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Antisepsis Techniques in Orthopedic Surgical Procedures: A Comparative Study*

Técnicas de antissepsia em procedimentos cirúrgicos ortopédicos: um estudo comparativo

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Abstract

Objective To compare antisepsis techniques using chlorhexidine-based soap associated with ethyl alcohol and alcohol-based chlorhexidine or chlorhexidine-based soap associated with alcohol-based chlorhexidine alone in surgical orthopedic procedures.
Methods This is a primary, randomized, analytical and single-center clinical trial consisting of 170 patients, who were divided into 2 groups. The combinations chlorhexidine-based soap + alcohol-based chlorhexidine (CSAC) and chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine (CSAAC) were tested in each group. The cultures were grown in mannitol and eosin methylene blue (EMB) after collection before skin preparation (time point 0), after skin preparation (time point 1) and at the end of the surgical procedure (time point 2).
Results There was no statistically significant difference regarding bacterial growth in mannitol and EMB between the groups at any time point. Moreover, there was no statistical difference between groups and time points regarding the type of bacterial growth in culture media.
Conclusion There was no difference between these antisepsis techniques for the prevention of surgical site infection in orthopedic procedures; in addition, a protocol containing measures to prevent infection in such procedures was developed.

Keywords
- chlorhexidine
- infection
- orthopedics
- operating rooms
- antisepsis
- surgical procedures

Resumo

Objetivo Comparar as técnicas de antissepsia utilizando clorexidina degermante associada a álcool etílico e a clorexidina alcoólica *versus* clorexidina degermante associada a clorexidina alcoólica, em procedimentos cirúrgicos ortopédicos.
Métodos Trata-se de um estudo clínico, primário, aleatorizado, analítico e de centro único, constituído por 170 pacientes ortopédicos submetidos a abordagem cirúrgica, alocados em 2 grupos aleatórios, nos quais foram testados clorexidina degermante +

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clorexidina alcoólica (grupo CDCA) e clorexidina degermante + álcool etílico a 70% + clorexidina alcoólica (grupo CDACA). Foram realizadas culturas nos meios manitol e eosina azul de metileno (EAM) de amostras colhidas nos períodos de pré-degermação (0), pós-degermação (1) e após a incisão suturada (2).

Resultados Em relação ao crescimento bacteriano nos meios de cultura manitol e EAM entre os grupos, em cada período de estudo (0, 1 e 2), não ocorreu diferença estatística significativa nesta pesquisa. Na avaliação do tipo de crescimento bacteriano nos meios de cultura manitol e EAM, também não foi constatada significância estatística entre os grupos.

Conclusão Não ocorreu diferença entre as técnicas utilizadas na antissepsia para prevenção de infecção de sítio cirúrgico em procedimentos ortopédicos, mas, ao final do trabalho, foi possível a elaboração de um protocolo de medidas para realização de prevenção infecciosa nesses procedimentos.

Palavras-chave
- clorexidina
- infecção
- ortopedia
- salas cirúrgicas
- antissepsia
- procedimentos cirúrgicos

Introduction

Surgical site infection (SSI) is among the most researched subjects, and it is frequently associated with surgical complications, affecting up to one third of patients undergoing surgical procedures in low- and middle-income countries.

Data from the Centers for Disease Control and Prevention estimates that nearly 500 thousand SSIs occur each year, representing almost a quarter of nosocomial infections in the United States annually.[1]

In Brazil, although there are no systematic data, SSIs are ranked third among causes of infection, being found in approximately 14% to 16% of hospitalized patients. In addition to the physical, psychological and financial damages to patients, SSI can prolong the hospital stay by an average of seven to eleven days; moreover, it increases the chances of hospital readmission and additional surgeries, resulting in an exorbitant increase in care expenses, which may reach US$ 1.6 billion per year.[2,3] Literature reviews provide historical data on antisepsis, from rudimentary procedures, which are evidently far from being safe and effective, to those known today.[4] In a systematic review, Lee et al[5] concluded that chlorhexidine-based compounds are more effective for surgical site antisepsis than iodine, leading to a significant cost reduction.

Mears et al,[6] Swenson et al,[7] Saltzman et al,[8] and Savage and Anderson[1] were able to prove the efficacy of chlorhexidine compared with iodine. Reichel et al[9] showed the effectiveness of alcohol + chlorhexidine in skin antisepsis.

It is agreed that the effectiveness of surgical preparation directly impacts the occurrence of SSIs, which depends on the antiseptic solution used and on the method of application. However, it is not clear which should be the antiseptic solution or association, the time for action, the application methodology, or the moment in which skin antisepsis should be performed. As such, the present study aims to compare the effectiveness of chlorhexidine-based soap + alcohol-based chlorhexidine (CSAC) and chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine (CSAAC) to evaluate the best way of skin preparation for orthopedic surgical procedures regarding bacterial growth and surgical time.

Materials and Methods

The present is a primary, randomized, prospective, analytical, single-blinded and single-centered clinical study to compare antisepsis techniques using CSAC and CSAAC in orthopedic surgical procedures. The data were collected in the operating room and in a research laboratory from a high-complexity hospital from the Brazilian Unified Health System (Sistema Único de Saúde, SUS, in Portuguese). After approval by the Ethics in Research Committee on May 9, 2017 (under opinion number 2.054.709), the study was conducted from June to November 2017.

In total, 190 patients were selected according to the eligibility criteria, and the final sample was composed of 170 patients who would undergo orthopedic surgical procedures.

The inclusion criteria were: both male and female patients; those older than 18 years of age; patients submitted to all elective orthopedic surgical procedures; and those who signed the informed consent form (ICF). The exclusion criteria were: patients undergoing urgent/emergency surgery; patients with a known history of chlorhexidine allergy or who had any kind of skin or systemic reaction during its application; those with existing skin lesions; patients from the intensive care center; those with open fractures at the time of the initial care; and patients using external fixators for fracture stabilization. Cases of preoperative death and of loss of material were also excluded.

The patients who met the eligibility criteria were separated through a random number table generated by the website http://www.randomization.com (# 25432, May 8, 2017) into two groups: CSAC and CSAAC. The patients were properly prepared for the surgical procedure following the Health Care Infection Prevention Measures of the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária, ANVISA, in Portuguese),[3] including a full-body bath two hours prior to surgery with the use of 4% chlorhexidine in those undergoing major elective surgery or receiving orthopedic implants; the patients undergoing elective minor or medium-sized surgeries used only neutral soap in the full-body bath. Patients using

plaster cast immobilizations were exempted from the full-body bath, since plaster removal would cause pain and discomfort, and it is associated with risks, including fracture-related skin perforation.

At the operating room, complying with the antibiotic prophylaxis protocol, the patients received intravenous (IV) cefazolin, 2 g diluted in 250 mL of saline solution, starting 30 minutes before the procedure; next, every 8 hours, 1 g of IV cephazolin was administered for 24 hours after surgery. The preoperative blood sugar level was measured 30 minutes before the procedure and immediately after surgery. Patients who had hair at incision sites underwent a hair clipping procedure using a 3M (Maplewood, MN, US) device; disposable blades were used for each patient, according to the previously mentioned Health Care Infection Prevention Measures.[3]

After anesthesia, sterile swabs were used to collect samples from the patient's skin microbiota at a previously selected location in the surgical site, in a 16-cm^2 area determined by a previously cut paper field sterilized at the Sterilization Center. The samples were collected at the three time points.

All samples were placed in test tubes with 1 mL of buffered phosphate solution and sent to the research laboratory, where they were cultivated on plates with mannitol or eosin methylene blue (EMB) agar media.

All test tubes containing the collected swabs and culture plates were sequentially numbered according to each patient, from 1 to 170. The time points were identified as 0, 1 and 2. The number 0 corresponds to the materials collected before skin preparation; number 1 refers to materials collected after skin preparation with 4% chlorhexidine followed by excess removal with dry gauze or gauze soaked in 70% ethyl alcohol; and number 2 refers to the materials collected at the end of surgery (►**Figure 1**).

In both groups, samples were collected from the surgical site before skin preparation (time point 0) with 4% chlorhexidine for 5 minutes. Any excess material was removed in a single, proximal to distal movement with a simple, sterile gauze soaked in 70% alcohol for the CSAAC group and a simple, sterile dry gauze for the CSAC group.

After skin preparation, sterile swabs were similarly used to collect samples in the previously studied area, followed by antisepsis with alcohol-based chlorhexidine and placement of surgical drapes (time point 1). At the end of the surgical procedure (after incision closure), while the patient was still at the sterile environment, a new sample was collected using the same technique at the same demarcated site (time point 2). The samples were placed separately in test tubes with 1 mL of buffered phosphate solution and sent to the laboratory for analysis.

After 48 hours of culture, the culture media were evaluated for organism growth. In case of growth, the number of colonies was counted, and Gram-positive (*Staphylococcus aureus* and non-*aureus*) and Gram-negative bacteria were identified. Samples from all time points, in both the mannitol and EMB media, were evaluated to verify if the number of colonies had decreased, increased or remained unaltered after skin preparation. In the case of growth in cultures from time point 2 (after incision closure), the plates were sealed with tape and sent to the Clinical Analysis Laboratory for sensitivity determination. Thus, all subjects were evaluated regarding the efficacy of the antisepsis, as well as the organisms growing at culture.

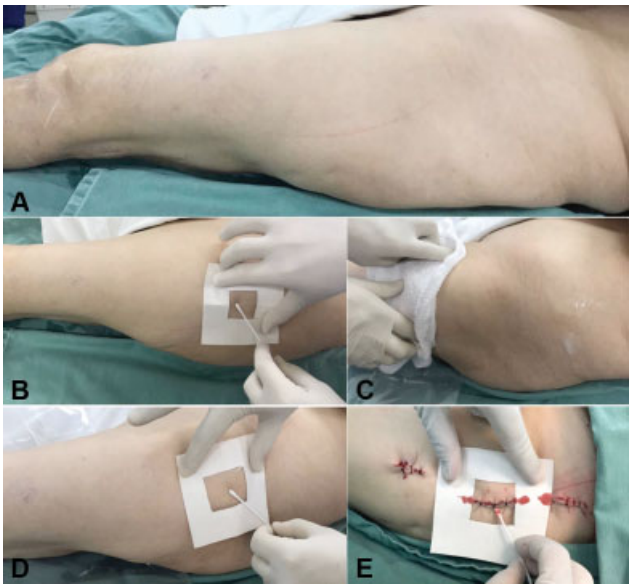

Fig. 1 Figures showing the time of sample collection. (**A**) Patient under anesthesia, with the surgical limb isolated with drapes; (**B**) sample collected before skin preparation; (**C**) skin preparation with chlorhexidine-based soap and excess removal; (**D**) sample collected after skin preparation; (**E**) sample collected at the end of the surgery, after surgical wound closure, with the patient still in the sterile environment.

The data were tabulated in Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, US) spreadsheets and submitted to statistical analysis. The Chi-squared test was performed using the Statistical Package for the Social Sciences (SPSS, IBM Corp. Armonk, NY, US), version 20.0.0, with the null hypothesis rejection level set at 5% ($p \leq 0.05$). The numerical variables were analyzed using descriptive statistics, calculating mean and median values.

Results

The present study compares the skin preparation performed at the Orthopedics and Traumatology Service using a chlorhexidine-based soap plus alcohol-based chlorhexidine and a chlorhexidine-based soap plus 70% ethyl alcohol and alcohol-based chlorhexidine. In total, 170 patients were eligible to participate in the study, and they were separated into 2 groups of 85 patients each. In the first group (CSAC), skin preparation was performed with chlorhexidine-based soap + alcohol-based chlorhexidine, whereas the skin preparation of the second group (CSAAC) was performed with chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine. During material collection, four sequential plates were contaminated; these plates were handled by the same resident, which justified the coincidence. Thus, these plates were eliminated, and the patients were excluded from the

study. In total, 4 patients were excluded, curiously 2 from each group; as such, the final sample consisted of 166 patients divided into 2 groups of 83 patients each.

Regarding bacterial growth in the mannitol and EMB culture media, significant differences were found between the second and third time points (1 and 2) and time point 0 (►**Table 1**); however, due to the lack of any intervention at this time point, this finding had no relevance for the present study. There were no statistically significant differences between other time points, indicating that there was no difference in the results of the two skin preparation methods (►**Table 2**).

The type of bacterial growth in the mannitol and EMB culture media from samples collected after incision closure did not depend on the skin preparation method (►**Tables 3** and **4**).

Both methods of skin preparation resulted in similar bacterial colony-forming unit (CFU) values (expressed as n x10 UFC/mL) obtained in both culture media (EMB and mannitol) and at all time points (0, 1 and 2). The mean CFU values were 27.3213×10 CFU/mL and 27.5874×10 CFU/mL for the CSAC and CSAAC groups respectively (►**Table 5**).

Bacterial growth in the mannitol and EMB culture media from samples obtained at time point 2 (after incision closure) was observed in 39% of the cases. These samples were sent to the Clinical Analysis Laboratory of our institution, which identified the prevalence of *Staphylococcus epidermidis* (58.33%), followed by *S. aureus* (13.88%) (►**Table 6**).

Table 1 Bacterial growth in the mannitol culture medium in the CSAC and CSAAC groups at each time point: before skin preparation (0), after skin preparation (1), and after incision closure (2)

Mannitol		Group					
		CSAAC		CSAC		Total	
		n	%	n	%	n	%
Time point 0– before skin preparation	Negative growth	6	7.3	16	19.3	22	13.3
	Positive growth	77	92.7	67	80.7	143	86.7
	Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**
Time point 1– after skin preparation	Negative growth	52	62.7	43	51.8	94	57.0
	Positive growth	31	37.3	40	48.2	71	43.0
	Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**
Time point 2– after incision closure	Negative growth	52	62.7	51	61.4	103	62.0
	Positive growth	31	37.3	32	38.6	63	38.0
	Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**

Abbreviations: CSAC, chlorhexidine-based soap + alcohol-based chlorhexidine; CSAAC chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine.
Note: There was a statistically significant difference between the groups regarding bacterial growth in the mannitol culture medium at time point 0–before skin preparation ($p = 0.024$). The growth rate was higher in the CSAAC group compared to the CSAC group. No statistically significant difference was observed between the groups at time points 1 ($p = 0.138$) and 2 ($p = 0.873$).

Table 2 Bacterial growth in the eosin methylene blue (EMB) culture medium in the CSAC and CSAAC groups at each time point: before skin preparation (0), after skin preparation (1) and after incision closure (2)

EMB		Group					
		CSAAC		CSAC		Total	
		n	%	n	%	N	%
Time point 0– before skin preparation	Negative growth	67	80.7	62	74.7	128	77.6
	Positive growth	16	19.3	21	25.3	37	22.4
	Total	**83**	**100.0**	**83**	**100.0**	**165**	**100.0**
Time point 1– after skin preparation	Negative growth	77	92.7	73	88.0	149	90.3
	Positive growth	6	7.3	10	12.0	16	9.7
	Total	**83**	**100.0**	**83**	**100.0**	**165**	**100.0**
Time point 2– after incision closure	Negative growth	75	90.4	74	89.2	149	89.8
	Positive growth	8	9.6	9	10.8	17	10.2
	Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**

Abbreviations: CSAC, chlorhexidine-based soap + alcohol-based chlorhexidine; CSAAC chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine; EMB, eosin methylene blue.
Note: There was no statistically significant difference between the groups regarding bacterial growth in the EMB culture medium at time points 0 ($p = 0.373$), 1 ($p = 0.305$) and 2 ($p = 0.798$).

Discussion

Widerström[10] evaluated the clinical importance of coagulase-negative staphylococci, particularly *S. epidermidis*, as a major cause of healthcare-associated infections. Its pathogenicity is favored by the natural niche in human skin, thus resulting in an opportune contamination point, which reinforces the importance of correct skin preparation.

Table 3 Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) growth in the mannitol culture medium in the CSAC and CSAAC groups at each time point: before skin preparation (0), after skin preparation (1) and after incision closure (2)

Bacteria	Group					
	CSAAC		CSAC		Total	
	n	%	n	%	N	%
Negative growth	49	59.1	43	51.8	92	55.4
GPC	29	35.8	31	37.4	60	36.1
GNB	2	2.4	2	2.4	4	2.4
GPC and GNB	3	3.6	7	8.4	10	6.1
Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**

Abbreviations: CSAC, chlorhexidine-based soap + alcohol-based chlorhexidine; CSAAC chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine.
Note: There was no statistically significant difference between the groups regarding the type of bacteria ($p = 0.536$) after incision closure.

Table 4 Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) growth in the eosin methylene blue culture medium in the CSAC and CSAAC groups at each time point: before skin preparation (0), after skin preparation (1) and after incision closure (2)

Bacteria	Group					
	CSAAC		CSAC		Total	
	n	%	n	%	N	%
Negative growth	51	61.4	52	62.6	103	62.0
GPC	26	31.3	27	32.6	53	31.9
GNB	0	.0	0	.0	0	.0
GPC and GNB	6	7.3	4	4.8	10	6.1
Total	**83**	**100.0**	**83**	**100.0**	**166**	**100.0**

Abbreviations: CSAC, chlorhexidine-based soap + alcohol-based chlorhexidine; CSAAC chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine.
Note: There was no statistically significant difference between the groups regarding the type of bacteria ($p = 0.783$) after incision closure.

The literature still debates the best association of antiseptic agents, as well as the method and time of application. Martínez et al[11] performed the first clinical trial to compare isopropyl alcohol and chlorhexidine in isopropyl alcohol for skin preparation to prevent blood culture contamination. These authors showed that blood contamination rates were not different when isopropyl alcohol and chlorhexidine were compared.[11]

A review of American English and French guidelines found that there is no consensus on how antiseptics should be applied. While the American and English guidelines are unclear about skin cleansing before antiseptic application (an approach that can improve the effectiveness of the

Table 5 Quantitative analysis of the samples in the culture media at the different time points

Time point	Medium	Group	Mean value (x 10 CFU/mL)
Before skin preparation	EMB	CSAC	17.0843
		CSAAC	12.1707
		Total	14.6424
	Mannitol	CSAC	116.7590
		CSAAC	133.6951
		Total	125.1758
	Total	CSAC	66.9217
		CSAAC	72.9329
		Total	69.9091
After skin preparation	EMB	CSAC	4.9518
		CSAAC	0.2317
		Total	2.6061
	Mannitol	CSAC	21.5542
		CSAAC	4.1707
		Total	12.9152
	Total	CSAC	13.2530
		CSAAC	2.2012
		Total	7.7606
After incision closure	EMB	CSAC	0.3976
		CSAAC	0.2439
		Total	0.3212
	Mannitol	CSAC	3.1807
		CSAAC	15.0122
		Total	9.0606
	Total	CSAC	1.7892
		CSAAC	7.6280
		Total	4.6909
Total	EMB	CSAC	4.4779
		CSAAC	4.2154
		Total	5.8566
	Mannitol	CSAC	47.1647
		CSAAC	50.9593
		Total	49.0505
	Total	CSAC	27.3213
		CSAAC	27.5874
		Total	27.4353

Abbreviations: CFU, colony-forming units; CSAC, chlorhexidine-based soap + alcohol-based chlorhexidine; CSAAC chlorhexidine-based soap + 70% ethyl alcohol + alcohol-based chlorhexidine; EMB, eosin methylene blue.

Table 6 Microbiological analysis of the samples obtained at time point 2 (after incision closure)

Bacterium	Frequency (%)
Staphylococcus epidermidis	58.33
Staphylococcus aureus	13.88
Acinetobacter iwoffii	11.14
Staphylococcus saprophyticus	4.16
Staphylococcus warneri	4.16
Staphylococcus hominis	2.77
Staphylococcus auricularis	1.39
Staphylococcus capitis-capitis	1.39
Staphylococcus haemolyticus	1.39
Staphylococcus capitis-ureolyticus	1.39

Table 7 Data from the hospital's Infection Control Center (ICC) regarding orthopedic surgeries and incidence of surgical site infections (SSIs) in 2017

Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Total
Number of surgeries	115	101	135	139	131	146	152	129	130	124	123	136	1,561
SSI	7	4	4	3	7	3	2	1	4	1	2	2	40
%	6.1	4.0	2.96	2.16	5.34	2.05	1.32	0.78	3.08	0.81	1.63	1.47	2.64

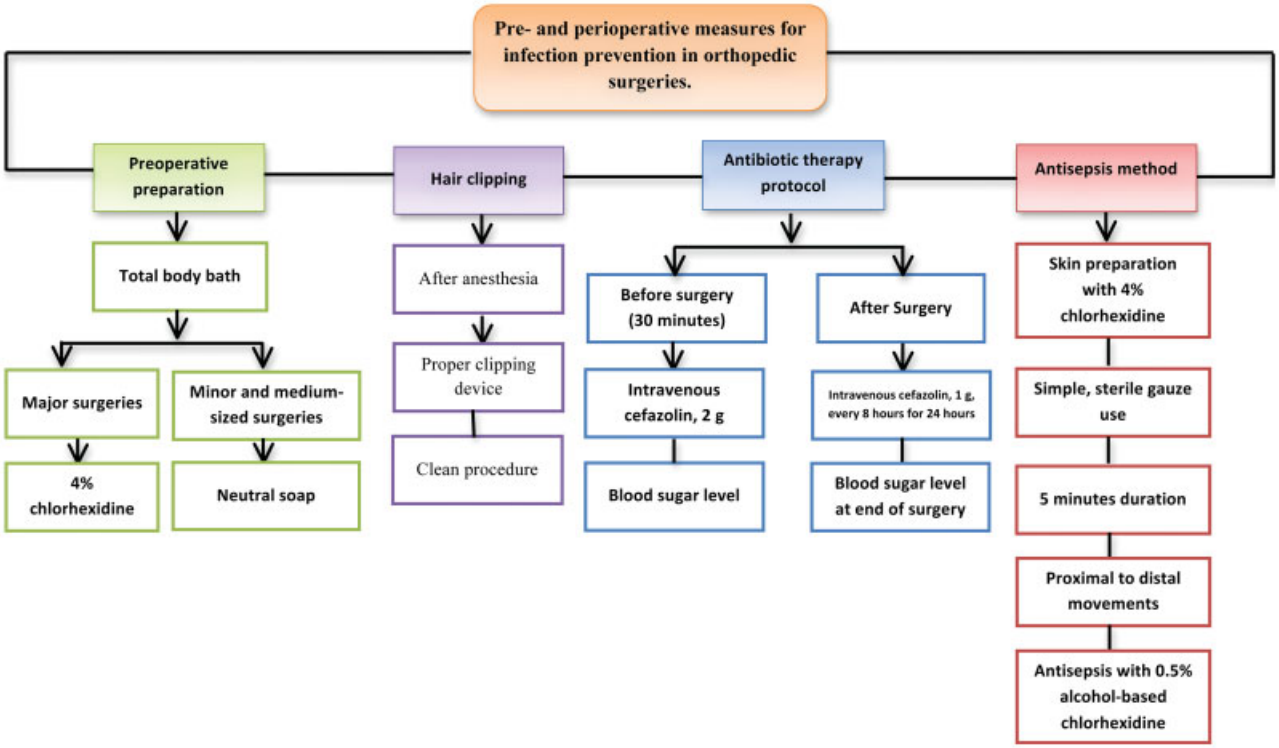

Fig. 2 Pre- and perioperative measures for infection prevention in orthopedic surgeries.

antiseptic by reducing the cutaneous amounts of bacteria and protein material), the French guidelines recommend cleansing the skin with a detergent before disinfection.[12]

The results of the present study do not determine which is the best antiseptic association for orthopedic patients, but data from our hospital's Infection Control Center (ICC) (►**Table 7**) obtained at the end of the study showed a reduction in ISS prevalence in such individuals, corroborating the principle that the development and adoption of a protocol (►**Figure 2**) can significantly lower ISS rates.

Conclusion

There was no statistical difference between skin preparation with chlorhexidine-based soap plus alcohol-based chlorhexidine or chlorhexidine-based soap plus 70% ethyl alcohol and alcohol-based chlorhexidine to prevent ISS in Orthopedics. However, the adoption of a pre-, peri- and postoperative protocol is effective in reducing SSI rates.

Further studies, with larger samples, may present more details regarding the best method for the application of antiseptics. Thus, the best agent and application method continue to be discussed.

Conflict of Interests

The authors have no conflict of interests to declare.

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