Received: 27 September 2021 | Revised: 3 March 2022 | Accepted: 10 March 2022

DOI: 10.1111/vsu.13810

ORIGINAL ARTICLE - CLINICAL

WILEY

Preoperative skin asepsis protocols using chlorhexidine versus povidone-iodine in veterinary surgery: A systematic review and meta-analysis

Emma Marchionatti DMV, MSc, DACVS-LA, DECVS[1] |
Caroline Constant DMV, MSc, MENG, DACVS-LA[2] |
Adrian Steiner Prof. Dr. Med. Vet., MS, DECVS, Dip. ECBHM[1]

[1]Vetsuisse Faculty, University of Bern, Bern, Switzerland

[2]AO Research Institute Davos, Davos, Switzerland

Correspondence
Emma Marchionatti, Vetsuisse Faculty, University of Bern, Bremgartenstrasse 109A, 3012 Bern, Switzerland.
Email: emma.marchionatti@vetsuisse.unibe.ch

Abstract

Objective: To provide a systematic assessment of the efficacy of preoperative skin asepsis using chlorhexidine versus povidone-iodine based protocols for surgical site infection (SSI) prevention in veterinary surgery.

Study design: Systematic meta-analytical review according to PRISMA-P guidelines.

Sample population: Studies comparing preoperative skin asepsis protocols using chlorhexidine versus povidone-iodine in veterinary surgery identified by systematic search between 1990 and 2020.

Methods: A search using MEDLINE/Pubmed, Web of Science and CAB Abstracts was performed, followed by secondary searches of Google Scholar, Proquest Dissertation and Theses, and relevant bibliographic articles. Primary and secondary outcome measures were the efficacy of skin asepsis protocols using chlorhexidine versus povidone-iodine on SSI incidence and skin bacterial colonization, respectively. A meta-analysis was performed with a random-effect model, with effect size calculated as risk ratio (RR) or mean standard deviation (MSD) with 95% CI. Statistical significance was set at $P < .05$.

Results: Among 1067 publications that met the initial search criteria, 9 relevant studies were eligible for analysis. No difference in the incidence of postoperative SSI or skin bacterial colonization between preoperative asepsis protocols using chlorhexidine versus povidone-iodine was found. Insufficient information and detail were frequent among studies and precluded a clear assessment of bias.

Conclusion: This study showed that asepsis protocols using chlorhexidine were comparable to povidone-iodine in preventing postoperative SSI and reducing skin bacterial colonization.

Clinical significance: Given the limitations of the studies that were included in terms of both quality and quantity, more high-quality randomized controlled trials are needed to confirm these conclusions.

1 | INTRODUCTION

Postoperative surgical site infection (SSI) is a leading cause of morbidity and mortality and represents a major economic and welfare burden in veterinary surgery.[1–3] Preoperative surgical site asepsis practice is based on the knowledge that pathogens leading to SSI are often acquired from the patient's endogenous flora. Hence, preoperative surgical site skin asepsis using appropriate products represents one of the most critical factors for SSI prevention. Aseptic protocols in veterinary surgery are traditionally based on methods used in humans. They typically involve the use of an aqueous or alcohol-based preparation of chlorhexidine or povidone-iodine. Despite chlorhexidine's wider range of antimicrobial activity compared to povidone-iodine, concerns may arise with its use, as methicillin-resistant *Staphylococcus aureus* (MRSA) and enterococci may develop acquired resistance to it.[4,5] Moreover, a longer residual effect and a greater skin tolerance have historically been attributed to chlorhexidine, characteristics that may have been overestimated.[6–9] Multiple veterinary studies have comparatively investigated SSI occurrence and/or bacterial reduction at the surgical site using chlorhexidine and povidone-iodine based protocols but were unable to draw conclusions about which surgical site antiseptic should be preferred.[10–17] According to recent systematic reviews in human patients, chlorhexidine appears superior to povidone-iodine in preventing SSI, with up to 30% reduction in its incidence, and in reducing skin bacterial colonization.[18,19] Nevertheless, criticism has arisen regarding metanalyses promoting the use of chlorhexidine-alcohol over povidone-iodine with or without alcohol in preventing SSI because of inclusion of studies with unknown active ingredient concentrations or concentrations below the active range.[20]

Despite some evidence in favor of chlorhexidine, this may not apply to veterinary surgery where patients present with different skin characteristics and microflora than human patients. As the choice of antiseptic should be based on the best available empirical data, including efficacy, patient tolerance and resistance development, or its potential, the objective of this study was to provide a systematic meta-analytic assessment of the efficacy of preoperative skin asepsis protocols using chlorhexidine versus povidone-iodine for SSI prevention and skin bacterial burden reduction in veterinary surgery. Considering the relationship between skin bacterial flora and SSI, and the aim of skin asepsis being reduction of skin flora, the evaluation of the reduction of both is necessary. We therefore, hypothesized that preoperative skin preparation with chlorhexidine-based protocols would be superior to that of povidone-iodine in both prevention of SSI and reduction of skin bacterial colonization.

2 | MATERIALS AND METHODS

This review was conducted according to the recommendations in the PRISMA-P 2015 statement.[21]

2.1 | Literature search strategy

A comprehensive literature search was carried out on February 4, 2021. The MEDLINE/Pubmed, Web of Science Core Collection and CAB Abstracts databases were searched, with University of Bern institutional access, for published veterinary literature comparing chlorhexidine and povidone-iodine based protocols for preoperative skin asepsis. Additional searches were performed for gray literature with Google Scholar, Proquest Dissertation and Theses Global, and hand searching of reference lists and book chapters. No language restrictions were applied. Retrieval strategy was a combination of keywords, free words, and subject words to include multiple animal species, methods, and endpoints. The complete search strategy used can be found in the supplementary material S1. The reference management software EndNote X9 (Clarivate, Philadelphia, Pennsylvania) was used to import references from searched databases, remove duplicate references, screen by title and abstract, retrieve and screen full text documents, and record reasons for exclusions.

2.2 | Selection criteria

Two reviewers (EM and CC) individually assessed studies to determine eligibility. Disagreements between reviewers were solved by consensus or by the decision of a third reviewer (AS) if consensus between the 2 main reviewers was not achieved. Articles were included if meeting the following criteria: (1) they were randomized controlled trials (RCTs) or observational studies on veterinary patients;

(2) they compared chlorhexidine-based and povidone-iodine-based preoperative skin asepsis protocols; (3) they assessed surgical patients; and (4) they assessed at least 1 of the outcomes of interest, being incidence of SSI or skin bacterial colonization. The latter was defined as a dichotomous variable being presence or absence of colonization, or as a continuous variable being the percentage of bacterial reduction. Human, noncomparative, in vitro or ex vivo studies, as well as reviews and meta-analyses were excluded. Further exclusion criteria included studies where relevant data could not be obtained from the published results and the raw data was not made available after contact with the corresponding authors. The primary and secondary outcome measures for this study were the efficacy of skin asepsis protocols using chlorhexidine versus povidone-iodine on the incidence of SSI and skin bacterial colonization respectively.

2.3 | Data collection and analysis methods

Data were collated in Excel (Microsoft, Redmond, Washington) and included authors' names, journal name, article title, year of publication, type of study, species, type of surgery, sample size of groups, type of skin aseptic protocols (formulations and application method), SSI rates, immediate and delayed bacterial colonization. When needed, missing information and clarification about the statistics presented was sought from the corresponding authors or was obtained using direct algebraic relationships with the available measures of variation.[22] Briefly, when not available, standard deviation of each group was obtained using the standard error of the mean and multiplying it by the square root of the sample size (Eq. 1) or by dividing the width of the 95% confidence interval (known to be 3.92 standard error wide; 3.92=2×1.96) by 3.92, and then multiplying it by the square root of the sample size (Eq. 2).

Eq. 1: Equation to obtain standard deviations from standard errors for group means

$$SD = SE \times \sqrt{N} \quad (1)$$

Eq. 2: Equation to obtain standard deviations from confidence intervals for group means

$$SD = \sqrt{N} \times (upperlimit\text{-}lowerlimit)/3.92 \quad (2)$$

For studies with only summary statistics calculated after a log-transformation has been applied to the raw data, statistical measures were obtained by finding the means and confidence intervals of the natural logs and taking their exponentials (antilogs). Separate statistical analyses using a random-effect model were performed using Revman 5.4 software (Review Manager, The Cochrane Collaboration 2020, Oxford, UK) to determine the risk ratio (RR) with 95% CI as the effect measure for dichotomous variables and the standard mean difference (SMD) with 95% CI as the effect measure for continuous data. The heterogeneity between the studies was analyzed using the χ^2 test, and the size of heterogeneity was quantified with I^2, with values of 25%, 50%, and 75% representing small, moderate and high heterogeneity. The significance of the I^2 value was determined after evaluation of magnitude and direction of effect and strength of evidence for heterogeneity (P value of the χ^2 test). The quality of RCTs was assessed using the Cochrane risk of bias tool, which includes random sequence generation, allocation concealment, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias.[23]

3 | RESULTS

3.1 | Quantity of research available

The literature search yielded 1291 results through database searching; 4 additional records were identified through other sources. After removing duplicates, 1067 articles were retained. After screening titles and abstracts, 30 potentially relevant articles were retained for full text review. Twenty-one studies did not meet the inclusion criteria (Figure 1). A total of 9 RCTs were judged eligible and were included in this review.[11–17,24,25]

3.2 | Study characteristics

An overview of the included studies is provided in Table S2 in the supplementary material. The articles selected for inclusion were published between 1990 and 2020. The species on which aseptic protocols efficacy was studied were small animals (4 studies, 446 animals), cattle (2, 164), laboratory mice (2, 72), and horses (1, 36). Surgery types included in the studies were classified as clean in 7 studies,[12,14–17,24,25] and as mixed clean and clean contaminated in 2.[11,13] One study reported SSI incidence as a measure of aseptic protocol efficacy and did not report skin bacterial colonization.[12] Three studies reported both SSI and skin bacterial colonization,[13,15,17] whereas 5 reported skin bacterial colonization only.[11,14,16,24,25] Diagnosis of SSI was made according to the Centers for Disease Control and Prevention (CDC) criteria in 2 studies;[13,17] in the

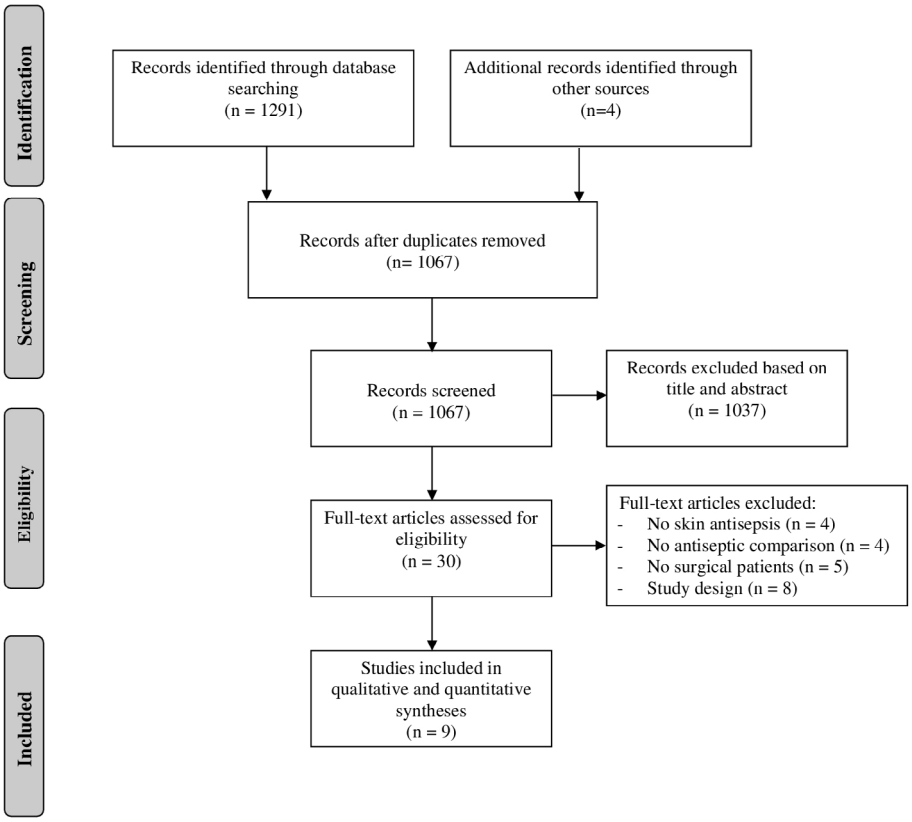

FIGURE 1 Flow chart of screening and selection of articles for the meta-analysis, detailing reasons for censorship at each stage

others, assessment was based on predefined clinical criteria.[12,15] The follow-up period for detection of SSI was 30 days in 3 studies[13,15,17] and limited to 14 days in 1 study.[12] Immediate skin bacterial colonization was measured at the preoperative timepoint in all studies, and delayed bacterial colonization was measured at the end-of-surgery timepoint in 5 studies[11,13,15,24,25] or at a predefined time (60, 180 min) in 2 studies.[14,16]

Formulation, concentration, and application method of antiseptics were not consistent across studies. Four studies reported use of 4% chlorhexidine gluconate,[11,13,15,16] 3 studies of 2% chlorhexidine gluconate,[14,17,24] and 1 study of 0.5% chlorhexidine acetate[12] in alternating order with alcohol and/or saline solution. In 1 study, 2 formulations of chlorhexidine were used, being either 4% gluconate or a hydro-alcoholic preparation (2% chlorhexidine gluconate/70% isopropyl alcohol) depending on the subgroup.[25] Four studies reported povidone-iodine formulations with a concentration of free iodine of 0.75%,[11,13,16,17] and 3 studies of 1%;[12,15,24] they were used alone or alternated with alcohol or saline solution. One study used povidone-iodine as a hydroalcoholic preparation (0.7% iodine/74% isopropyl alcohol)[14] and another study either as 1% or as a hydroalcoholic solution depending on the subgroup.[25] When alcohol was alternated with chlorhexidine or povidone-iodine, it was 70% isopropanol in 7 studies[11,13–17,25] and 70% ethanol in one study.[24]

3.3 | Surgical site infection

One study reported no SSI occurrence in either group[17] and the remaining 3 found no significant statistical difference between the SSI rates for the 2 aseptic protocols.[12,13,15] Meta-analysis indicated no difference in the incidence of postoperative SSI between preoperative asepsis protocols using chlorhexidine versus povidone-iodine (RR, 0.90; 95% CI, 0.38-2.12; $P = 0.82$, $I^2 = 0\%$; Figure 2).

3.4 | Skin bacterial colonization

Skin bacterial colonization was reported as presence or absence of >5 colony-forming units (CFU) in the immediate and delayed period in 2 studies,[14,25] or as immediate and delayed reduction factors in 2 studies;[13,15] in 4 studies both measures were reported.[11,14,16,24] All studies reported no difference in skin bacterial colonization. Two studies, however, reported a trend toward a reduction in skin bacterial colonization with the use of chlorhexidine and alcohol,[13,24] while the use of chlorhexidine and saline or povidone-iodine and alcohol performed slightly better than chlorhexidine and alcohol in 2 other studies.[11,16] Of the 8 studies that evaluated skin bacterial colonization, only 4 used neutralizing agents in sampling.[11,13,15,16]

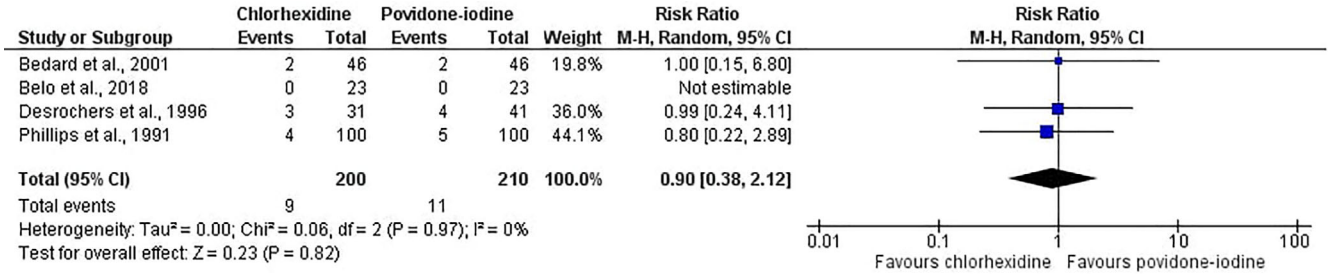

FIGURE 2 Forest plot of the efficacy of chlorhexidine-based versus povidone-iodine-based aseptic protocols for the prevention of surgical site infection (SSI) events. A risk ratio (RR) of 1 indicates that there is no difference between groups; RR >1 indicates that povidone-iodine-based asepsis protocol is associated with a lower incidence of SSI, whereas RR <1 indicates that chlorhexidine-based asepsis protocol is associated with a lower incidence of SSI. Confidence intervals that overlap a RR of 1 suggest lack of association between aseptic protocol and SSI

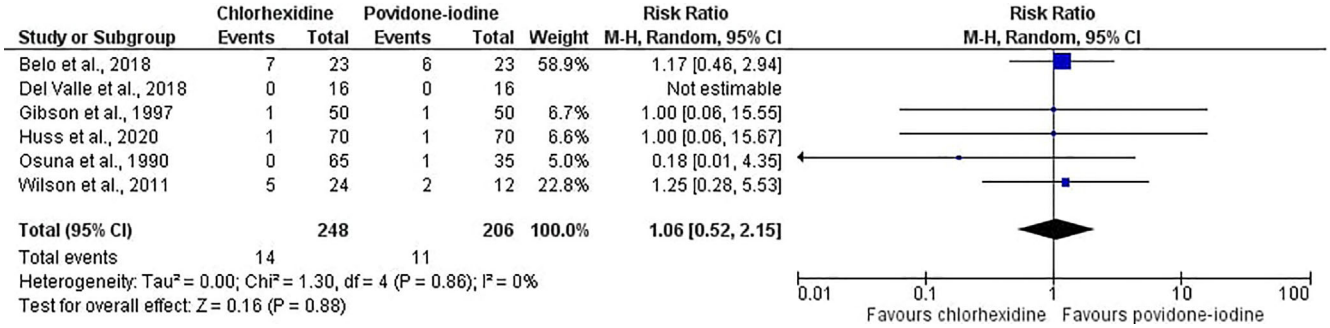

FIGURE 3 Forest plot of the efficacy of chlorhexidine-based versus povidone-iodine-based aseptic protocols for the immediate skin bacterial colonization (>5 CFU) events. A risk ratio (RR) of 1 indicates that there is no difference between groups; RR >1 indicates that povidone-iodine-based asepsis protocol is associated with lower immediate skin bacterial colonization, whereas RR <1 indicates that chlorhexidine-based asepsis protocol is associated with lower immediate skin bacterial colonization. Confidence intervals that overlap a RR of 1 suggest lack of association between aseptic protocol and immediate skin bacterial colonization

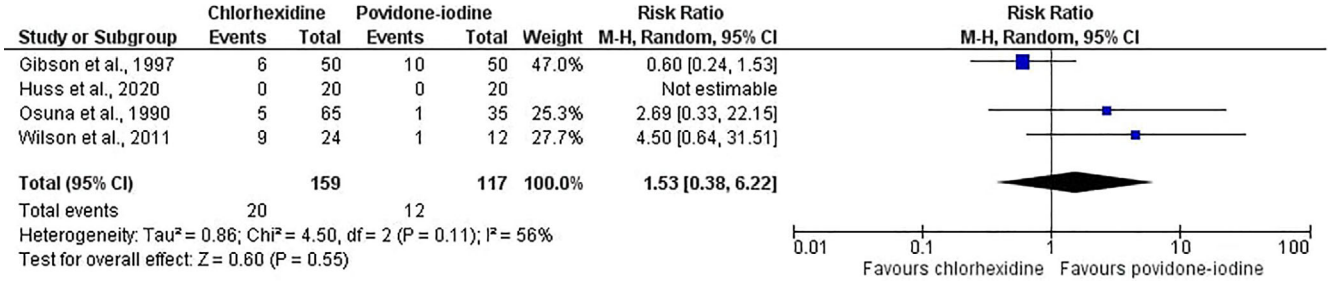

FIGURE 4 A forest plot of the efficacy of chlorhexidine-based versus povidone-iodine-based aseptic protocols for the delayed skin bacterial colonization (>5 CFU) events. A risk ratio (RR) of 1 indicates that there is no difference between groups; RR >1 indicates that povidone-iodine-based asepsis protocol is associated with lower delayed skin bacterial colonization, whereas RR <1 indicates that chlorhexidine-based asepsis protocol is associated with lower delayed skin bacterial colonization. Confidence intervals that overlap a RR of 1 suggest lack of association between aseptic protocol and delayed skin bacterial colonization

Meta-analyses showed no difference for the presence/absence of skin bacterial colonization at immediate (RR, 1.06; 95% CI, 0.52-2.15; $P = 0.88$, $I^2 = 0\%$; Figure 3) or delayed timepoints (RR, 1.53; 95% CI, 0.38-6.22; $P = 0.55$, $I^2 = 56\%$; Figure 4), nor for the immediate (SMD, −0.16; 95% CI, −0.41-0.09; $P = 0.22$, $I^2 = 0\%$; Figure 5) or delayed (SMD, 0.05; 95% CI, −0.20-0.29; $P = 0.72$, $I^2 = 0\%$; Figure 6) percentage of skin bacterial reduction.

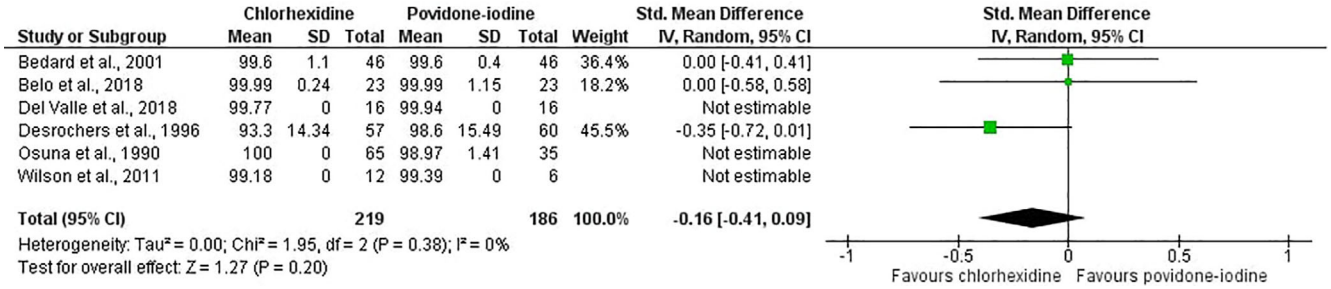

FIGURE 5 A forest plot of the efficacy of chlorhexidine-based versus povidone-iodine-based asepsis protocol for the immediate skin bacterial reduction (%) events. A standard mean difference (SMD) of 0 indicates that there is no difference between groups; on the right side of the forest plot are studies that favor povidone-iodine-based asepsis protocol and on the left side there are studies that favor a chlorhexidine-based asepsis protocol. Confidence intervals that overlap 0 suggest lack of association between asepsis protocol and immediate skin bacterial reduction

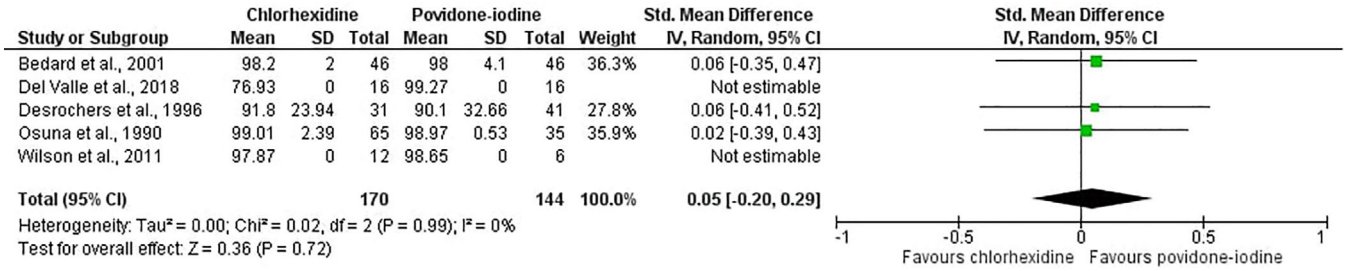

FIGURE 6 A forest plot of the efficacy of chlorhexidine-based versus povidone-iodine-based asepsis protocol for the delayed skin bacterial reduction (%) events. A standard mean difference (SMD) of 0 indicates no difference between groups; on the right side of the forest plot are studies that favor povidone-iodine-based asepsis protocol and on the left side studies that favor chlorhexidine-based asepsis protocol. Confidence intervals that overlap the 0 suggest a lack of association between asepsis protocol and delayed skin bacterial reduction

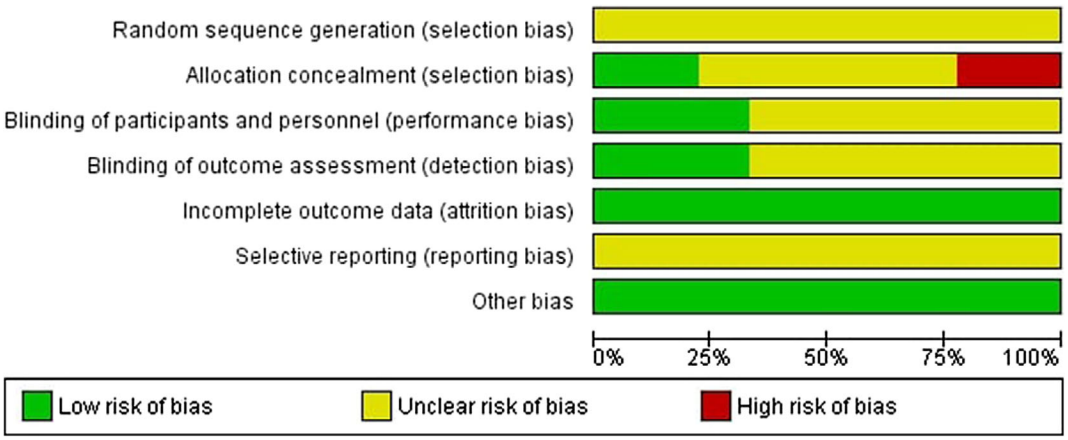

FIGURE 7 Risk of bias graph: reviewers' judgment about each risk of bias item presented as percentages across all studies that were included

3.5 | Risk of bias assessment

The proportions of the studies with low, high, and unclear risks of bias in each domain based on reviewers' judgment is depicted in Figure 7, and the risk of bias judgment of each study in each domain is illustrated in Figure 8. There was an unclear risk of bias due to insufficient information and detail provided

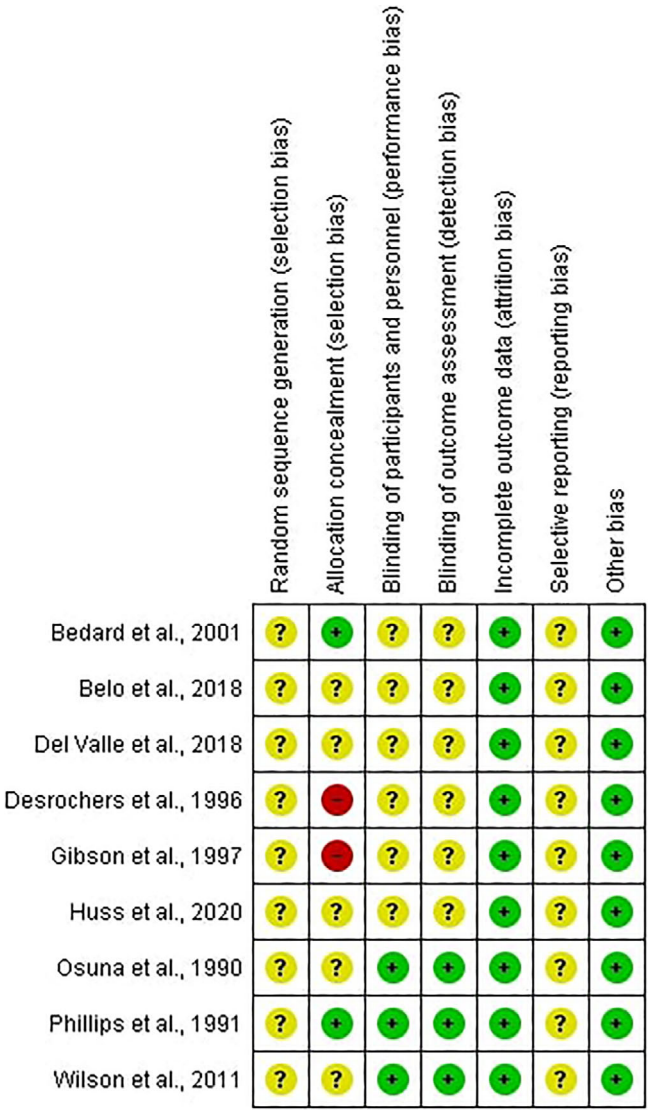

FIGURE 8 Risk of bias summary: reviewers' judgment about each risk of bias item for each study that was included

in the articles in 2 or more domains in all the included studies. Randomization was judged to have an unclear risk of bias in all the studies as the authors did not clearly state the method of random sequence generation. For allocation concealment, 2 studies had a high risk of bias as they allocated animals either using an alternate sequence or based on the hospital registration number.[13,14] Three studies clearly stated the blinding of personnel and outcome assessors,[11,12,16] while the other studies did not specify. However, blinding is considered unlikely in these studies as they compare skin antiseptics with different appearance and clinical evaluation of SSI might have been affected by lack of blinding. All studies were judged to have low risk of attrition bias as loss of subjects from study groups was <20% and, when present, equal between groups.

4 | DISCUSSION

The occurrence of SSI is multifactorial. Skin preparation and surgical site bacterial colonization are factors to consider.[26] Human studies have provided some evidence supporting the use of chlorhexidine for preoperative skin asepsis and its association with lower bacterial colonization when compared to povidone-iodine.[18,19] This is the first systematic meta-analytical review comparing preoperative asepsis protocols using chlorhexidine versus povidone-iodine in veterinary surgery. The results of the current study, however, were not able to provide evidence that chlorhexidine-based protocols were superior to povidone-iodine-based protocols in reducing both rates of SSI and bacterial colonization in veterinary surgery. Clinicians may, therefore, consider other characteristics such as costs, potential side effects for both patients and health care professionals, and potential antiseptic resistance development when choosing the most appropriate preoperative aseptic protocol.

The overall quality of evidence provided by the eligible studies contained within this systematic review was low, which could partially be due to the small number of studies included in each comparison. The variable risk of bias of the included studies could also have affected our ability to estimate effects. Moreover, lack of power in the analysis, as evidenced by the small number of studies and the small sample sizes in each comparison, may affect the confidence in interpreting the results because of the inability to determine whether results that are not statistically significant are indicative of true effects or merely of insufficient data for detecting differences.

Multiple other limitations related to the studies that were included must also be considered when interpreting the meta-analysis results. Variations in the concentration, formulation and application method of the antiseptics constitute a source of clinical heterogeneity in both the individual study protocols and the meta-analysis itself, which makes it difficult to draw strong conclusions. Many antiseptics can be used singly or in combination in a variety of products that may vary considerably in efficacy. This review was intended to compare chlorhexidine- and povidone-iodine-based asepsis protocols rather than individual antiseptics. Results regarding immediate effect of asepsis protocols should therefore be interpreted carefully when alcohols are used in association with chlorhexidine and povidone-iodine to prevent overestimation of the efficacy of the latter.[7] Evidence on delayed efficacy of chlorhexidine and povidone-iodine asepsis protocols may reflect more reliably the true effect of the individual antiseptic because, even if used in combination with alcohols, these latter do not show a sustained effect. When interpreting data on SSI occurrence in correlation with antiseptic use, one must

consider that multiple factors, patient related and not patient related, may influence the potential development of SSI, and therefore draw careful conclusions. Moreover, absence of neutralizing agents in sampling media may foster misinterpretation of results as residual bacteriostatic or bactericidal activity may persist therefore rendering impossible to distinguish whether low/absent skin bacterial colonization was obtained before or after sampling.[8]

Likewise, although all studies included were RCTs, the differences in methodology are another source of variability that can affect the meta-analysis. Although the evidence gathered in this review does not suggest that asepsis protocols using chlorhexidine are superior to povidone-iodine, it highlights the paucity of the available research, and further trials in preoperative skin asepsis are warranted. Future studies should be planned as rigorous RCTs to reduce bias by ensuring presence of comparable groups through appropriate randomization methods and allocation concealment, as well as by guaranteeing blinding of personnel and outcome accessors. The inclusion of primary research into meta-analyses strongly relies on systematic, appropriate, and transparent reporting of data and detailed description of methodology used. Therefore, high quality standards and compliance with guidelines describing study design, sample size determination, methods of randomization and blinding, will increase the soundness and quality of future meta-analyses.

Studies of skin asepsis tend to use variable endpoints, with most of the studies that were included relying on quantitative skin cultures to determine the antiseptic efficacy as the aim of skin asepsis is to reduce skin flora. However, these outcomes are difficult to correlate with clinical infection, rendering comparison of the results difficult. Postoperative SSI is a clinical diagnosis and is dependent on the recorder. The lack of appropriate and uniform SSI definitions could again make the results difficult to compare. In addition, a large number of SSI could be underreported if superficial and mild, and diagnosed and treated by referring veterinarians after hospital discharge. In fact, a prospective SSI surveillance study in dogs has shown that only 65% of SSI are reported in the medical record, which could have reduced the chances to detect a significant difference between the aseptic protocols.[27]

Because of the comprehensive search strategy employed in this review, it is unlikely that eligible published studies were missed. However, there may be relevant unpublished research that was not included. Screening of studies, data extraction and bias assessment were carried out by 2 review authors, limiting potential bias in the review process.

In conclusion, this study showed that preoperative asepsis protocols using chlorhexidine appear to be comparable to povidone-iodine in preventing postoperative SSI and in reducing bacterial colonization in veterinary surgery. Given the limitations of included studies in quality and quantity, more high-quality RCTs with larger sample sizes are needed to further confirm or reject these conclusions.

ACKNOWLEDGMENTS

The authors would like to thank Tania M. Rivero, who provided insight on search strategy development and technique. Open access funding provided by Universitat Bern.

Author Contributions

Marchionatti E, DMV, MSc, DACVS-LA, DECVS: Study design, data collection and analysis, and manuscript preparation. Constant C, DMV, MSc, MENG, DACVS-LA: Study design, data collection and analysis, and manuscript preparation. Steiner A, Prof. Dr. Med. Vet., MS, DECVS, Dip. ECBHM: Data collection and analysis, and manuscript preparation.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this report.

ORCID

Emma Marchionatti https://orcid.org/0000-0002-9113-5829
Caroline Constant https://orcid.org/0000-0002-7846-5612
Adrian Steiner https://orcid.org/0000-0003-2415-3768

REFERENCES

1. Nicoll C, Singh A, Weese JS. Economic impact of tibial plateau leveling osteotomy surgical site infection in dogs. *Vet Surg*. 2014;43:899-902.
2. Curtiss AL, Stefanovski D, Richardson DW. Surgical site infection associated with equine orthopedic internal fixation: 155 cases (2008-2016). *Vet Surg*. 2019;48:685-693.
3. Espinel-Ruperez J, Martin-Rios MD, Salazar V, et al. Incidence of surgical site infection in dogs undergoing soft tissue surgery: risk factors and economic impact. *Vet Rec Open*. 2019;6:e000233.
4. Block C, Robenshtok E, Simhon A, et al. Evaluation of chlorhexidine and povidone iodine activity against methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcus faecalis using a surface test. *J Hosp Infect*. 2000;46:147-152.
5. Kampf G. Acquired resistance to chlorhexidine - is it time to establish an 'antiseptic stewardship' initiative? *J Hosp Infect*. 2016;94:213-227.
6. Maiwald M, Petney TN, Assam PN, et al. Use of statistics as another factor leading to an overestimation of chlorhexidine's role in skin antisepsis. *Infect Control Hosp Epidemiol*. 2013;34:872-873.
7. Maiwald M, Chan ES. The forgotten role of alcohol: a systematic review and meta-analysis of the clinical efficacy and perceived role of chlorhexidine in skin antisepsis. *PLoS One*. 2012;7:e44277.

8. Kampf G. Effect of chlorhexidine probably overestimated because of lack of neutralization after sampling. *Infect Control Hosp Epidemiol*. 2009;30:811-812 author reply 812-813.
9. Wittczak T, Dudek W, Walusiak-Skorupa J, et al. Chlorhexidine–still an underestimated allergic hazard for health care professionals. *Occup Med (Lond)*. 2013;63:301-305.
10. Osuna DJ, DeYoung DJ, Walker RL. Comparison of three skin preparation techniques in the dog. Part 1: experimental trial. *Vet Surg*. 1990;19:14-19.
11. Osuna DJ, DeYoung DJ, Walker RL. Comparison of three skin preparation techniques. Part 2: clinical trial in 100 dogs. *Vet Surg*. 1990;19:20-23.
12. Phillips MFV, Gregory CR. Chlorhexidine diacetate versus povidone-iodine for preoperative preparation of the skin: a prospective randomized comparison in dogs and cats. *J Am Anim Hosp Assoc*. 1991;27:105-108.
13. Desrochers A, St-Jean G, Anderson DE, et al. Comparative evaluation of two surgical scrub preparations in cattle. *Vet Surg*. 1996;25:336-341.
14. Gibson KL, Donald AW, Hariharan H, et al. Comparison of two pre-surgical skin preparation techniques. *Can J Vet Res*. 1997;61:154-156.
15. Bedard S, Desrochers A, Fecteau G, et al. Comparison of four protocols for preoperative preparation in cattle. *Can Vet J*. 2001;42:199-203.
16. Wilson DGH, Carter VR, Klohnen A, MacWilliams PS. Comparison of three preoperative skin preparation techniques in ponies. *Eq Vet Educ*. 2011;23:462-465.
17. Belo L, Serrano I, Cunha E, et al. Skin asepsis protocols as a preventive measure of surgical site infections in dogs: chlorhexidine-alcohol versus povidone-iodine. *BMC Vet Res*. 2018;14:95.
18. Chen S, Chen JW, Guo B, et al. Preoperative antisepsis with chlorhexidine versus povidone-iodine for the prevention of surgical site infection: a systematic review and meta-analysis. *World J Surg*. 2020;44:1412-1424.
19. Privitera GP, Costa AL, Brusaferro S, et al. Skin antisepsis with chlorhexidine versus iodine for the prevention of surgical site infection: a systematic review and meta-analysis. *Am J Infect Control*. 2017;45:180-189.
20. Maiwald M, Widmer AF. WHO's recommendation for surgical skin antisepsis is premature. *Lancet Infect Dis*. 2017;17:1023-1024.
21. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4:1.
22. Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021), in Higgins JPT, Thomas J, Chandler J, et al (eds), Vol Cochrane, 2021. www.training.cochrane.org/handbook, 2021.
23. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
24. Del Valle JM, Fisk EA, Noland EL, et al. Comparison of aqueous and alcohol-based agents for Presurgical skin preparation methods in mice. *J Am Assoc Lab Anim Sci*. 2018;57:401-414.
25. Huss MK, Casey KM, Hu J, et al. Evaluation of 3 alcohol-based agents for Presurgical skin preparation in mice. *J Am Assoc Lab Anim Sci*. 2020;59:67-73.
26. Wong ES. Surgical site infections. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control*. 3rd ed. Lippincott, Williams, and Wilkins; 2004:287-310.
27. Turk R, Singh A, Weese JS. Prospective surgical site infection surveillance in dogs. *Vet Surg*. 2015;44:2-8.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Marchionatti E, Constant C, Steiner A. Preoperative skin asepsis protocols using chlorhexidine versus povidone-iodine in veterinary surgery: A systematic review and meta-analysis. *Veterinary Surgery*. 2022;51(5):744-752. doi:10.1111/vsu.13810