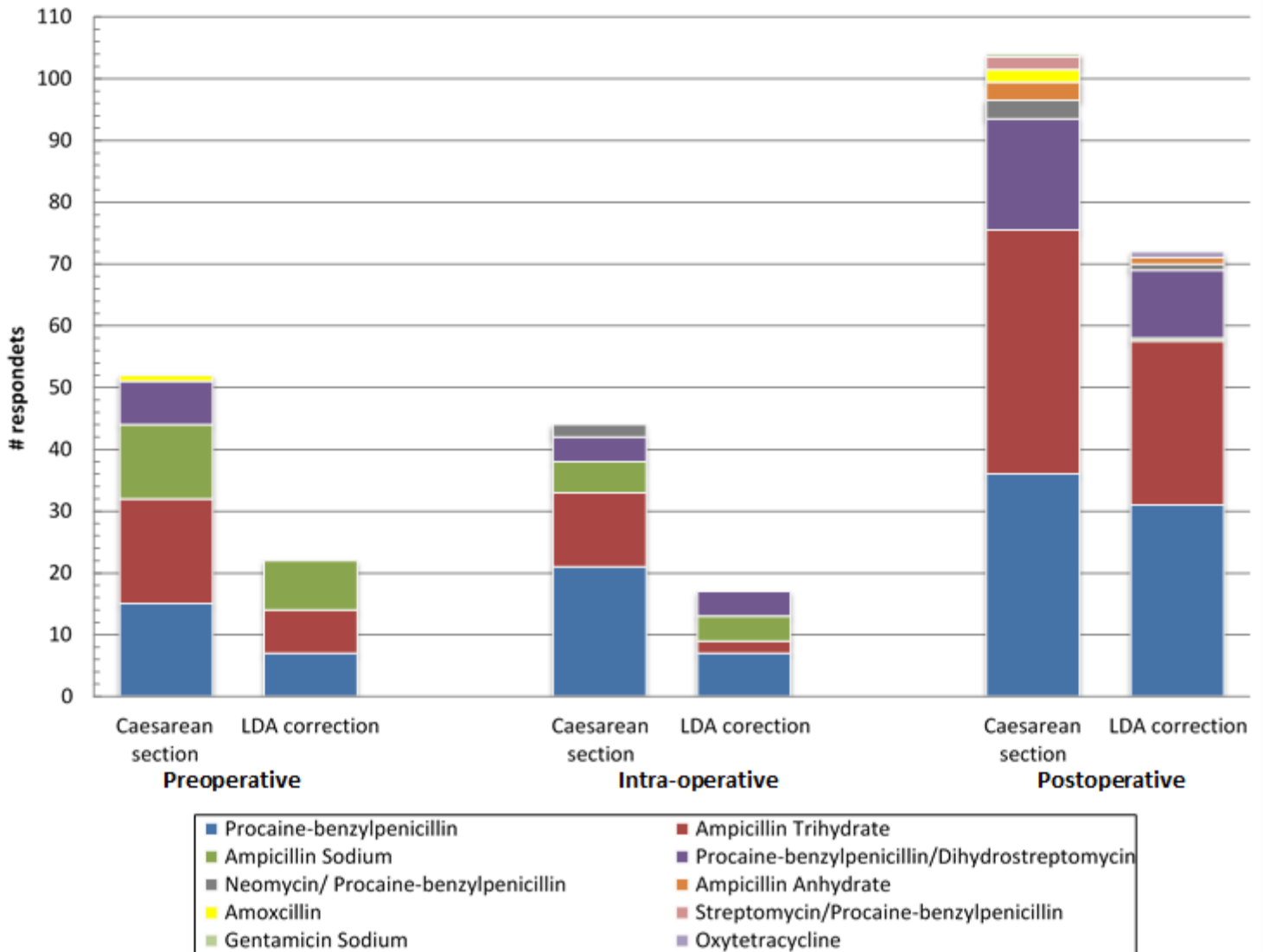


Figure 2. Frequency of perioperative antibiotic use for CS and LDA correction

Furthermore, these studies also described the role of veterinarians and other factors in the successful reduction of antibiotic use in animals. However, none of these studies focused on the prudent use of prophylactic antibiotics surrounding bovine abdominal surgeries. The survey response rate of 30% is comparable to other studies with online surveys (Hardefeldt et al., 2017; David C. Speksnijder et al., 2015). Apart from sending reminders after two weeks no other incentives were offered for filling in the online survey. The addressed veterinarians were 373 members of the specialist-ruminant sub-department of the KNMvD, although the estimated number of Dutch farm

animal veterinarians is 1100 (D. C. Speksnijder et al., 2015a). These sub-department members might be better informed than other farm animal veterinarians and the results might therefore not reflect the same antibiotic attitude as that of non-members or non-respondents. Furthermore, veterinarians who are interested in the subject may be over-represented because they are more likely to fill in the survey than veterinarians who are not. In addition, respondents can also work in the same clinic following the same protocols which might lead to some response bias in this study that could have influenced the results. We asked the respondents about their latest performed

surgery which could have led to recall bias. The situation that a veterinarian would submit more than one questionnaire was prevented because every veterinarian received a personal survey entrance code. The survey and data handling were confidentially and anonymously to decrease the trend of giving politically correct answers instead of true answers. While some of these features might have influenced our findings, our results improved our knowledge of current practices on the use of antibiotic prophylaxis in CSs and LDA corrections in the Netherlands.

The prudent use of prophylactic antibiotics is justified around CS, as the surgery is classified as clean-contaminated and in the event of peritoneum contamination with uterine fluid as contaminated. On the other hand, an uncomplicated LDA correction is classified as clean surgery (Mangram et al., 1999) and therefore does not necessarily require antibiotic prophylaxis, as illustrated in a recent clinical trial (Jorritsma et al., 2018). The anticipated risks in the field may be perceived as not represented in the clinical study. We found a high frequency of prophylactic antibiotic use surrounding bovine abdominal surgeries. In CSs, 100% of the respondents reported the use of prophylactic antibiotics and 72% of the respondents reported prophylactic antibiotic use for LDA corrections. Similar studies in Canada and Australia investigating the use of prophylactic antibiotics surrounding bovine abdominal surgeries reported comparable antibiotic usage (Chicoine et al., 2008; Hardefeldt et al., 2017). These results indicate that the use of prophylactic antibiotics is more routinely rather than anticipation on specific problems experienced during most surgeries, since 75% of the CSs and 85% of the LDA corrections were performed without complications in aseptic technique. The reason for this routine prophylactic antibiotic use may be due to expected complications and associated economic loss.

A negative aspect of the misuse of antibiotics is for example the interaction

with the commensal microbiome at the surgical site. We found that 29% of the respondents used an antibiotic spray on the wound after CSs and 35% after LDA corrections. The usage of antibiotics locally and systemically does not only affect pathogens but also the commensal microbiome. The interaction of antibiotics with the ecological balance at the surgical site might have more negative consequences for the patient than wounds that are not treated with antibiotics (Romano-Bertrand et al., 2015). From our results we can conclude that the use of prophylactic antibiotics was significantly lower around LDA corrections than CSs (odds ratio=0.29; CI 0.15-0.52). When we look at the disease-specific antibiotic guidelines for dairy cattle of the KNMvD, the use of prophylactic antibiotics is only indicated prior to surgeries with an increased risk on infections. Surgeries that comply with this constraint are abdominal surgeries with opening of a cavity or contaminated ones (gastrointestinal, caesarian sections, umbilical hernia repairs) and claw operations (Bierens et al., 2016). Therefore, the use of prophylactic antibiotics is indicated prior to both surgeries, although a LDA correction does not necessarily require antibiotic prophylaxis (Jorritsma et al., 2018). Following on these guidelines, appropriate preoperative antibiotic administration is preferable given the importance for adequate surgical prophylaxis at the time of certain surgeries (Classen et al., 1992; de Jonge et al., 2017). The suitability of antibiotics for preoperative administration should be based on the pharmacodynamic in combination with the pharmacokinetic and the expected pathogens (Boothe and Boothe, 2015). Endogenous Gram-negative bacteria like *Prevotella spp.*, and *Butyrivibrio spp.* are primarily isolated from the abomasum, while a mixed population of Gram-negative and Gram-positive bacteria is frequently isolated from uterus at the time of CS (Mao et al., 2015; Mijten et al., 1997). Further, exogenous Gram-positive bacteria, such as *Streptococcus spp.*, *Staphylococcus spp.*, and *Bacillus spp.*, are frequently

isolated from the skin of cattle. Other bacteria like *Trueperella pyogenes*, *Escherichia coli*, and *Fusobacterium necrophorum* were cultured from peritoneal and incisional infections (Hoeben et al., 1997). The previously mentioned bacteria could play a role in surgical site infections and in the event of peritoneal contamination with abomasal or uterine fluid, a peritoneal inflammation could occur after surgery (Dumas et al., 2016). Therefore, antibiotics used for surgical prophylaxis should preferably be broad-spectrum, since the endogenous and exogenous bacteria could be Gram-positive or Gram-negative. Some broad-spectrum antibiotic classes such as aminopenicillins, 3rd and 4th generation cephalosporins, tetracyclines, amphenicols and fluoroquinolones are effective against Gram-positive and Gram-negative bacteria but most of these antibiotics are not registered for surgical prophylaxis. In the Netherlands, ampicillin sodium is the only antibiotic that is registered for antibiotic prophylaxis in dairy cattle prior to surgeries (Cbg-Med, 2014). In addition to the appropriate antibiotic type, the success of surgical prophylaxis depends on the application method, dose, and timing to achieve effective concentration levels of these antibiotics at the time of surgery (Classen et al., 1992). Successful antibiotic prophylaxis requires effective concentrations of antibiotics against the expected pathogens in the operative tissue before the incision (Klein et al., 1989; Liu et al., 2002). In our survey, procaine-benzylpenicillin, ampicillin trihydrate and ampicillin sodium were the most frequently reported preoperative antibiotics. Most respondents administered antibiotics I.M. in CSs and LDA corrections between 0-30 minutes prior to surgery. In previous studies, I.M. administration of procaine-benzylpenicillin achieved maximum plasma concentrations after more than three hours post injection (Dubreuil et al., 2001). In case of I.M. administration of ampicillin trihydrate in postpartum Holstein cows, the highest plasma concentration was measured between 4 and 6 hour post injection (Credille et al., 2015). On the other

hand, I.M. administration of ampicillin sodium in cows and neonatal calves achieved the highest plasma concentration already within 20 minutes and 11 minutes after injection. In both studies, the plasma concentration levels rapidly declined within the first 4 hours (Fernández-Varón et al., 2005; Klein et al., 1989). The pharmacokinetics of the previously mentioned antibiotics suggests that only ampicillin sodium will reach an adequate plasma concentration when administered I.M. 0-30 minutes prior to surgery. Administration of procaine-benzylpenicillin or ampicillin trihydrate should be performed a few hours before the incision to achieve effective concentration levels at the time of surgery (Credille et al., 2015; Dubreuil et al., 2001; Plumb, 2005). Additionally, the time between I.M. antibiotic administration and effective tissue concentrations may be more than the previous mentioned times to achieve maximum plasma concentration levels due to drugs distribution (Mouton et al., 2008). These big differences between time of injection and the highest plasma concentration levels (the pharmacokinetics) of the most applied antimicrobial drugs, consistent with the most frequently reported antibiotics in our study, imply that more considerations than just active substance and dose should be taken into consideration before the appropriate surgical prophylaxis can be chosen. These features together suggest that in most of the reported surgeries no effective antibiotic concentrations were present in the operative field at the time of surgery and therefore the success of an infection free operation was not attributable to the prophylaxis.

Additional to preoperative antibiotic administration, also intra-abdominal and intra-incisional administration during LDA corrections and CSs is reported. However, higher efficacy of intra-abdominal and intra-incisional antibiotic administration is not shown in literature (Lyons et al., 2013). There are even studies that reported inflammatory reactions after intra-abdominal administration of ampicillin anhydrate (Klein et al., 1989). Furthermore, administration of

intra-abdominal or intra-peritoneal administration is off label leading to divergent withdrawal times. In our survey, postoperative antibiotic use was the most frequently used administration strategy for both surgeries (odds ratio= 10.27; CI 6.38-17.04) despite 85% of the LDA corrections and 75% of the CS were performed without complications. However, postoperative antibiotic prophylaxis is not in line with the disease-specific antibiotic guidelines of the KNMvD (Bierens et al., n.d.). In addition, postoperative antibiotic administration does not contribute to effective concentration levels at the time of surgery, so the effect of postoperative antibiotic use for surgical prophylaxis is limited compared with preoperative antibiotic administration (Haven et al., 1992). We did not exactly ask the respondents towards the cow's recovery after surgery, so it is hard to conclude whether the prophylactic antibiotic therapies were successful or not, especially since most preoperative treatments were followed by intra-operative or postoperative treatments.

In our study, there was a difference in the prophylactic antibiotic use during CS between the different years of work experience. Recent graduated veterinarians (0-10 years of work experience) used less frequently antibiotics during CSs than older graduates. Furthermore, they seem to use less intra-operative antibiotics during both operations, but these findings were not significant. It is remarkable that less than half of the respondents applied preoperative antibiotics around CSs, whereas almost every veterinarian administered postoperative antibiotics. Although the veterinarians used significant less antibiotics around LDA corrections even in this surgery postoperative administration was still the most reported strategy. In general, the administered prophylactic antibiotics in bovine abdominal surgeries are not the most critically important ones for human medicine such as polymyxins, 3rd and 4th generation cephalosporins and fluoroquinolones.

CONCLUSION

The results of this study improve our knowledge of prophylactic antibiotic usage surrounding bovine abdominal surgeries in the Netherlands. All the respondents reported the use of prophylactic antibiotics surrounding CSs and 72% surrounding LDA corrections. Forty-seven percent used preoperative antibiotics in CSs and 20% in LDA corrections but in most surgeries the type of preoperative antibiotics and timing of administration were not appropriate to achieve effective prophylaxis at the time of surgery. A good strategy for adequate antibiotic prophylaxis in bovine abdominal surgeries would be administration of ampicillin sodium 15-30 minutes prior to surgery. After surgery, 94% administered antibiotics in CSs and 65% in LDA corrections. The postoperative antibiotic administration is justified in surgeries with complications but unnecessary in uncomplicated CSs and LDA corrections. Given the results of this study, more education of veterinarians is needed to improve a more prudent use of prophylactic antibiotics around CSs and LDA corrections in the Netherlands.

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REFERENCES

- Bierens, J.J.M., van Beijnum, L.M., Dierikx, C.M., Parlevliet, J.M., van Rossum, R.J.W., Vendrig, J.C., 2016. *Formularium melkvee*
- Boothe, D.M., Boothe, H.W., 2015. Antimicrobial Considerations in the Perioperative Patient. *Vet. Clin. North Am. Small Anim. Pract.*, Soft Tissue Surgery 45, 585–608.
- Cbg-Med, 2014. Geneesmiddeleninformatiebank - College ter Beoordeling van Geneesmiddelen <http://www.cbg-meb.nl/geneesmiddeleninformatiebank> (accessed 4.3.19)
- Chicoine, A.L., Dowling, P.M., Boison, J.O., Parker, S., 2008. A survey of antimicrobial use during bovine abdominal surgery by western Canadian veterinarians. *Can. Vet. J.* 49, 1105–1109.
- Classen, D.C., Evans, R.S., Pestotnik, S.L., Horn, S.D., Menlove, R.L., Burke, J.P., 1992. The Timing of Prophylactic Administration of Antibiotics and the Risk of Surgical-Wound Infection. *N. Engl. J. Med.* 326, 281–286.
- Credille, B.C., Giguère, S., Vickroy, T.W., Fishman, H.J., Jones, A.L., Mason, M.E., DiPietro, R.O., Ensley, D.T., 2015. Disposition of ampicillin trihydrate in plasma, uterine tissue, lochial fluid, and milk of postpartum dairy cattle. *J. Vet. Pharmacol. Ther.* 38, 330–335.
- de Jonge, S.W., Gans, S.L., Atema, J.J., Solomkin, J.S., Dellinger, P.E., Boermeester, M.A., 2017. Timing of preoperative antibiotic prophylaxis in 54,552 patients and the risk of surgical site infection: A systematic review and meta-analysis. *Medicine (Baltimore)* 96, e6903.
- Dubreuil, P., Daigneault, J., Couture, Y., Guay, P., Landry, D., 2001. Penicillin concentrations in serum, milk, and urine following intramuscular and subcutaneous administration of increasing doses of procaine penicillin G in lactating dairy cows. *Can. J. Vet. Res.* 65, 173–180.
- Dumas, S.E., French, H.M., Lavergne, S.N., Ramirez, C.R., Brown, L.J., Bromfield, C.R., Garrett, E.F., French, D.D., Aldridge, B.M., 2016. Judicious use of prophylactic antimicrobials to reduce abdominal surgical site infections in periparturient cows: part 1 – a risk factor review. *Vet. Rec.* 178, 654–660.
- Fernández-Varón, E., Escudero-Pastor, E., Cárceles-Rodríguez, C.M., 2005. Pharmacokinetics of an ampicillin–sulbactam combination after intravenous and intramuscular administration to neonatal calves. *Vet. J.* 169, 437–443.
- Grave, K., Torren-Edo, J., Mackay, D., 2010. Comparison of the sales of veterinary antibacterial agents between 10 European countries. *J. Antimicrob. Chemother.* 65, 2037–2040.
- Hardefeldt, L.Y., Browning, G.F., Thursky, K.A., Gilkerson, J.R., Billman-Jacobe, H., Stevenson, M.A., Bailey, K.E., 2017. Cross-sectional study of antimicrobials used for surgical prophylaxis by bovine veterinary practitioners in Australia. *Vet. Rec.* 181, 426–426.
- Haven, M.L., Wichtel, J.J., Bristol, D.G., Fetrow, J.F., Spears, J.W., 1992. Effects of antibiotic prophylaxis on postoperative complications after rumenotomy in cattle. *J. Am. Vet. Med. Assoc.* 200, 1332–1335.
- Hoeben, D., Mijten, P., Kruif, A. de, 1997. Factors influencing complications during caesarean section on the standing cow. *Vet. Q.* 19, 88–92.
- Jorritsma, R., Geijlswijk, I.M. van, Nielen, M., 2018. Randomized prospective trials to study effects of reduced antibiotic usage in abdominal surgery in cows. *J. Dairy Sci.* 101, 8217–8223.
- Klein, W.R., Firth, E.C., Kievits, J.M., De Jager, J.C., 1989. Intra-abdominal versus intramuscular application of two ampicillin preparations in cows. *J. Vet. Pharmacol. Ther.* 12, 141–146.
- Lam, T.J.G.M., Jansen, J., Wessels, R.J., 2017. The RESET Mindset Model applied on decreasing antibiotic usage in dairy cattle in the Netherlands. *Ir. Vet. J.* 70, 5.
- Lam, T.J.G.M., van den Borne, B.H.P., Jansen, J., Huijps, K., van Veersen, J.C.L., van Schaik, G., Hogeveen, H., 2013. Improving bovine udder health: a national mastitis control program in the Netherlands. *J. Dairy Sci.* 96, 1301–1311.
- Liu, P., Müller, M., Derendorf, H., 2002. Rational dosing of antibiotics: the use of plasma concentrations versus tissue concentrations. *Int. J. Antimicrob. Agents* 19, 285–290.
- Lyons, N.A., Karvountzis, S., Knight-Jones, T.J.D., 2013. Aspects of bovine caesarean section associated with calf mortality, dam survival and subsequent fertility. *Vet. J.* 197, 342–350.
- Mangram, A.J., Horan, T.C., Pearson, M.L., Silver, L.C., Jarvis, W.R., 1999. Guideline for Prevention of Surgical Site Infection, 1999. *Am. J. Infect. Control, Outcomes Management* 27, 97–134.

- Mao, S., Zhang, M., Liu, J., Zhu, W., 2015. Characterising the bacterial microbiota across the gastrointestinal tracts of dairy cattle: membership and potential function. *Sci. Rep.* 5, 16116.
- MARAN, 2018: Monitoring of antimicrobial resistance and antibiotic usage in animals in the Netherlands in 2017.
- Mijten, P., van den Bogaard, A.E., Hazen, M.J., de Kruif, A., 1997. Bacterial contamination of fetal fluids at the time of cesarean section in the cow. *Theriogenology* 48, 513–521.
- Mouton, J.W., Theuretzbacher, U., Craig, W.A., Tulkens, P.M., Derendorf, H., Cars, O., 2008. Tissue concentrations: do we ever learn? *J. Antimicrob. Chemother.* 61, 235–237.
- Plumb, D.C., 2005. *Plumb's veterinary drug handbook*. Fifth edition. Stockholm, Wis. : PhrmaVet ; Ames, Iowa : Distributed by Blackwell Pub., [2005] ©2005.
- Postma, M., Speksnijder, D.C., Jaarsma, A.D.C., Verheij, T.J.M., Wagenaar, J.A., Dewulf, J., 2016. Opinions of veterinarians on antimicrobial use in farm animals in Flanders and the Netherlands. *Vet. Rec.* 179, 68.
- Romano-Bertrand, S., Licznar-Fajardo, P., Parer, S., Jumas-Bilak, E., 2015. Environmental impact on human microbiota: Focus on hospitalization effects on skin and surgical microbiota.
- Smith, R., 2015. Regulation (EC) No 764/2008 of the European Parliament and of the Council, in: *Core EU Legislation*. Macmillan Education UK, London, pp. 183–186.
- Speksnijder, D. C., Jaarsma, A.D.C., van der Gugten, A.C., Verheij, T.J.M., Wagenaar, J.A., 2015a. Determinants associated with veterinary antimicrobial prescribing in farm animals in the Netherlands: a qualitative study. *Zoonoses Public Health* 62 Suppl 1, 39–51.
- Speksnijder, David C., Jaarsma, D.A.C., Verheij, T.J.M., Wagenaar, J.A., 2015. Attitudes and perceptions of Dutch veterinarians on their role in the reduction of antimicrobial use in farm animals. *Prev. Vet. Med.* 121, 365–373.
- Speksnijder, D. C., Mevius, D.J., Brusckke, C.J.M., Wagenaar, J.A., 2015b. Reduction of veterinary antimicrobial use in the Netherlands. The Dutch success model. *Zoonoses Public Health* 62 Suppl 1, 79–87.
- Zinn, J.L., 2012. Surgical Wound Classification: Communication Is Needed for Accuracy. *AORN J.* 95, 274–278.