Efficacy of surgical skin preparation solutions in hip arthroplasty: a prospective randomized trial

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Background: The use of an effective antimicrobial preoperative skin preparation solution is essential in preventing infections after surgery, but the findings in the literature regarding efficacy are not necessarily applicable to surgery involving the hip. The purpose of the present study was twofold: 1) to examine the native bacteria on the skin at the hip and 2) to determine the efficacy of 2 surgical skin preparation solutions at eliminating bacteria from the hip site in patients undergoing total hip arthroplasty.

Methods: We conducted a prospective randomized controlled trial in consecutive adult patients who underwent primary total hip arthroplasty at a single institution from October 2014 to December 2015. Each patient was randomly allocated to be treated with 1 of 2 commonly used surgical skin preparation solutions: ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol) or DuraPrep (0.7% iodophor and 74% isopropyl alcohol). Aerobic and anaerobic samples were obtained for culture before skin preparation, immediately after skin preparation and after skin closure.

Results: Full data were obtained for 105 patients: 54 in the ChloraPrep group and 51 in the DuraPrep group. *Staphylococcus epidermidis*, *Corynebacterium* and *Micrococcus luteus* were the organisms most commonly isolated from the hip before skin preparation. Positive bacterial culture results were obtained in 50 patients (93%) in the ChloraPrep group and 48 patients (94%) in the DuraPrep group. Immediately after skin preparation, the overall proportion of positive culture results was significantly lower in the DuraPrep group than the ChloraPrep group (14% v. 35%, adjusted relative risk 0.40, 95% confidence interval 0.18–0.85). After wound closure, there was no significant difference in the rate of positive culture results between the 2 groups.

Conclusion: DuraPrep was more effective than ChloraPrep at eliminating skin flora at the hip initially on application, but the 2 solutions were equally effective at the time of closure. Further study with larger samples is required to identify any influence of skin preparation solution on the incidence of prosthetic joint infection.

Contexte : L'utilisation d'une solution antimicrobienne efficace pour la préparation cutanée préopératoire est essentielle à la prévention des infections après une opération, mais les constats publiés sur l'efficacité d'un tel produit ne s'appliquent pas nécessairement aux interventions chirurgicales à la hanche. La présente étude avait 2 objectifs : 1) examiner les bactéries endogènes sur la peau de la hanche et 2) déterminer l'efficacité de 2 solutions de préparation chirurgicale pour la peau dans l'élimination des bactéries sur la hanche chez les patients et patientes subissant une arthroplastie totale de la hanche.

Méthodes : Nous avons mené un essai clinique randomisé prospectif auprès de patients adultes consécutifs ayant subi une arthroplastie primaire totale de la hanche dans un seul établissement entre octobre 2014 et décembre 2015. Chaque patient a été aléatoirement traité avec 1 de 2 solutions de préparation chirurgicale pour la peau couramment utilisées : ChloraPrep (gluconate de chlorhexidine à 2 % et alcool isopropylique à 70 %) ou DuraPrep (polyvidone iodée à 0,7 % et alcool isopropylique à 74 %). Des échantillons d'organismes aérobies et anaérobies ont été obtenus pour réaliser une culture avant la préparation cutanée, immédiatement après la préparation cutanée et après la suture de la plaie.

Résultats : Des données complètes ont été recueillies pour 105 patients : 54 du groupe ChloraPrep et 51 du groupe DuraPrep. *Staphylococcus epidermidis*, les bactéries du genre *Corynebacterium* et *Micrococcus luteus* étaient les organismes les plus fréquemment isolés sur la hanche avant la préparation cutanée. Des résultats de culture bactérienne positifs ont été obtenus chez 50 patients (9 %) du groupe ChloraPrep et chez 48 patients (94 %) du groupe DuraPrep. Immédiatement après la préparation cutanée, la proportion globale de résultats de culture positifs était significativement plus faible

dans le groupe DuraPrep que dans le groupe ChloraPrep (14 % c. 35 %; risque relatif ajusté 0,40, intervalle de confiance de 95 %, 0,18–0,85). Après la fermeture de plaie, il n'y avait aucune différence significative dans le taux de résultats de culture positifs entre les 2 groupes.

Conclusion : DuraPrep était plus efficace que ChloraPrep pour éliminer la flore cutanée de la hanche à la première application, mais les 2 solutions présentaient la même efficacité lors de la fermeture de plaie. D'autres études comportant de plus grands échantillons seront nécessaires pour déterminer l'influence des solutions de préparation cutanée sur la fréquence des infections de prothèse articulaire.

Postoperative infections are relatively uncommon after arthroplasty, with reported rates ranging between 0.25% and 2.0%.[1] When postoperative infections do occur, they can lead to considerable patient morbidity and cost.[2,3] A potential risk factor for the development of postoperative wound infection is the amount of bacterial skin flora present at the operative site at the time of surgery. Human skin is home to a diverse community of microorganisms. Therefore, it is critical to use an effective antimicrobial preoperative skin preparation solution to prevent contamination at the surgical site and, in turn, the surgical wound.

Several different types of antimicrobial skin preparation solutions are currently available. Guidelines published by the Centers for Disease Control and Prevention and the World Health Organization state that alcohol-based preparations combining chlorhexidine or iodophors with alcohol are recommended in preference to aqueous-based solutions.[4,5] However, these guidelines do not provide consensus regarding which agent to combine with alcohol, and, thus, controversy still exists as to which solution is superior.

Several authors have investigated bacterial cultures before and after skin preparation for orthopedic surgery; however, the procedures were performed on the foot, shoulder, lumbar spine, knee or hand.[6–10] The topography of the hip is quite different from that of other sites, and different native bacterial flora likely reside in this region.[11,12] In addition, the hip is adjacent to several distinct areas, including the inguinal fold, buttock and perineum. Thus, the findings in the literature are not necessarily applicable to surgery involving the hip.

The purpose of this study was twofold: to examine the native bacteria present on the skin around the hip, and to assess the efficacy of 2 of the most commonly used surgical skin preparation solutions, ChloraPrep (chlorhexidine–alcohol) and DuraPrep (iodine–alcohol), at eliminating bacteria from the hip site.

Methods

Study design and participants

This prospective randomized trial included consecutive adult patients who underwent elective primary total hip arthroplasty at a single institution from October 2014 to December 2015. A 3-month moratorium (July–September 2015) was imposed on the study owing to limitations of supply of the neutralization agent. All procedures were performed by 1 of 3 fellowship-trained arthroplasty surgeons (K.P.D., D.P., C.C.) using the lateral or posterior approach. Research ethics board approval was obtained from the institution. All patients gave informed consent to participate in the study and were required to be able to communicate in English.

Patients were formally interviewed by a clinical trials nurse to obtain information about confounding variables such as smoking history and chronic disease, including diabetes. Patients were excluded if they had had previous hip surgery, had evidence of an abrasion or open wound at the incision site, had an active infection at or near the incision site or elsewhere in the body, or were chronically immunosuppressed.

All patients were seen at 6 weeks and 3 months postoperatively to evaluate for any wound complications.

Skin preparation

Hair within the surgical region was removed with clippers just before surgery. No antimicrobial bathing cleanser was used preoperatively. Perioperative antibiotics were given to all patients (1 or 2 g of cefazolin, depending on weight, within 1 h of surgery; if allergic to penicillin, they received 600 or 900 mg of clindamycin, depending on weight). No antimicrobial adhesive drape was used for any of the procedures.

Immediately before surgery, patients were randomly assigned to receive 1 of 2 commonly used surgical skin preparation agents: ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol; Enturia) or DuraPrep (0.7% iodophor and 74% isopropyl alcohol; 3M Healthcare). Randomization, with an allocation ratio of 1:1, was performed by a clinical trial nurse by opening a sealed envelope that indicated the agent to be used. Each hip region was then prepared according to the manufacturer's instructions by trained operating room staff and allowed to dry. Patients and surgeons were not blind to treatment group; however, culture specimens did not identify which treatment group the participant belonged to in order to blind those performing the laboratory analysis and reporting the results of bacterial culture.

Sampling and culture

All patients had culture specimens obtained before skin preparation, after skin preparation and immediately after skin closure. Both aerobic and anaerobic cultures were done; therefore, 6 specimens were obtained for each patient. All culture specimens were collected with premoistened, sterile rayon-tipped swabs (aerobic: Copan Diagnostics; anaerobic: Starplex Scientific). A validated neutralization agent was used to ensure that the antimicrobial activity of the skin preparation solution was stopped immediately upon sampling. The specimens obtained before skin preparation were premoistened with sterile saline, and those obtained after skin preparation and after skin closure were premoistened with neutralization agent, since these were the samples that incorporated the skin preparation agent.

A 4 cm × 4 cm area adjacent to the proposed incision site was sampled before preparation. Once the skin was prepared with agent, the square was divided in half; one half was used for sampling after skin preparation, and the other half for sampling after skin closure. This ensured that neutralization solution would not be applied to the postclosure section before sampling. Swab sampling was performed by the surgeon with a firm motion for a minimum of 10 seconds on the skin. The swab was placed in a sterile container and immediately transported to the microbiology laboratory at our hospital.

All cultures were incubated for 7 days. Swab samples of neutralization agent were analyzed weekly and served as negative controls. Neutralization agent was supplied by an independent laboratory (MicroBioTests) not affiliated with the study. Details of the neutralization agent have been previously described.[8]

Statistical analysis

Sample size requirements were based on the findings of a prospective randomized study evaluating the rate of positive results of culture of specimens from the shoulder after skin preparation.[7] On the basis of the assumption that a 20% difference in positive culture rates would be clinically relevant, the number of participants required to achieve 80% power at $\alpha = 0.05$ would be at least 50 per group. We used descriptive statistics (means and proportions) to present baseline patient characteristics including age, sex, body mass index, and proportions of smokers, patients with diabetes and patients diagnosed with rheumatoid arthritis. We presented proportions of positive culture results overall and for the most common bacteria for the prepreparation, postpreparation and postclosure stages. We computed the relative risk (RR) of a positive culture result for the 2 skin preparation solution groups by time (after surgical skin preparation and after skin closure) using a generalized linear model. Within the model, we adjusted for patient characteristics (age, sex, body mass index), duration of surgery and culture result (positive or negative) at prepreparation. For the most common bacteria, we calculated RRs comparing group by time (after skin preparation and after skin closure). We also examined percent reduction and associated RR of the most common bacteria by group by time (before v. after skin preparation; after skin closure v. after skin preparation). Significance was defined as $p < 0.05$.

Results

Between October 2014 and December 2015, 347 patients consented for total hip arthroplasty. Of the 347, 115 were enrolled in the study (Figure 1). Ten patients were excluded after randomization; reasons for exclusion were no neutralization agent available ($n = 5$), use of a contaminated neutralization agent (negative control for the lot returned with a positive result) resulting in a spurious microbiologic profile ($n = 3$), antimicrobial skin wash used ($n = 1$) and withdrawal from study before surgery ($n = 1$) (Figure 1). The trial ended when the last follow-up visit was completed, in May 2016. Full data were obtained for 105 patients: 54 in the ChloraPrep group and 51 in the DuraPrep group.

The study included 58 male and 47 female patients with an average age of 65.8 (range 36–86) years, average body mass index of 29.9 (range 27.1–47.1) and average duration of surgery of 60 (range 23–103) minutes. Twelve patients (11.4%) were active smokers, 18 (17.1%) had diabetes, and 10 (9.5%) had been diagnosed with rheumatoid arthritis. The 2 groups were similar across patient characteristics (Table 1).

Culture results

Culture of specimens obtained before surgical skin preparation gave positive results in 50 (93%) and 48 (94%) of patients allocated to the ChloraPrep and DuraPrep groups, respectively (Table 2). The most common bacterial organisms isolated were *Staphylococcus epidermidis* (50 isolates), *Corynebacterium* (47 isolates), *Micrococcus luteus* (40 isolates), *S. hominis* (38 isolates) and *S. capitis* (22 isolates) (Figure 2). *Propionibacterium acnes* was cultured in 5 isolates. A mean of 3.4 different organisms were isolated from the site. Two or more isolates were obtained in 76 patients (72.4%), and 3 or more were identified in 66 (62.8%). *Corynebacterium* was present in 32 patients (63%) in the DuraPrep group, compared to 17 (31%) in the ChloraPrep group. No other differences in organism distribution were identified between the 2 groups.

Immediately after skin preparation, the overall proportion of positive culture results was significantly lower in the DuraPrep group than in the ChloraPrep group (14%

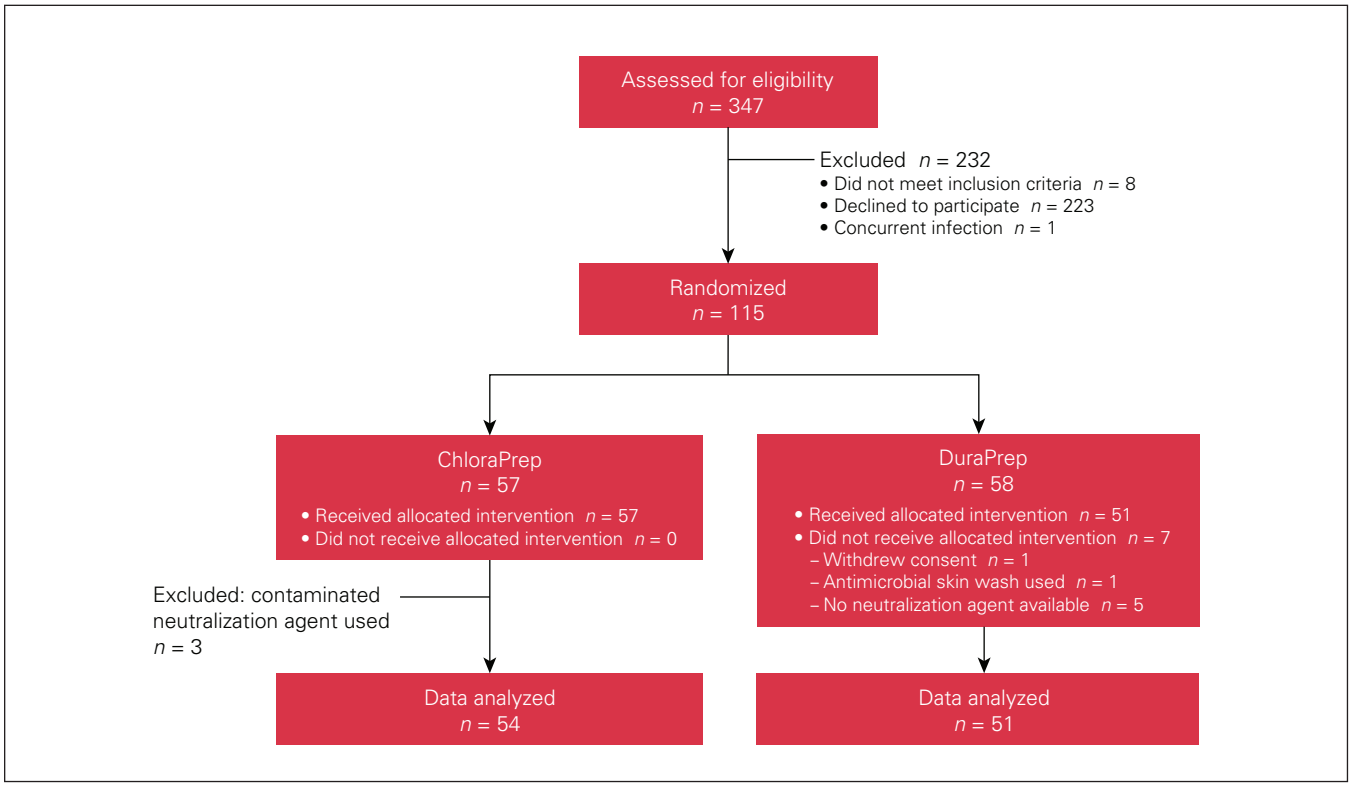

Fig. 1. Flow diagram showing patient allocation.

Table 1. Baseline characteristics of patients who underwent total hip arthroplasty, by surgical skin preparation solution

Characteristic	Group; no. (%) of patients* ChloraPrep n = 54	DuraPrep n = 51
Sex		
Male	30 (56)	28 (55)
Female	24 (44)	23 (45)
Age, mean ± SD, yr	65.6 ± 11	65.9 ± 11
Body mass index, mean ± SD	30.0 ± 5.6	30.1 ± 5.6
Smoker	6 (11)	6 (12)
Diabetes	7 (13)	11 (22)
Rheumatoid arthritis	6 (11)	4 (8)
Surgery duration, mean ± SD, min	59 ± 19	60 ± 19

SD = standard deviation.
*Except where noted otherwise.

Table 2. Overall positive culture results

Time	Group; no. (%) of patients ChloraPrep	DuraPrep	Adjusted RR* (95% CI)
Before skin preparation	50 (93)	48 (94)	—
After skin preparation	19 (35)	7 (14)	0.40 (0.18–0.85)
After closure	19 (35)	15 (29)	0.83 (0.48–1.44)

CI = confidence interval; RR = relative risk.
*Adjusted for patient age, sex, body mass index, surgery duration and prepreparation culture status.

[*n* = 7] v. 35% [*n* = 19], adjusted RR 0.40, 95% confidence interval [CI] 0.18–0.85) (Table 2). The most common bacterial organisms isolated at this stage were *M. luteus* (15 isolates), *Corynebacterium* (4 isolates) and *S. epidermidis* (3 isolates) (Figure 2).

After wound closure, there was no significant difference in the positive culture rate between the DuraPrep and ChloraPrep groups (29% [*n* = 15] v. 35% [*n* = 19], adjusted RR 0.83, 95% CI 0.48–1.44). There was a 114% increase in the proportion of positive culture results after wound closure compared to immediately after skin preparation in the DuraPrep group (adjusted RR 2.10, 95% CI 1.12–3.95). The most common bacterial organisms isolated after wound closure were *M. luteus* (15 isolates), *Staphylococcus* (5 isolates) and *Corynebacterium* (3 isolates) (Figure 2).

The rates of positive culture results for the most common organisms are shown in Table 3. After skin preparation, 14 specimens (26%) in the ChloraPrep group and 1 specimen (2%) in the DuraPrep group yielded *M. luteus* (adjusted RR 0.08, 95% CI 0.01–0.55). Similar proportions were seen after closure (24% v. 4%, adjusted RR 0.16, 95% CI 0.04–0.69). There was a greater reduction in the proportion of cultures positive for *M. luteus* in the DuraPrep group than in the ChloraPrep group after skin preparation (95% v. 21%, adjusted RR 0.06, 95% CI 0.01–0.43) and after closure (91% v. 27%, adjusted RR 0.13, 95% CI 0.03–0.55). No

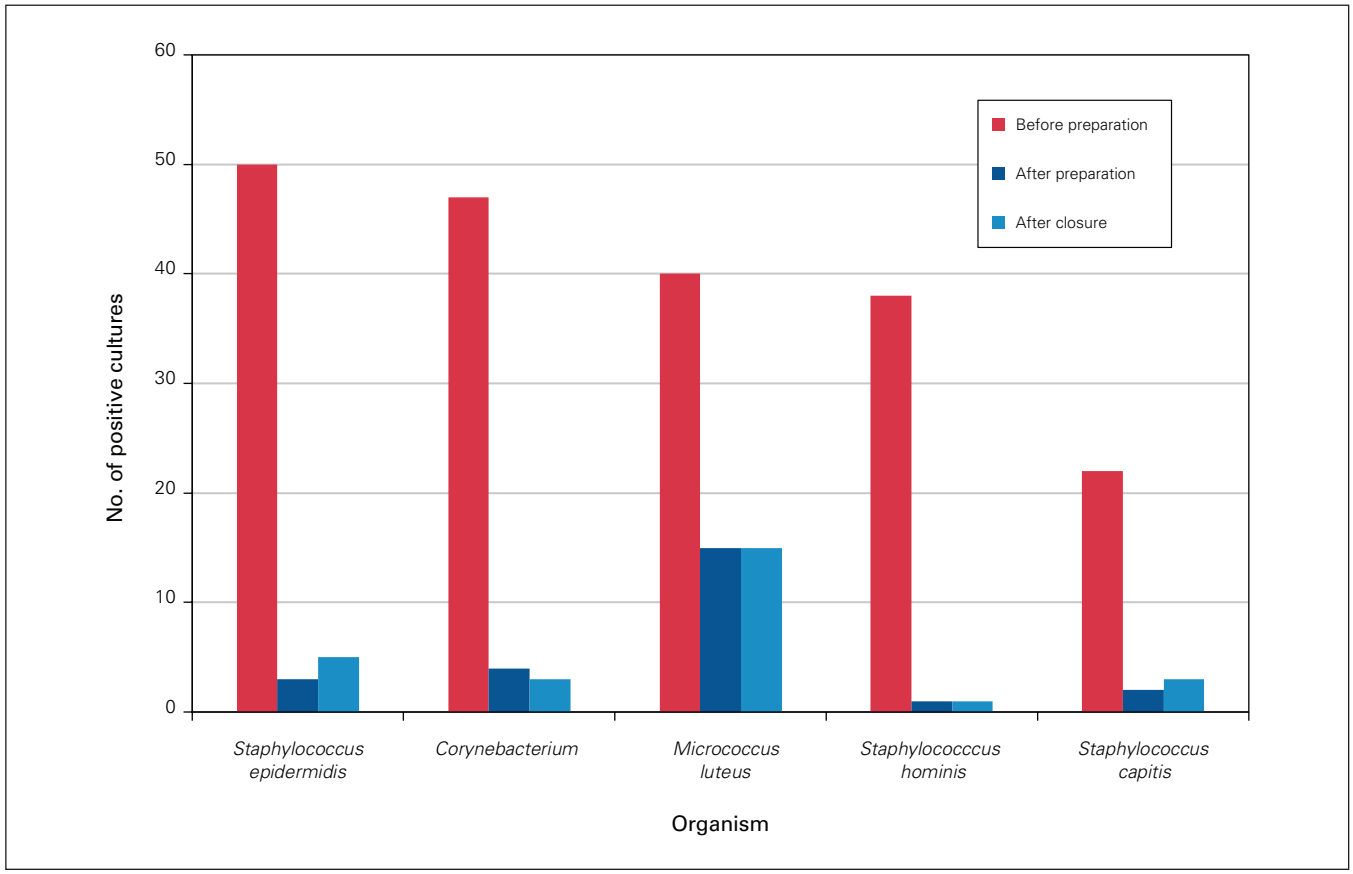

Fig. 2. Bacterial culture results.

Table 3. Positive culture results for common bacteria, by time and group

Organism	Total *n* = 105	Time; no. (%) of patients: Before skin preparation ChloraPrep *n* = 54	Before skin preparation DuraPrep *n* = 51	After skin preparation ChloraPrep *n* = 54	After skin preparation DuraPrep *n* = 51	After closure ChloraPrep *n* = 54	After closure DuraPrep *n* = 51
Staphylococcus epidermidis	50 (47.6)	27 (50)	24 (47)	2 (4)	1 (2)	2 (4)	3 (6)
Corynebacterium	47 (44.8)	17 (31)	32 (63)	1 (2)	3 (6)	1 (2)	2 (4)
*Micrococcus luteus**†	40 (38.1)	18 (33)	23 (45)	14 (26)	1 (2)	13 (24)	2 (4)
S. hominis	38 (36.2)	16 (30)	23 (45)	0 (0)	1 (2)	0 (0)	1 (2)
S. capitis	22 (21.0)	11 (20)	12 (24)	0 (0)	2 (4)	1 (2)	2 (4)

*$p < 0.05$ for difference between DuraPrep and ChloraPrep groups after preparation and after closure.
†$p < 0.01$ for reduction in positive culture results in the DuraPrep group compared to the ChloraPrep group after preparation and after closure.

differences were observed after skin preparation for the other common organisms between the 2 groups.

Association with confounding variables/ complications

Male patients had an 85% increased risk of a positive culture result overall compared to female patients (adjusted RR 1.85, 95% CI 1.05–3.24). Age ($p = 0.6$), body mass index ($p = 0.8$), positive culture result before skin preparation ($p = 0.2$) and duration of surgery ($p = 0.8$) were not significantly associated with increased risk of positive culture results.

Three patients had superficial wound complications within 6 weeks of surgery, 1 (2%) in the ChloraPrep group and 2 (4%) in the DuraPrep group ($p = 0.6$). No superficial wound complications were identified at 3 months, and no deep wound infections were encountered during the duration of the study.

Discussion

We found that the most common bacteria cultured from the hip area in patients undergoing total hip arthroplasty were *S. epidermidis* (48% of samples), *Corynebacterium*

(45%), *M. luteus* (38%), *S. hominis* (36%) and *S. capitis* (21%). Collectively, coagulase-negative *Staphylococcus* was the most prevalent organism. In contrast to reports evaluating the bacteria around the shoulder, lumbar spine and hand,[7,8,10] there was a paucity of *P. acnes* at the hip.

In a recent randomized controlled trial (RCT) comparing alcohol-based skin preparations after hip and knee arthroplasty, no difference was observed in the incidence of superficial wound complications.[13] However, in an analysis of secondary outcomes, a significant difference was found in favour of iodine–alcohol for the prevention of surgical site infections (SSIs).[13] The rate of SSIs was 1.0% and 3.1% in the alcohol and chlorhexidine groups, respectively (OR 3.06, 95% CI 1.26–7.46). These results are in contrast to the World Health Organization guidelines, which recommend that chlorhexidine-based preparations be used.[5]

In several recent meta-analyses, investigators aimed to evaluate the efficacy of chlorhexidine- and iodine-based alcohol solutions for the prevention of SSI after surgery. Based on 9 RCTs, Privitera and colleagues[14] reported in favour of chlorhexidine (RR 0.70, 95% CI 0.52–0.92). Chen and colleagues[15] examined 19 RCTs and reported a lower SSI rate with chlorhexidine than with povidone–iodine (RR 0.57, 95% CI 0.47–0.70). Although these results are promising, they should be interpreted with caution, as the formulation, concentration and application of the antiseptic solutions were variable and not consistent across studies. Furthermore, a range of procedure types were included, with limited data from orthopedic studies. A meta-analysis based on 13 RCTs showed an overall reduction in the risk of SSI with the use of chlorhexidine compared to iodine (RR 0.79, 95% CI 0.67–0.93); however, in a subgroup analysis examining only bone and joint data (5 RCTs), chlorhexidine was associated with an increased risk of SSI (RR 2.67, 95% CI 1.05–6.8).[16] Thus, the efficacy of antiseptic solutions may differ according to the surgical procedure.

Since the incidence of SSI is very low after hip arthroplasty,[1] most studies assessing colonization or culture rates (including the present study) are underpowered to detect differences in SSI rates between skin preparations. However, they are powered to detect differences in the reduction of skin flora, which may serve as a potential surrogate measure of efficacy. Ostrander and colleagues[6] and Saltzman and colleagues[7] concluded that ChloraPrep was at least twice as effective as DuraPrep in eliminating bacteria from the forefoot and shoulder regions, respectively. Neither group used a neutralization agent before sampling. Contamination with antiseptic on the culture swab likely led to ongoing bacterial death and exaggerated efficacy, particularly in the ChloraPrep group, as it is a non–film-forming antiseptic.[17] Savage and colleagues[8] reported that ChloraPrep and DuraPrep were equally effective at eradicating bacteria on the skin overlying the lumbar spine region. Although they used a neutralization agent, they reported a relatively low prepreparation positive culture rate of 82%, which suggests that the sampling technique or the laboratory plating process was not ideal, and, as a result, culture results after skin preparation were underrepresented. In a study evaluating the flora on the hand, Xu and colleagues[10] reported that the rate of positive culture results after skin preparation was 26% in the ChloraPrep group, 4% in the DuraPrep group and 1% in the Betadine group ($p < 0.001$). They, too, had a low prepreparation rate of positive culture results, 38%, and did not control for antimicrobial hand washing by the patients before surgery. Consequently, it remains unclear whether a specific solution is superior.

The rate of positive culture results before skin preparation in the current study (93% in the ChloraPrep group and 94% in the DuraPrep group) suggests a more robust sampling and culturing process than in the previous studies. Furthermore, presurgical cleansing soap and adhesive sealant drapes were not used in order to eliminate any potential confounding effects. DuraPrep was more effective than ChloraPrep at eradicating bacteria initially on application. However, there was no difference between the preparation solutions after wound closure. This initial difference was largely due to the continued presence of *M. luteus* in the ChloraPrep group. Continued presence of *Micrococcus* was also observed on the skin overlying the lumbar spine, as Savage and colleagues[8] reported a reduction of only 30% of *Micrococcus* isolates after skin preparation. The clinical significance of this finding is unclear, as periprosthetic infections from *M. luteus* are relatively rare.[18]

Limitations

This study was not powered to show a correlation between prosthetic joint infection and type of skin preparation solution. The rate of prosthetic joint infection in elective total hip arthroplasty is very low.[1] The overall rate of superficial and deep wound infection in our study was 3% and 0%, respectively. A much larger patient population would be required to show a significant correlation. Second, qualitative rather than quantitative culture data were used. Perhaps the number of residual colonies is more representative of solution efficacy and, in turn, the risk of postoperative infection. Last, contamination was encountered, which resulted in 3 false-positive results; the data from the affected patients were excluded.

Conclusion

This study successfully identified the native bacteria present on the skin around the hip. In addition, DuraPrep was more effective than ChloraPrep at reducing bacteria at the hip immediately after skin preparation for surgery. At the time of wound closure, there was no longer a difference

between the 2 solutions. Further study with larger samples is required to identify any influence of skin preparation solution on the incidence of prosthetic joint infection.

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Contributors: K. Droll, M. Abouassaly, C. Cullinan and D. Puskas designed the study. S. Dubois analyzed the data. K. Droll wrote the manuscript, which M. Abouassaly, C. Cullinan, D. Puskas and S. Dubois critically revised. All authors gave final approval of the article to be published.

Data sharing: Data are available on request from the corresponding author.

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