Use of Simini Protect Lavage as an Adjuvant in the Antiseptic Protocol for Revision Surgeries Involving Total Hip Replacement

Ida Forzisi[1] Luca Vezzoni[1] Milo Bozzerla[2] Aldo Vezzoni[1]

[1] Surgical Department, Clinica Veterinaria Vezzoni, Cremona, Italy
[2] Surgical Deparment, AniCura - Clinica Veterinaria Malpensa, Samarate, Italy

Address for correspondence Ida Forzisi, DVM, Clinica Veterinaria Vezzoni, Via delle Vigne 190, Cremona 26100, Italy (e-mail: idaforzisi@gmail.com).

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Abstract

Objectives Despite advances in surgical asepsis and improvements in sterile surgical techniques, surgical site infection occurs in 0.8 to 15.8% of surgical wounds. Most infections are caused by microorganisms forming biofilms that adhere to implants or dead bone and can evade host immunity and antimicrobial agents. Simini Protect Lavage (SPL) is a hypertonic aqueous solution designed to break cross-links within the extracellular polymeric substance of biofilms produced by bacteria. This study aimed to report the outcome of our total hip replacement (THR) revision cases using an SPL in addition to our standard antiseptic protocol.

Methods The medical records of patients at Vezzoni Veterinary Clinic were searched for animals undergoing a revision orthopaedic surgery involving a THR that included the use of SPL. In all patients, a minimum of 1-year follow-up and culture and a sensitivity test pre- and post-Simini Lavage were required.

Results SPL was used in 36 cases. At the beginning of surgery, culture and sensitive tests were positive in eight patients, and at the end of surgery, seven dogs were still positive for bacterial infection. Only one case, which experienced three revision surgeries, underwent explantation due to persistent, clinically evident infection. The other dogs showed neither clinical nor X-ray signs of infection over a long period.

Clinical Significance The use of SPL can be considered as an adjuvant in the antiseptic protocol for the one-stage revision THR surgeries without a plan of prosthesis explanation. Nevertheless, further studies are needed to objectively evaluate the efficacy of SPL in eradicating the postoperative infections.

Keywords
- infections
- surgical site infection
- revision surgery
- intraoperative antiseptic lavage

Introduction

Surgical site infection (SSI) is costly and associated with poor patient outcomes, increased morbidity, and high reoperation rates. The complications posed by SSI are particularly challenging to resolve, especially in orthopaedic cases. Despite advances in surgical asepsis, the rate of SSI ranges from 0.8 to 18.1%, depending on patient characteristics, the degree of wound contamination, the surgical environment, and the type of surgical procedure.[1,2] Factors increasing the risk of SSI include prolonged anaesthesia and surgery times, body weight, the number of people in the operating suite, hospitalization time, the physical status score according to the American Society of Anaesthesiologists physical status classification system, hypotension, type of surgery, and open fractures.[3–7]

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The management of periprosthetic joint infection is a significant challenge, with irrigation and debridement playing a pivotal role in addressing SSI. Therefore, meticulous mechanical and chemical debridement of nonviable tissue and judicious selection of irrigation solutions are imperative in minimizing the presence of infected debris.

Total hip replacement (THR) is considered the gold standard treatment for some of the common canine coxofemoral joint diseases like end-stage osteoarthritis and severe hip dysplasia.[8–11] Predisposing factors for infection in dogs following THR include revision surgery, preexisting hip infection, prolonged surgical time, and hematogenous spread secondary to an infection in a remote area.[12,13]

In both veterinary and human medicine, the gold standard for treating SSI in orthopaedic surgery involves the removal of implants, antibiotic therapy, and, if required, a two-stage surgical revision procedure.[14,15]

The most difficult infections to treat in orthopaedic surgery are those caused by microorganisms that adhere to implants or dead bone (sequestra), forming a biofilm that makes them resistant to host defence mechanisms and most antimicrobial agents.[16–18] Curing an existing infection is difficult because, although antibiotics can kill planktonic or free-living bacteria, they are usually ineffective against bacteria in biofilms.[19]

Costerton et al first proposed that communities of bacteria embedded in a highly hydrated polysaccharide matrix called a "biofilm," mediated adhesion to solid–liquid interfaces. These functionally heterogeneous microcolonies or single-cell aggregates are enclosed in a matrix of self-produced extracellular polymers, which may adhere to biotic or abiotic surfaces.[20,21] In the 1980s, it was shown that most bacteria and fungi can form a biofilm, which protect them from biotic and abiotic stresses, providing a survival mechanism in hostile environments.[22–25] It has been reported that biofilm-producing bacteria encapsulated in an extracellular polymeric substance (EPS), which may also contain components derived from the host, are more tolerant to antibiotics and antiseptics, resisting antimicrobial concentrations 100 to 1,000 times higher than those effective against their planktonic counterparts.[26–29]

The bacteria most frequently involved in SSI in veterinary medicine are *Staphylococcus* spp.,[30] *Streptococcus* spp., and *Escherichia coli*,[31] with S*taphylococcus pseudintermedius* being the most common in dogs. Based on recent studies, approximately 50% of bacteria isolated from implant-associated osteomyelitis were methicillin-resistant *Staphylococcus* spp. strains.[3,32–34]

Various strategies are utilized to mitigate the risk of SSIs. These encompass perioperative antibiotic prophylaxis, applying specific antiseptic solutions for skin preparation, intraoperative topical adjuvants, antiseptic irrigation, meticulous tissue handling, ensuring effective hemostasis, and adhering to rigorous aseptic techniques.[35] Intraoperative irrigation is a commonly employed technique advocated in all surgical disciplines before incision closure. Irrigation hydrates the surgical bed, facilitates examination of the area immediately before closure, removes blood clots and contaminants from both superficial and deep incisional layers, and lowers the bioburden to expedite healing. This practice theoretically reduces the risk of infection. However, irrigation has not been standardized or definitively proven to reduce the risk of SSI, and the ideal lavage solution remains undetermined.[36–39]

Povidone–iodine has been recommended as an irrigation solution due to its potent oxidizing properties, which inactivate cell membranes and intracellular constituents in a concentration-dependent manner. In a recent study evaluating largely index THR surgeries, no postoperative infections developed after 3-minute lavage with 0.35% povidone–iodine solution, followed by rinsing with sterile saline before closing the incision in 97 primary THR and five revisions for luxation.[40]

Recent studies have indicated that a 0.35% solution of povidone–iodine is effective in eradicating methicillin-susceptible *Staphylococcus aureus* and *E. coli*, also showing the ability to remove periprosthetic joint infection bacteria biofilm on orthopaedic material, with negligible cytotoxic effects on osteoblasts, chondrocytes, and fibroblasts.[36,38,41–46]

Chlorhexidine gluconate (CHG) is a cationic bisbiguanide that binds to the negatively charged cell wall of bacteria, disrupting their osmotic equilibrium. Chlorhexidine gluconate has a broad spectrum of activity and is highly effective against various microorganisms responsible for SSI, including methicillin-susceptible *S. aureus*, methicillin-resistant *S. aureus*, coagulase-negative *Staphylococcus*, Gram-negative bacteria, fungi, and mycobacteria. The bactericidal effect of CHG is almost immediate, with maximum uptake occurring within 20 seconds of exposure. The duration of effect is directly related to the duration of exposure and concentration. The antimicrobial activity of CHG may last for an extended period, preventing the attachment and growth of other bacteria on surfaces. Although the optimal CHG dilution for intraoperative irrigation is debated, concentrations of 0.05 to 0.5% may effectively reduce bacterial load without being cytotoxic.[47,48]

In human medicine, a surgical lavage solution called Bactisure Wound Lavage (Zimmer Biomet) has recently been shown to reduce the bacterial load within the surgical site. Bactisure is a preformulated combination solution of ethanol, acetic acid, sodium acetate, and benzalkonium chloride in water. The acetic acid chelates the metal ions in the exopolysaccharide matrix, and the sodium acetate acts as a buffer to maintain an ideal pH. Benzalkonium chloride is a surfactant that reduces the surface tension of the biofilm and lyses bacterial cells. This lavage solution deconstructs EPS, which facilitates the exposure of the bacteria to antibiotics and the innate immune system, potentially leading to their subsequent eradication through lavage.[49,50] An identical solution was developed for use in veterinary medicine: Simini Protect Lavage (SPL). It is a hypertonic aqueous solution composed of ethanol (solvent), acetic acid (pH modifier), sodium acetate (buffer), benzalkonium chloride 0.13% (surfactant), and water. SPL is designed to break cross-links within the EPS of biofilms. Its effects become effective within 1 minute and must be removed by rinsing with an equal or greater volume of saline solution.

To the authors' knowledge, available information about the most effective treatment for SSI following orthopaedic surgery, which would also allow for one-stage revision surgery, is limited. Therefore, the purpose of this study was to report the short- and long-term clinical outcome of our THR revision case series while using the SPL added to our standard antiseptic protocol.

Methods

Case Selection

The medical records of dogs that underwent a revision orthopaedic surgery involving Zurich Cementless THRs (Kyon, CH) from November 2019 to December 2022, where SPL was used at Vezzoni Veterinary Clinic (Cremona, Italy), were retrospectively evaluated. To be included in the study, animals were required to have a clinical and radiographic follow-up evaluation a minimum of 1 year postoperatively, along with culture and sensitivity tests both before and after Simini lavage. Data collected included signalment, indication for the surgery, number of revisions surgeries, culture and antimicrobial susceptibility testing results before and after SPL, type and class of bacteria isolated, and outcome at the last reevaluation.

Surgical Procedure

All surgeries were performed by one of the authors (A.V.). The animals underwent a preoperative antibiotic prophylaxis protocol that included 20 mg/kg cefazolin sodium (Cefazolina 1 g, Teva, Italy) administered intravenous 30 minutes before the skin was incised and then every 90 minutes until the end of surgery. After the induction of general anaesthesia, the hair was clipped according to the procedure required, and the animals were moved to the operating theatre and positioned on the surgical table. Preoperative skin asepsis was achieved using a solution of 4.0% chlorhexidine digluconate and 2.6% isopropyl alcohol, followed by applying a solution of 0.5% CHG and 66.0% denatured ethyl alcohol. This procedure was repeated at least four times with a contact time of 8 minutes. Before draping, a coloured propanol-based skin antiseptic solution (Cutasept G; propan 2 of 72% + benzalkonium chloride; Bode-Chemie, Germany) was applied with a contact time of 2 minutes. SPL was used after debridement and implant removal and again after new implant positioning immediately before closing. SPL was employed in every surgical revision surgery and consistently in dogs undergoing multiple revision surgeries. The volume of SPL fluid used in each case was sufficient to cover the surgical wound. It was allowed to remain in contact with the wound for 1 minute, after which it was removed by rinsing with an equal or greater volume of saline solution (►**Figs. 1**, **2**). Two samples were collected for culture: the first at the beginning of the surgical procedure, from the synovial membrane, and the second from the joint before its closure. In all cases, a gentamicin-impregnated collagen sponge (Genta-coll Resorb) was applied after SPL and after the culture sample before suturing of the deep tissues (►**Fig. 2**).

All animals received 20 mg/kg of amoxicillin/clavulanic acid (Konclav, Fatro, Italy) orally, three times a day, until the culture and antimicrobial susceptibility testing results were available. Antibiotic therapy was then discontinued or adjusted based on the test results. In case with a positive culture at the end of surgery, antibiotic therapy was continued for 10 days.

Given on the retrospective observational nature of the study, ethical approval was not required; however, signed informed owner consent was obtained before all surgeries.

Results

Simini Protect Lavage was used in 36 cases of THR revision surgery between November 2019 and December 2022. The indication for surgery included dislocation of the prosthetic head ($n = 21$), cup loosening ($n = 5$), periprosthetic femoral fracture following THR ($n = 2$), stem breakage ($n = 4$), revision with THR of a capital physeal fracture previously treated with internal fixation ($n = 1$), revision of double pelvic osteotomy to implant the THR ($n = 1$), revision of extra-articular iliofemoral suture to implant the THR ($n = 1$), revision of infected THR ($n = 1$).

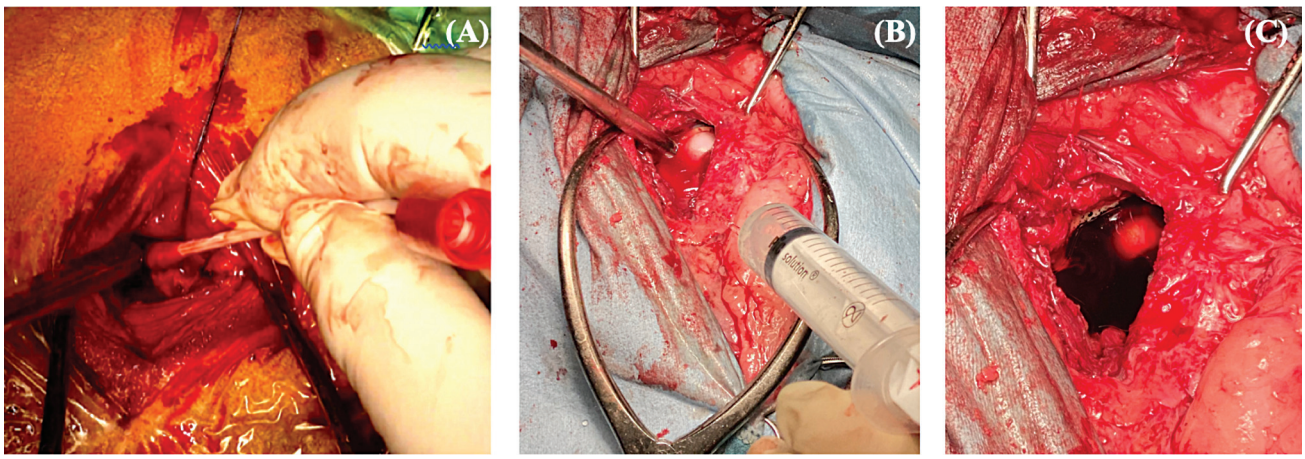

Fig. 1 Intraoperative images showing collection of a sample for microbial culture after debridement (**A**) and application of Simini Protect lavage fluid (**B**) using enough lavage fluid to cover the surgical wound (**C**).

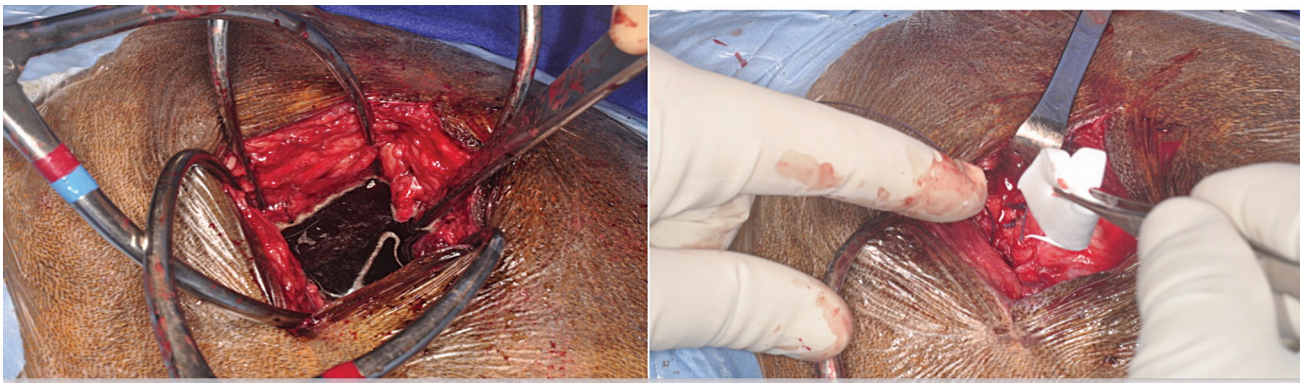

Fig. 2 Intraoperative images showing that Simini Protect Lavage fluid becomes black during 1 minute of contact with the surgical wound (left) and application of a Genta-coll Resorb sponge before closure (right).

Five dogs experienced three revision surgeries in a short period (cases: 1, 6, 7, 11, 21), 8 had two revision surgeries (cases: 2, 3, 4, 5, 13, 30, 32, 33), and the remaining 23 underwent one THR revision surgery (cases: 8, 9, 10, 12, 14, 15, 16, 17, 18, 19, 20, 22, 23, 24, 25, 26, 27, 28, 29, 31, 34, 35, 36).

The mean time of anaesthesia was 118.47 ± 47.08 minutes (range: 70–80 minutes, median: 100 minutes). The mean time of surgery was 79.58 ± 46.86 minutes (range: 25–240 minutes, median 60 minutes).

The bacterial culture results at the beginning of surgery were positive in 8 cases (cases: 1, 2, 6, 7, 8, 9, 10, 11) and negative in 28 (cases: 3, 4, 5, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36). At the end of the surgery, 7 dogs were still positive for bacterial infection (cases: 1, 2, 3, 4, 5, 6, 7), whereas the other 29 dogs had a negative culture and sensitive test with no postoperative infection developing (cases: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36).

The bacteria isolated at the beginning of surgery included *S. pseudintermedius* (methicillin-resistant *S. pseudintermedius* [MRSP, $n = 5$]), *Pseudomonas aeruginosa* ($n = 2$), and *Enterococcus faecalis* ($n = 1$). At the end of the surgery, after SPL was applied, the bacteria isolated were *Enterobacter cloacae* ($n = 1$) *and S. pseudintermedius* MRSP ($n = 6$).

Regarding the seven dogs with a positive swab at the end of the surgery, three underwent three consecutive revision surgeries (cases: 1, 6, 7), and four dogs underwent two consecutive revision surgeries due to recurrent luxation (cases: 2, 3, 4, 5). Only one case (case 1), which experienced three revision surgeries, required total implant explantation. The bacteria isolated at the end of the first revision surgery was the same as the bacteria isolated at the end of the following revision surgery in all seven cases.

In the other two cases (cases: 6, 7), the implant removal was carried out not for reasons related to infections, as the swabs were negative at the beginning and end of surgery, but due to the recurrence of THR dislocation.

The other dogs showed neither clinical nor radiographic signs of infection, with good outcomes over a long period (►**Table 1**).

In our cases, no complications, such as adverse tissue or bone reactions, delayed bone healing, or surgical wounds, were observed.

The mean duration of the last clinical and radiographic follow-up in cases where implants were not removed ($n = 33$) was 865.27 days (range: 612–1,557 days).

Of the 36 patients who received treatment, 34 showed no clinical or radiographic signs of infection, with only two cases exhibiting such signs. In one case (case 2) that underwent two surgical revision surgery with a positive swab for *S. pseudintermedius* MRSP at the beginning and end of the surgery, still showed signs of lysis around the stem screws. However, it was not clinically significant, and was managed conservatively.

Contrary to another case (case 1) that underwent three surgical revisions, with a positive swab for *S. pseudintermedius* (MRSP) at the beginning and at the end of the surgery for each surgical revision, which instead required explantation.

Discussion

Surgical site infection is an infection that occurs within 30 days of surgery and affects the incision, organs, or spaces in the body where the operation occurred.[51]

SSI is particularly challenging to resolve in orthopaedic surgery due to the possibility of bacterial biofilm formation on the implants. Biofilm adheres to implants, resists eradication, and necessitates implant removal to eliminate the infection.[32,52–54] For this reason, cases of revision surgeries were used to evaluate the effect of SPL on biofilms as an adjuvant to all previous measures.

In our study, only one case (case 8) underwent a positive preoperative culture and sensitivity test before the revision surgery, suggesting the probable presence of biofilm on the implants. This dog had previously experienced unsuccessful antibiotic treatment for the infection. However, using the SPL as an adjuvant during the revision surgery resulted in a successful outcome, effectively resolving the infection without requiring the removal of the prosthesis.

A preoperative culture and sensitivity test were not performed before the surgical revision for the other seven cases. However, the swab taken at the beginning of the

Table 1 Summary of the cases for surgical revision of total hip replacement in which Simini Protect Lavage was used

ID case	Number of revision surgery	Coculture and sensitive test before the use of Simini Protect Lavage	Coculture and sensitive test after the use of Simini Protect Lavage	Outcome
1	3	*Staphylococcus pseudintermedius* MRSP	*Staphylococcus pseudintermedius* MRSP	Explant
2	2	*Staphylococcus pseudintermedius* MRSP	*Staphylococcus pseudintermedius* MRSP	Good
3	2	Negative	*Staphylococcus pseudintermedius* MRSP	Good
4	2	Negative	*Enterobacter cloacae*	Good
5	2	Negative	*Staphylococcus pseudintermedius* MRSP	Good
6	3	*Staphylococcus pseudintermedius* MRSP	*Staphylococcus pseudintermedius* MRSP	Good
7	3	*Staphylococcus pseudintermedius* MRSP	*Staphylococcus pseudintermedius* MRSP	Good
8	1	*Pseudomonas aeruginosa*	Negative	Good
9	1	*Pseudomonas aeruginosa*	Negative	Good
10	1	*Staphylococcus pseudintermedius* MRSP	Negative	Good
11	3	*Staphylococcus pseudintermedius* MRSP	Negative	Good
12	1	Negative	Negative	Explant
13	2	Negative	Negative	Explant
14	1	Negative	Negative	Good
15	1	Negative	Negative	Good
16	1	Negative	Negative	Good
17	1	Negative	Negative	Good
18	1	Negative	Negative	Good
19	1	Negative	Negative	Good
20	1	Negative	Negative	Good
21	3	Negative	Negative	Good
22	1	Negative	Negative	Good
23	1	Negative	Negative	Good
24	1	Negative	Negative	Good
25	1	Negative	Negative	Good
26	1	Negative	Negative	Good
27	1	Negative	Negative	Good
28	1	Negative	Negative	Good
29	1	Negative	Negative	Good
30	2	Negative	Negative	Good
31	1	Negative	Negative	Good
32	2	Negative	Negative	Good
33	2	Negative	Negative	Good
34	1	Negative	Negative	Good
35	1	Negative	Negative	Good
36	1	Negative	Negative	Good

Abbreviation: MRSA, methicillin-resistant *Staphylococcus pseudintermedius*.

revision surgery tested positive for SSI, which may have compromised the surgical revision. The authors believe that using SPL as an adjuvant helped to avoid or limit the progression of these infections.

In the 28 cases where infection was not present at the beginning of the surgery, the authors suggest that the aseptic techniques, including the use of SPL, facilitated multiple surgical revisions, up to three in the same patient, without the occurrence of SSIs. Only two cases required implant removal, but this was for reasons unrelated to infection.

Out of the 28 cases, three presented with a negative swab prior to surgery but later exhibited signs of infection with a

positive swab postsurgery. These three cases underwent two surgical revisions, and subsequent swabs consistently returned positive results. Nonetheless, none of the three cases displayed clinical or radiographic signs of infection. The authors believe that the intraoperative technique utilized to disrupt the biofilm played a crucial role in allowing the antibiotics to eliminate the infection. However, it is important to recognize that, at this time, there is a lack of concrete evidence to substantiate this assertion.

Simini Protect Lavage was developed in veterinary medicine to remove planktonic bacteria and biofilms. It destroys the EPS matrix, exposing the bacteria to host defence mechanisms and antibiotics, and promotes eliminating bacteria from the surgical site. Ethanol, a key component, dehydrates and denatures proteins, interferes with the cell plasma membrane, disrupts cell metabolism, and halts bacterial growth.[55,56]

Specific procedures and patient-related factors can increase the risk of SSI. Operative time is often a predictor factor, with increased times associated with more complex surgical procedures. It is well known that longer operative times predispose patients to increased bacterial contamination. Eugster et al[57] reported that the risk of infection increased 1.01 times for each additional minute of surgery. Pratesi et al found that the risk of infection in orthopaedic surgeries increased by 2% for each additional minute of anaesthetic time.[58] That is an important consideration, especially when planning for the revision surgery. The estimated time of any revision surgery is difficult to predict due to the altered anatomy, need for implant removal and its replacement, which can result in longer anaesthetic times and a higher risk of postoperative infection.

In our study, gentamicin-impregnated collagen sponges were also applied, and antibiotic therapy was administered to all patients. Indeed, this represents a limitation of this study, as its purpose was not to compare the different additives but only to report our clinical experience using a new preformulated irrigation solution that allows surgical revisions to be carried out without the need to remove existing implants in which a biofilm had likely formed.

In our study, seven dogs had a positive culture and sensitivity test after using SPL. However, only one case that experienced three consecutive revision surgeries developed a clinical infection requiring THR explantation. The literature describes the possibility of a positive swab at the end of the surgery due to the duration of the surgery and anaesthesia. It has also been described as a positive swab after using antiseptic solution irrigation, particularly in human medicine after using Bactisure Wound Lavage. The authors reported that there was not a statistically significant increase in culturable bacteria after the wash, which may indicate only the liberation of bacteria from the biofilm, thus allowing antibiotic therapy to act.[13,59] Based on the findings above, it is plausible that the SPL exerted an effect in six out of the seven patients who tested positive for SSI, thereby permitting the antibiotic to function without leading to a long-term infectious condition.

The ideal volume, pressure, and irrigation duration for treatment or prevention of SSI need to be better defined. In human medicine, pulsed lavage with Bactisure Wound Lavage is reported to remove wound debris. Low-pressure lavage may be adequate for SSI with low bacterial load but may not be effective for deep SSI where bacteria and biofilm adhere to the implants and tissues.[12] Our study only applied the SPL to the wound without a pulse lavage. This procedure is based only on our subjective observation and should be verified with further studies.

Another essential aspect of antiseptic lavage is that not all commercially available antiseptic solutions are sterile, leading to nonsterile or multiuse containers harbouring contaminants. An advantage of the SPL is that it is dispensed in single-use 20-mL vials, which helps maintain the solution's sterility.

No complications directly related to SPL were observed. Wound healing and implant osseointegration were uneventful, suggesting that SPL was clinically nonirritating and noncytotoxic.

Conclusions

Simini Protect Lavage was used in 36 cases of surgical THR revisions with no signs of SSI based on both radiographic and clinical long-term observation in 35 cases. Only one dog, which underwent three revision surgeries, exhibited clinical and radiographic signs of persistent infection, requiring a THR explant.

In the context of surgical revision procedures, implementing a valid protocol for maintaining a sterile environment is of utmost importance. The incorporation of SPL into the antiseptic protocol in our total hip replacement revision case series seemed safe without causing further disruption to the osteointegration of the preserved implants or without negatively influencing postoperative surgical wound healing. The use of SPL as an adjuvant in the antiseptic protocol can be considered in THR revision surgeries even without a plan for prosthesis explantation. According to the conclusions of the in vitro study by Marquez-Gomez and colleagues, the use of several antiseptic agents in the same operation may be the most effective solution to treat and prevent periprosthetic infections.[59]

This work describes a protocol employed in a case series. One notable limitation of this study pertains to its retrospective nature and the absence of a control group.

Further studies are needed to objectively evaluate the efficacy of SPL in eradicating postoperative infections.

Author's Contribution

A.V. and I.F. contributed to the conception of the study. A.V., I.F., L.V., and M.B. contributed to the study design, acquisition of data, data analysis, and interpretation. All authors drafted, revised, and approved the submitted manuscript.

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Conflict of Interest

None declared.

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