An Overview of Skin Antiseptics Used in Orthopaedic Surgery Procedures

Abstract

Surgical site infections (SSIs) in orthopaedics are a common complication, with more than half a million SSIs occurring in the United States each year. SSIs can carry a notable burden for patients and physicians alike. Skin antiseptic solution plays an important role in preventing SSI. Many studies have looked at different skin antiseptic solution in preventing SSIs. Different surgical preps can decrease bacterial loads at surgical sites in varying degrees. Yet, the amount of bacterial load does not always correlate with a lower risk of infection. Chlorhexidine, for example, has been shown to cause markedly less SSIs compared with povidone-iodine prep in general surgery cases. Whereas chlorhexidine with alcohol may best work in the forefoot, iodine povacrylex with alcohol is equivalent in the spine. Conversely, joint arthroplasty SSIs were markedly decreased with a combination of preps. Because of all these differences, understanding which prep solution to use and when can be invaluable to the orthopaedic surgeons.

More than half a million surgical site infections (SSIs) occur in the United States each year. SSIs have been reported to occur in 2.8% of surgical procedures. Some risk factors that may help predict SSIs include age, diabetes, obesity, urinary incontinence, and prolonged surgical time. Not only are SSIs costly surgical complications, they also carry a notable burden for patient well-being and quality of life. SSIs are associated with revision surgeries, delayed wound healing, increased or prolonged antibiotic use, and increased length of hospital stay. One of the most common nosocomial infections is the SSI, which leads to mortality in thousands of patients each year. SSIs not only cause morbidity to the patients but also drive health-care costs up. Hospital-acquired complications receive limited reimbursement, and SSIs account for 38% of nosocomial infections. In an effort to stave this trend, perioperative skin preparation has become an important quality performance measure in the Centers for Disease Control and Prevention and Centers for Medicare and Medicaid-initiated Surgical Care Improvement Project.

Skin antiseptic solution (SAS) plays an important role in preventing SSIs. The three main antiseptics most commonly used in the operating room (OR) for skin prepping include chlorhexidine, iodine, and alcohol. This review covers the most commonly used SASs and their cost. It then summarizes the use and efficacy of these antiseptic agents in the various subspecialties of orthopaedic surgery.
Skin Antiseptic Solutions: A Brief Background

Chlorhexidine

Chlorhexidine, also known as 1,6-bis(4-chloro-phenylbiguanido)hexane, is a cationic polybiguanide. Its mechanism of action is based on releasing a positively charged chlorhexidine cation, which can then bind to the negatively charged bacterial cell wall, thus exerting its bactericidal effect. At high concentrations, it can cause membrane disruption, resulting in cell death. It is active against gram-positive and gram-negative organisms, facultative anaerobes, aerobes, and yeast. Although it is effective against gram-positive organisms at low concentrations, higher concentrations are needed for gram-negative bacteria and fungi.\(^5\)

Chlorhexidine can have both bactericidal and bacteriostatic effects and is often used in combination with alcohol. A study published in the *New England Journal of Medicine* in 2010 found that infection in general surgery cases occurred markedly less in patients who had chlorhexidine-alcohol antiseptics used than in patients who had povidone-iodine used as a surgical site preparation solution.\(^6\) The authors attributed the increased protection offered by chlorhexidine-alcohol to its more rapid action, persistent activity despite exposure to bodily fluids, and residual effect. Limitations of chlorhexidine-alcohol include its slow onset of antimicrobial activity, skin irritation, and potential to damage tissue on contact.\(^7\)

The purchase price of chlorhexidine antiseptic was reported to be $6.07 per 26-mL single-use applicator of 2% chlorhexidine gluconate 70% isopropyl alcohol and $1.68 per 113 g bottle of 4% chlorhexidine, which is higher than a comparable iodine surgical antiseptic solution. The reported cost of povidone-iodine solution is $1.42 per 118-mL surgical scrub with 7.5% povidone-iodine (Table 1).

### Iodine

Two main SASs contain iodine: povidone-iodine and iodine povidone-iodine. Iodine works in conjunction with the carrier polymer povidone, forming the skin antiseptic agent povidone-iodine. Povidone is used to prolong the effects of iodine. Povidone-iodine, also sold as Betadine, covers a broad spectrum for its antiseptic use. It has bactericidal effects against bacteria, fungi, and viruses. Povidone-iodine contains 9% to 12% iodine and works by releasing iodine, which results in the death of microorganisms.\(^8\)

Povidone-iodine can be used for the prevention of infections for surgical skin preparation and management of infections in decubitus and stasis ulcers. Nonsterile povidone-iodine has limited use because of a long history of contamination with *Propionibacterium cepacia*.\(^9\) Thus, sterile povidone-iodine should always be used, especially in open wounds. It should be noted that iodine is absorbed into the body in varying degrees depending on the condition of the patient’s skin. Therefore, it can interact with diagnostic tests of the thyroid, including radiiodine diagnostics. It is contraindicated in patients with hyperthyroidism or other thyroid diseases after patients have been treated with radioiodine.\(^10\)

The other iodine SAS is iodine poviacylex, which is combined with alcohol for added antiseptic effect. Some downsides of iodine include less persistence on skin compared with chlorhexidine antiseptics and slow onset of its antimicrobial effects.

### Alcohol

Alcohol provides the most rapid reduction in bacterial count of all the antiseptic solutions. In fact, some articles attribute much of the efficacy of chlorhexidine-alcohol antiseptics to the alcohol component, which is often overshadowed by the conversation regarding whether chlorhexidine or iodine antiseptic solutions are superior.\(^11\) Despite its more rapid onset, alcohol also tends to have a shorter duration of action than chlorhexidine and iodine, explaining why it is often used in combination with other antiseptic agents. Although it is also a broad-spectrum antibiotic like chlorhexidine and iodine antiseptics, alcohol is poorly sporicidal.\(^12\)

In addition, alcohol antiseptics are highly flammable and require drying before progression of surgery for risk of fire in the OR. Additional deliberation should be taken when considering using alcohol-based antiseptics for surgeries involving the use of cautery for making deeper incisions.

Orthopaedic Surgery Specialties

Hand Surgery

Hand surgery infection rates are generally low, and multiple studies have shown an infection rate of less than 1%.\(^13,14\) Some factors associated with SSIs in hand surgery include diabetes, immunosuppression, severe burns, malnutrition, open fractures, animal or human bites, and severely crushed or contaminated wounds.\(^15,16,17\) *Staphylococcus aureus* is the organism most commonly associated with postoperative infection.\(^18\) There is no general agreement on which skin antiseptic is the best to minimize SSIs in hand surgery.

Although there is a shortage of studies looking at the association between skin preparation solution used and SSIs in hand surgery, the results of a 2016 study comparing the efficacy of surgical preparation solutions in clean elective hand surgery by analyzing post-preparation bacterial cultures found that DuraPrep (iodine povacrylex and isopropyl alcohol) and Betadine (povidone-iodine...
iodine) were markedly better than ChloraPrep (chlorhexidine gluconate and isopropyl alcohol) for skin decontamination. However, no SSIs were noted within 30 days of surgery in any of the 119 patients studied.

Another 2016 study from researchers in Iran showed that non-rinse alcoholic hand disinfectants had superior immediate effects on disinfecting bacterial colonies than 7.5% povidone-iodine, but ultimately no notable difference exists in colony-forming units between the two groups after 2 hours. The authors suggested that alcohol-based solutions may be preferable to povidone-iodine solution in emergency situations.

Seigerman et al reported on two methods of applying antiseptic solutions to the skin of the hand and found that two fellowship-trained orthopaedic hand surgeons left markedly less areas of the skin unprepared when using 4 × 4 inch sterile gauze sponges relative to when they used commercially available prep-stick applicators.

Because of the low infection rates in hand, there is no consensus on what prep solution is best used. However, we can infer from the studies that using 4 × 4 inches sterile gauze sponges may have a better ability to get into the crevices of the hand because of the more complicated nature of prepping the hand (Table 2).

### Joint Arthroplasty

SSIs after joint arthroplasty can be potentially devastating, and the morbidity associated with them can be enormous. Thus, preventing SSIs in joint arthroplasty is of utmost importance. Rasouli et al reported an SSI rate of 1.31% in 6,111 total joint arthroplasties analyzed, with the highest rates occurring in revision total knee arthroplasty (4.57%), followed by revision hip arthroplasty (1.94%). Risk factors for infection include higher Charlson Comorbidity Index, revision total knee arthroplasty, and a low preoperative hemoglobin level. The most commonly detected microbes causing joint infection are staphylococci, including *S. aureus* and coagulase-negative staphylococci.

Preoperative skin preparation in joint arthroplasty surgeries is a

<table>
<thead>
<tr>
<th>Prep</th>
<th>Cost</th>
<th>Coverage</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhexidine (aqueous)</td>
<td>$1.68/118 mL bottle</td>
<td>Excellent for gram-positive bacteria, good for gram-negative bacteria and virus, fair for fungi, and poor for Mtb</td>
<td>Cost</td>
<td>Lower antimicrobial activity against gram-negative bacteria and fungi</td>
</tr>
<tr>
<td>Povidone-iodine (aqueous)</td>
<td>$1.42/118 mL bottle</td>
<td>Excellent for gram-positive bacteria and good for gram-negative bacteria, fungi, virus, and Mtb</td>
<td>Cost</td>
<td>Short duration of action (2 hr) and longer prep time</td>
</tr>
<tr>
<td>ChloraPrep (alcohol-chlorhexidine)</td>
<td>$6.07/26 mL applicator</td>
<td>Improved gram-negative, Mtb, and fungal activity</td>
<td>Rapid onset, long duration of action (48 hr), one-step prep, and easier application</td>
<td>Flammability and expensive</td>
</tr>
<tr>
<td>DuraPrep (alcohol-iodophor)</td>
<td>$4.27/26 mL applicator</td>
<td>Improved gram-negative bacteria and Mtb</td>
<td>Rapid onset, long duration of action (48 hr), one-step prep, easier application, and enhanced adhesion between drapes and skin</td>
<td>Flammability and expensive</td>
</tr>
</tbody>
</table>

*Mtb = Mycobacterium tuberculosis*
The study found a fourfold reduction in superficial surgical site infections (SSIs) using chlorhexidine, iodine, or povidone-iodine. This study was published in the Journal of the American Academy of Orthopaedic Surgeons.

Another study compared iodophor-in-impregnated skin preparation trays with a povidone-iodine solution. Both studies showed superior drape adherence to skin with the iodine alcohol solution relative to its aqueous counterpart.

Finally, a 2016 prospective study analyzed whether the application of an additional surgical site preparation solution with iodine povacrylex and isopropyl alcohol before application of the final adhesive drape would result in lower SSI rates in patients undergoing total hip and total knee arthroplasty. The study found a notable reduction in the incidence of superficial SSIs in the intervention group compared with the control group that only received a single surgical site preparation solution with alcohol and povidone-iodine before draping. This study brings up an important point of second skin prep. Often the process of draping may contaminate either those draping the patient or the surgical site. A second prep right after draping can help ensure that the surgical site is adequately sterilized. This does not mean that if the surgical site is contaminated during draping, a second prep would suffice. In fact, if contamination is noted during draping, everything should be taken down and re-prepped. But in cases where surgical infection is more likely or of greater morbidity, such as in total joint surgery, a second prep is a prudent and well-advised step.

The literature on joint surgery has multiple more recommendations with regard to draping and preoperative shaving, which is beyond the scope of this article. But the conclusions we can draw in joint surgery are that (1) an additional surgical site preparation before the final drape is beneficial in reducing SSIs and (2) although iodine-based solutions have been shown to have consistent and similar bactericidal effects, drapes adhere better to skin with iodine alcohol solution. So if using drapes with self-adhesive, iodine alcohol solution may be best to provide a more robust barrier.

Foot and Ankle Surgery

Foot and ankle surgery has been associated with higher infection rates than many of the other subspecialties of orthopaedics, with infection rates as high as 6.5% being reported. Risk factors for SSIs in foot and ankle surgery include diabetes, peripheral neuropathy, Charcot neuroarthropathy, current or past smoking, and increased length of surgery. Some potential explanations suggested for these elevated rates of infection in foot and ankle surgery include the resident microbiota of this region of the body and the wearing of shoes which may facilitate a favorable environment for bacteria to grow. Staphylococcus aureus was found to be the main microbe at fault for wound infection in one study on foot and ankle surgery infection rates.

Surgical preparation solutions have been shown to be an effective way of eliminating bacteria from feet. A 2005 study of 125 patients undergoing surgery of the foot and ankle compared the efficacy of DuraPrep (0.7% iodine and 74% isopropyl alcohol), Techni-Care (3.0% chloroxylenol), and ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol). The authors found ChloraPrep to be the most effective prep solution for eliminating bacteria from the forefoot before surgery.

### Table 2

**Skin Antiseptic Recommendations**

<table>
<thead>
<tr>
<th>Area</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand</td>
<td>Sterile 4 × 4s using chlorhexidine, iodine, or alcohol-based solutions.</td>
</tr>
<tr>
<td>Foot and ankle</td>
<td>Chlorhexidine with alcohol.</td>
</tr>
<tr>
<td>Spine</td>
<td>ChloraPrep or DuraPrep with adequate time for drying.</td>
</tr>
<tr>
<td>Hip arthroscopy</td>
<td>Insufficient evidence to make recommendation.</td>
</tr>
<tr>
<td>Shoulder arthroscopy</td>
<td>No difference between ChloraPrep, DuraPrep, and Betadine.</td>
</tr>
<tr>
<td>Knee arthroscopy</td>
<td>Insufficient evidence to make recommendation.</td>
</tr>
<tr>
<td>Joint arthroplasty</td>
<td>Iodine-based surgical preps, with an additional skin prep before final drapes.</td>
</tr>
<tr>
<td>Oncology</td>
<td>Insufficient evidence to make recommendation; however, recommend following above-mentioned guidelines based on area of the body and procedure type.</td>
</tr>
</tbody>
</table>
A randomized, prospective study looked at skin preparation before foot and ankle surgery using one of two preparation routines. One group, called isopropyl alcohol group, was prepped with a 4% chlorhexidine gluconate application, followed by an alcohol rinse. The other group, chlorhexidine gluconate group, was prepped with alcohol, followed by chlorhexidine. The study found no notable difference in the level of postoperative culture swab growth and no difference in SSIs between each group. These studies looked at different prep solutions on different parts of the foot. Although no study found a notable difference in post-SSIs between any of the preps, ChloraPrep was found to markedly reduce bacteria in the forefoot in one study. Based on these studies, we conclude that the combination of chlorhexidine and alcohol should be used when disinfecting the skin of the foot before surgery. Although this is our recommendation, it is worth mentioning that all preps in the foot and ankle surgery have been shown to be equivalent with regard to preventing SSIs.

Joint Arthroscopy

The incidence of infection in arthroscopic surgery is likely the lowest among all orthopaedic subspecialties. Infection rates after knee arthroscopy range from 0.04% to 0.42%. An article published in June 2017 found a number of variables associated with postoperative infection, including younger age, morbid obesity, tobacco use, inflammatory arthritis, chronic kidney disease, hemodialysis, depression, and a hypercoagulable disorder. Because of the minimally invasive nature of arthroscopy, not much information is available about skin preparation practices in joint arthroscopic surgery. Shoulder arthroscopy is no exception. Cutibacterium acnes, which is a major causative agent of SSIs in spinal surgery as well, has been associated with pain and stiffness after shoulder arthroscopy. This bacterium has been found more commonly in patients who are male, have preexisting shoulder arthropathy, prosthesis, and revision, as well as in patients with a greater density of hair follicles and sebum. Even with the use of a 4% chlorhexidine scrub, followed by a 2% chlorhexidine gluconate and 70% isopropyl alcohol paint applied to the entire shoulder preoperatively, C. acnes has been found in deep tissue of patients undergoing shoulder arthroplasty at a rate of 19.6%. Because C. acnes causes poor outcomes postoperatively, measures have been taken to decrease C. acnes skin colonization preoperatively.

A 2017 study analyzed bacterial cultures taken from patients undergoing shoulder arthroscopy before and after surgery. The study concluded that applying topical benzoyl peroxide 5% and clindamycin 1% gel at night within the 10 days before surgery is effective in reducing both superficial and deep C. acnes in shoulder arthroscopy. It found that shoulder joint inoculation with C. acnes decreased from 19.6% to 3.1% in 65 patients enrolled. Another 2015 study found that treating patients with benzoyl peroxide cream 48 hours before surgery in conjunction with standard chlorhexidine skin preparation reduced C. acnes before and after surgery, which may result in lower postoperative infection rates.

The effectiveness of DuraPrep (iodine povacrylex and isopropyl alcohol), ChloraPrep (chlorhexidine and isopropyl alcohol), and Betadine (povidone-iodine) in eradicating bacteria in shoulder surgery (137 of 150 procedures were shoulder arthroscopies) was studied by Saltzman et al. They found an overall positive culture rate after skin preparation being highest in the povidone-iodine and paint group (0.75% iodine scrub and then 1.0% iodine paint), followed by DuraPrep. ChloraPrep had the lowest positive bacterial cultures. However, no infections occurred in any of the 150 patients undergoing shoulder surgery in this study at a minimum of 10-month follow-up. Although the above-mentioned studies confirm that benzoyl peroxide cream administered before surgery decreases inoculation with C. acnes, there has been no proof that this leads to a decreased level of infections. This lack of statistical difference is likely because of the very low rate of infection inherent in arthroscopy. To detect one infection, a much larger population would be needed. Thus, we recommend benzoyl peroxide cream before surgery along with a chlorhexidine skin prep solution to lower the risk of infection.

No studies could be found comparing the efficacy of different skin preparation solutions in knee arthroscopy. Despite the lack of variability in SSIs in arthroscopy, a 2006 study found that presurgical disinfection of the patient’s skin with povidone-iodine was shown to be
completely effective, with 100% of 30 samples taken from patients’ knees perioperatively being negative for bacterial infection. Another study comparing preoperative preparation of the knee with povidone-iodine scrub with a two-stage preparation of preoperative iodine scrub, followed by painting with aqueous povidone-iodine, found no notable difference in SSIs between 300 patients in the two groups (no SSIs in either group). Based on the above-mentioned studies and lack of sufficient evidence, we do not have a formal recommendation, though povidone-iodine is an adequate and proven skin prep for knee arthroscopy.

Just as in patients undergoing knee arthroscopy, iodine solutions such as DuraPrep (iodine povacrylex) are used to prepare the skin in patients undergoing hip arthroscopy. In a large systematic review by Harris et al,14 infection rate of less than 1% was found in hip arthroscopy cases. Infection in patients after hip arthroscopy has been associated with intra-articular hip injection in 3 months before the procedure. No research compares the efficacy of different SASs in preventing infection after hip arthroscopy.

**Spine Surgery**

Spine surgery carries a high risk for postoperative infection. A possible explanation for this large SSI range is that many variations exist in surgical factors such as implant usage and surgical approach. SSIs in spine surgery are associated with obesity, diabetes, cigarette smoking, obesity, steroid use, alcohol abuse, extremes of ages, and transfusion of blood products. S aureus was the most commonly isolated pathogen in spinal SSIs; however, gram-negative organisms accounted for a considerable number of SSIs among lower lumbar and sacral spinal procedures in one study. A 2012 study comparing the efficacy of an iodine-alcohol solution (DuraPrep) against a chlorhexidine gluconate-alcohol solution (ChloraPrep) in eliminating bacterial flora overlying the lumbar spine found that the two are equally successful antiseptic agents. Variations exist also in timing and techniques for skin preparation before spine surgery, which have been investigated for their efficacy in eliminating bacteria. One of the most commonly used skin antiseptic agents is povidone-iodine. Yasuda et al conducted a study comparing bacterial cultures in two groups: group A which received povidone-iodine directly before skin incision, after the surgeon’s hands were scrubbed, and group B which had povidone-iodine applied at least 5 minutes before skin incision, before the surgeon’s hands were scrubbed. In the latter group, povidone-iodine had enough time to dry, leading to markedly lower positive culture rates than in the former group.

Thus, we conclude that ChloraPrep or DuraPrep used as the surgical preparation solution are both equally effective. The study by Yasuda highlights the importance of letting the prep solution dry for it to exert its effects on the skin. For spine surgery, we recommend that the prep be allowed to dry before incision. This recommendation can be carried to all surgical prep applications.

**Orthopaedic Oncology**

Orthopaedic oncology surgery cases can necessitate a large incision and long surgical time, both of which predispose a patient to SSIs. Thus, these patients are at higher risk for infection and necessitate a careful skin preparation routine. An analysis of 1,521 orthopaedic oncologic surgery procedures in 1,304 patients in 2014 showed a 10.1% SSI rate. This 2014 study identified eight patient-related variables associated with SSIs in orthopaedic oncology surgery: body mass index, age, number of preexisting implants or allografts, infection at another site on the date of surgery, malignant disease, and hip region infected. The study also had access to information pertaining to the preparation solution used. A comparison between “triple” (soap, povidone-iodine [Betadine], and alcohol), DuraPrep, and “other” (representing any other SAS) showed no notable difference in SSI rates.

Because orthopaedic oncology cases vary greatly and can range anywhere from large pelvic reconstructions to arthroscopy cases, we recommend that preps for oncology cases follow the specific area of the body previously discussed, so that large knee reconstructions should follow skin prep guidelines for arthroplasty, whereas tumor excisions in the hand and upper extremity would be suited by following guidelines under hand procedures.

**Summary**

There appears to be no consensus in many fields of orthopaedic surgery on which SAS is superior. Furthermore, literature on each area of orthopaedic surgery has different evidence of which preparation methods and solutions are best. One explanation for the wide range of findings across these subspecialties is that each part of the body being operated on often has its own microbiota, which may display different responses to the same SAS. In addition, because of the varying nature of procedures undertaken in different orthopaedic subspecialties, different precautions and skin preparation methods may need to be undertaken depending on the surgery planned within a subspeciality of orthopaedics. Further subspecialty-and procedure-specific studies on the
efficacies of surgical site antiseptic solutions may help create more clear guidelines on surgical antiseptic usage and consequently reduce SSI rates in the future.

In addition to cost, other factors are seldom included in the discussion around SSSs, but that are nonetheless very relevant. This includes fire risk and the time difference in application. As discussed previously, alcohol is often an additional active ingredient, such as with Chloraprep. However, with alcohol being highly flammable, this increases concern for the risk of an intraoperative fire. This can bare devastating complications, especially because the oxygen source is at the face. The use of Chloraprep should be strongly reconsidered if the risk of intraoperative fire risk is high. When an SAS containing alcohol is used, it is important to prevent any pooling of the solution and sufficient amount of time is given to let this dry and for the alcohol to evaporate. This adds additional time which increases the nonsurgical time in the OR.

References

References printed in bold type are those published within the past 5 years.

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