Subdermal Betadine to Reduce Microbacterial Bioburden During Posterior Spinal Fusion

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A. Background and Significance

Adolescent idiopathic scoliosis (AIS) occurs in approximately 1-3% of the population, while other underlying conditions are associated with scoliosis as well, such as neuromuscular disorders, congenital anomalies, and syndromes such as Marfan's.[1,2] Large magnitude scoliosis curves are typically managed with posterior spinal fusion (PSF).

Surgical site infections (SSI) are a leading cause of nosocomial infection that can contribute to significant patient morbidity or even mortality, negatively impact patient well-being and quality of life, and are a significant drain on health care resources.[3,4] In patients undergoing PSF for scoliosis, SSI occur at rates of 1-2% in AIS patients, and in 15-20% of higher risk populations, such as those with spinal deformity due to myelomeningocele and/or neuromuscular scoliosis.[5] In addition to patient morbidity, SSI are a costly complication, with a mean additional cost of $154,537 per patient related to hospitalization and treatment of infection.[6] Given that PSF is a relatively common procedure with >100 cases performed at Akron Children's Hospital annually, we are continuously working towards process improvement for decreasing infection risk.

One method to reduce SSI is perioperative skin preparation, as skin antiseptics decrease skin flora and kill superficial bacteria that otherwise could enter the wound and contribute to infection. Prior studies have demonstrated that bacterial contamination from the patient's skin is a major presumed source of postoperative infection, especially with an implanted biomaterial, as the bacteria can form a biofilm that protects the bacteria from the host cellular defense system and antibiotics.[7-9] Skin antisepsis to decrease bacterial wound contamination has been shown to decrease incidence of SSI.[10] Thus, skin preparation is an important quality performance measure in the Centers for Disease Control and Prevention and Centers for Medicare and Medicaid initiated Surgical

Care Improvement Project.[4,11] The most common skin antiseptics used in the operating room are chlorhexidine, iodine, and alcohol; however, there is no consensus in the literature regarding the most effective option, including for spine surgery.[12]

Skin antiseptic solutions are applied to the skin prior to incision. However, while skin preparation is effective at reducing bioburden on the skin (3% microbial growth rate), there is a high rate of bacterial contamination at the dermal layer following skin incision (32% microbial growth), with contamination that remains abundant deeper in the spinal wound throughout the case.[13] This is likely due to lack of deeper penetration of the topical skin preparation into the sweat glands or sebaceous glands, as evidenced in larger culture studies.[14] Bacteria may then enter the wound upon making incision, resulting in contamination that could contribute to surgical site infection.

SSI's are always a substantial concern and therefore there is a need to investigate possible mitigation strategies. This project has the potential to have an immense impact by demonstrating a reduction in bacterial contamination by utilizing 10% povidone-iodine at the dermal layer of the skin.

B. Study Purpose and Objective(s)

The goal of this project is to evaluate the efficacy of subdermal 10% povidone-iodine at reducing bacterial contamination from the dermal layer of skin during posterior spinal fusion. Our institution has standardized 2% chlorhexidine gluconate (CHG) and 70% isopropyl alcohol (IPA) solution (ChloraPrep™) for orthopedic surgeries, including spine surgery, as alcohol-based skin preparations are widely considered standard of care.[12] It is possible that a second application of surgical antisepsis with a topical povidone-iodine in the subdermal layer after making incision could decrease bacterial contamination that could enter the deeper wound and contribute to surgical site infection (SSI). However, this has not been previously studied in this manner, so the effect of secondary wound preparation with subdermal povidone-iodine on bacterial contamination within the surgical wound is unknown.

The purpose of this study is to evaluate the effect of this second preparation in terms of microbial bioburden reduction. We hypothesize that povidone-iodine application in the dermal/ subdermal layer will significantly reduce microbial growth in the dermis and in the deeper surgical wound when compared to control patients. We also hypothesize that reducing microbial contamination in the wound with subdermal povidone-iodine will directly reduce incidence of surgical site infection; however, this will require future studies with large populations given the relative rarity of this complication.

The primary outcome of this study will be incidence of positive bacterial growth in several layers of the surgical wound: the skin (after preparation with ChloraPrep™), the subdermis (before and after application of povidone-iodine versus control with saline), and the deep surgical wound after exposure and before closure (Figure 1).

Secondary outcomes will be complications, including allergic reactions, contact dermatitis, surgical site infection and wound complications (Figure 1). Tertiary outcomes are the effect of other patient and surgical variables on microbial growth, including age, gender, comorbidities, body mass index (BMI), operative time, blood loss, fusion levels, scoliosis etiology, curve type, curve magnitude (Cobb angle), use of prophylactic antibiotics, hospital length of stay, complications to include readmissions and reoperations (Figure 1).

Figure 1. Objectives

Objectives	
Primary	To assess incidence of positive bacterial growth in five layers of the surgical wound. 1. The skin, along the length of the planned incision 2. The subdermis before application of povidone-iodine versus control with saline 3. The subdermis after application of povidone-iodine versus control with saline) 4. The deep surgical wound after exposure 5. The deep surgical wound after all corrective maneuvers are complete, before closure
Secondary	To evaluate complications, including allergic reactions, contact dermatitis, surgical site infection and wound complications.
Tertiary	To determine the effect of other patient and surgical variables on microbial growth, including • Age • Gender • Comorbidities • Body mass index (BMI) • Operative time • Blood loss • Fusion levels • Scoliosis etiology • Curve type • Curve magnitude (Cobb angle) • Use of prophylactic antibiotics • Hospital length of stay • Complications, including readmissions and reoperations.

C. Human Subject Study Population

- This will be a single institution randomized controlled trial and will include all English-speaking patients ≤ 26 years old with scoliosis undergoing primary posterior spinal fusion of the thoracic and/or lumbar spine. We will exclude patients who have undergone prior spinal surgery, are undergoing procedures other than primary posterior spinal fusion of the thoracic and/or lumbar spine (cervical fusion, anterior surgery, growth-friendly instrumentation), or for any contraindication to povidone-iodine, including pregnancy, allergy, or prior treatment with radioiodine.[12]
- The target enrollment for this study is 60 subjects. Patients who meet the inclusion criteria will be offered enrollment. Patients and their legal guardians will be informed of the nature of this study. The risks, benefits, advantages, and disadvantages of this study will be detailed with the patient and guardians, as a part of their routine pre-operative visit with their doctor. If the family wishes to enroll in the study, the informed consent process will be undertaken, and the patient will be enrolled.
- We estimate a 75% rate of consent for patients who meet eligibility criteria. Given that there are >100 cases performed at Akron Children's Hospital annually, our goal is to complete enrollment within 1 year of the start date. An enrollment log will be kept documenting rate of consent and if a patient declines, their reason for no consent.
- Research material will include consent forms, electronic medical records, review of radiographs via PACS, and electronic data. As described in section D, five bacterial swab cultures will be obtained throughout the surgical procedure regardless of their treatment group and sent to the microbiology lab for processing, storage, and discarded per their standard protocols.
- The following vulnerable populations will be included:

☒Minors
- Parent/guardians will sign the consent form, and assent will be obtained in children who are ≥10 years old, unless cognitively or decisionally-impaired

☒Cognitively or decisionally impaired individuals
- Cognitively or decisionally-impaired patients will be included if their parent/guardian is present and has the ability to understand and consent for the study.

☒Students/employees of ACH
- They will be included only if they meet all inclusion criteria with planned spinal surgery.

☒Illiterate individuals
- The surgeon and research coordinator will verbally explain the study, and an impartial witness will attest that the study was fully explained, and that the patient voluntarily agreed to participate. The patient signs in whatever way is customary for them (e.g., making their mark). The witness signs the consent on the witness line.

☒Economically or educationally disadvantaged individuals

- Individuals who are economically disadvantaged are not being specifically targeted for this study but will be allowed to participate if they so choose. Compensation is not being offered, so this will not unduly influence participation in the research.

D. Research Design and Methods

- This is a prospective, one site, randomized controlled trial. Patients will be identified by ICD-10 diagnosis for scoliosis with a case request for posterior spinal fusion. Eligible patients will be identified by the clinical research coordinators who typically review all planned spine surgeries for determining eligibility for spine registries (Figure 2).
- Patients will be invited to participate at their preoperative orthopedic visit. The study will be discussed by both the primary surgeon and the clinical research coordinator. The risks, benefits, advantages, and disadvantages of this study will be detailed with the patient and family, as a part of their routine pre-operative visit with their doctor. If the family wishes to enroll in the study, the informed consent process will be undertaken, and the patient will be enrolled.
- After enrollment, patients will be automatically randomized. Randomization schedules will be provided prior to initiation of the trial to balance treatment and control arms (Appendix A). The clinical research coordinator will provide the surgeon with a sealed envelope with their group determination (povidone-iodine vs control).
- On the day of surgery, the surgeon will verbally confirm with the patient and family that they still wish to move forward with study participation. A blank copy of the consent form will be available for review.
- All female patients undergoing surgery (including patients not enrolled in a research study) undergo a pregnancy test on the morning of surgery according to standard surgical protocol. If a patient enrolled in this study has a positive pregnancy test, they will be administratively withdrawn from the study.
- Intraoperatively, patients will follow the standardized spine pathway, including standard antibiotics and skin preparation with isopropyl alcohol followed by ChloraPrep™ and sterile draping (Figure 3).
- Bacterial cultures will be obtained with the use of an Eswab on the skin by rubbing along length of the planned incision, before standard placement of an antimicrobial adhesive drape known as a 3M™ Ioband™. An Eswab is a swab cleared by the FDA to aid as a transport system for your sample utilizing a plastic tube, containing an eluting liquid with a screw cap. All patients will be swabbed in the same fashion for each Eswab to assure consistency across patients.
- Prior studies have demonstrated no difference in culture positivity based on the level of the spine (cephalad/caudal thoracic and/or lumbar spine).[7] Therefore, each swab will be taken along the entirety of the posterior spinal incision and accordingly swabs may vary slightly in levels as each patients' levels will be individually determined case by based upon the planned thoracic and/or lumbar fusion levels.
- The surgeon will make incision with a scalpel and then obtain a bacterial culture in the subdermal layer in all patients by rubbing an Eswab along the subdermis.
- A nurse will open the sealed envelope. At this time the surgeon will be notified which

group the patient is in and the surgeon will proceed accordingly. If patients were randomized to the povidone-iodine group, then a single-use sealed packet of 10% povidone-iodine swabs will be opened via standard sterile technique. Three 10% povidone-iodine swabs are provided in each packet, and thus all three will be utilized for this study according to manufacturer recommendations. If patients are in the control group, then sterile swabs will be provided for soaking in sterile saline as a sham. Three saline swabs will be utilized so as to match the application technique as used with povidone-iodine swabs.

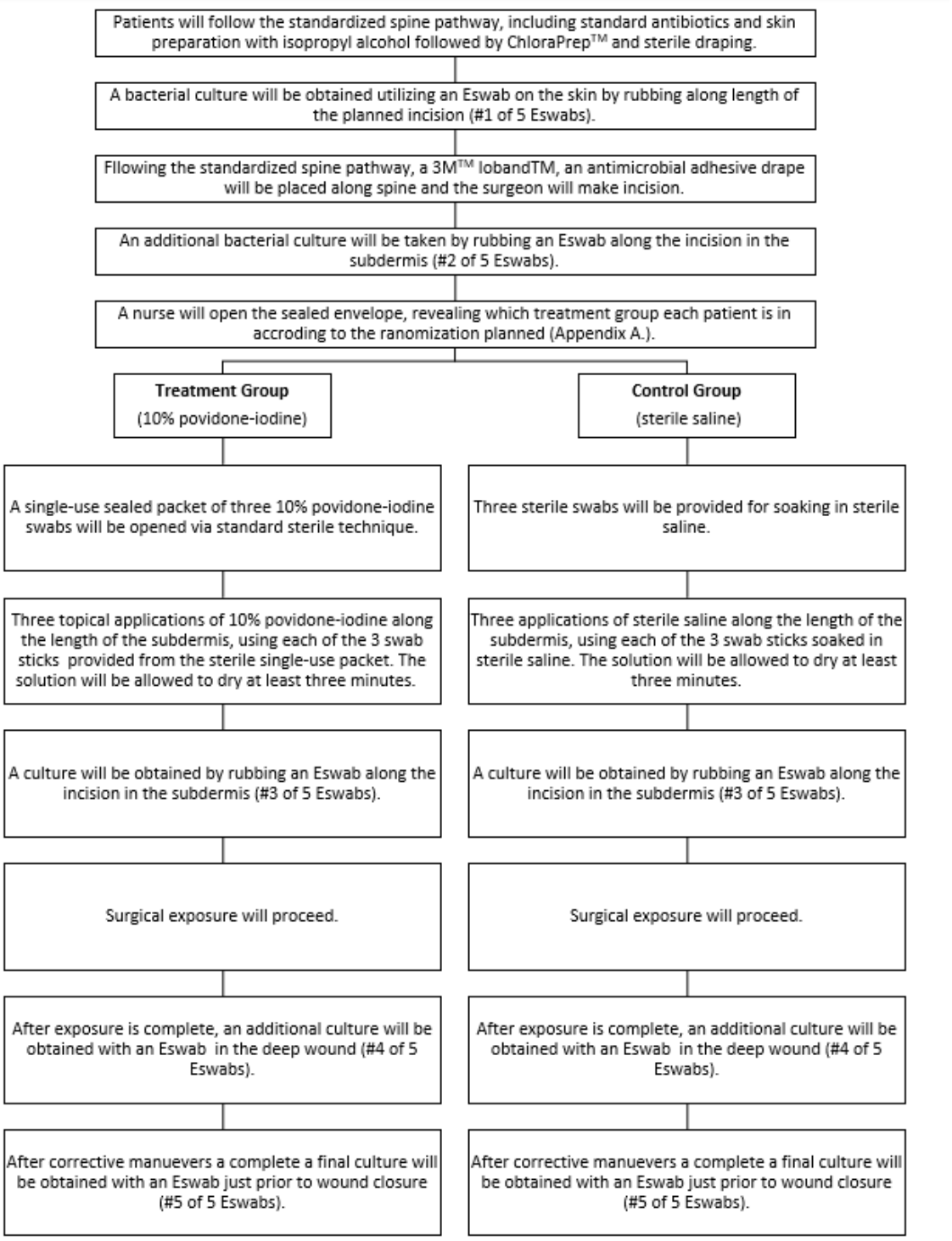
- Patients who were randomized to the povidone-iodine group will then have three topical applications of 10% povidone-iodine along the length of the subdermis, using each of the 3 swab sticks provided from the sterile single-use packet. Following the 10% povidone-iodine application, the solution will be allowed to dry at least three minutes. Patients who were randomized to the control group will then have three applications of sterile saline along the length of the subdermis, using each of the 3 swab sticks soaked in sterile saline.
- Following application of either 10% povidone-iodine or saline and waiting 3 minutes for drying time, an additional culture will be obtained by rubbing another Eswab along the incision in the subdermis.
- Surgical exposure will proceed in all patients, and an additional culture will be obtained with an Eswab along the length of the deep wound after exposure is complete, and a final culture along the length of the deep wound just prior to wound closure.
- All Eswabs will be labeled and sent to the microbiology lab for cultures. Culture growth will be recorded after final results have been reported. To mitigate competing interest, the investigators or surgeons delivering patient care, administering the treatment or control, and obtaining the bacterial culture swabs will be blind prior to surgery and only to the culture results. Each of the five samples per patient will receive a separate sample ID from the biorepository blinding the investigators or surgeons delivering patient care to the culture results only.
- Routine postoperative care of patients will not change according to culture results, with standard-of-care prophylactic antibiotic dosing. Therefore, routine antibiotics will not be extended or changed from standard prophylactic protocol unless there is otherwise a clinical indication, such as for any clinical evidence of infection (superficial or deep), as per standard of care and clinician discretion. Patients will be closely followed via the standard postoperative spine clinical schedule as noted in Figure 2.
- Research coordinators will not be blinded to the results as they will provide and document data, sources of data for adherence metrics (the electronic medical record), screening, and enrollment logs when needed.
- All spine surgeons will be included for participation in this study, including the primary and co-investigator. It is not possible to blind surgeons to the treatment group, given that povidone-iodine is administered into the surgical wound intraoperatively. This must be performed by the treating surgeon, as it would not be considered reasonable for the surgeon to exit the operating room for blinding, and/or for a non-surgeon to perform this procedure on an open wound intraoperatively. Therefore, surgeons will not be blinded to the treatment group, but all surgeons will be blinded to culture results of both control and test patients to mitigate risk of bias of competing interests.

- The duration of participation for patients will be only on the surgical day, though we will prospectively follow patients clinically to report postoperative course, including occurrence of any complications.

Figure 2. Schedule of Activities

Procedures	Screening Day -7 to -1 Prior To Pre-Op	Enrollment/ Baseline	Day Of Surgery	First Erect	2nd Errect	3 Month	6 Month	1-Year
Inclusion/Exclusion	X	-	-	-	-	-	-	-
Informed consent	-	X	-	-	-	-	-	-
Randomization	-	X	-	-	-	-	-	-
Demographics	-	X	-	-	-	-	-	-
Medical history	-	X	-	-	-	-	-	-
Initial Physical Examination	-	X	-	-	-	-	-	-
Vital signs including height and weight	-	X	X	X	X	X	X	X
Pain Scale	-	X	-	X	X	X	X	X
Surgical variables	-	-	X	-	-	-	-	-
Surgeon confirms patient enrollment	-	-	X	-	-	-	-	-
Urine HCG (females of childbearing age)	-	-	X	-	-	-	-	-
Coordinator gives surgeon sealed treatment envelope	-	-	X	-	-	-	-	-
Standard antibiotic, skin preparation and incision will be completed prior to nurse opening sealed envelope, revealing treatment	-	-	X	-	-	-	-	-
Administer study intervention/medication	-	-	X	-	-	-	-	-
Five cultures will be taken via Eswabs	-	-	X	-	-	-	-	-
1. After skin preparation, prior to incision, along the length of incision				-	-	-	-	-
2. Post incision, along the subdermis				-	-	-	-	-
3. Post control or treatment application, along the subdermis				-	-	-	-	-
4. Post surgical exposure, along the deep wound				-	-	-	-	-
5. Prior to wound closure, along the deep wound				-	-	-	-	-
Prospectively following patients clinically, including occurance or complications	-	-	-	X	X	X	X	X

Figure 3. Intraoperative Schema



Study Variables. For patients meeting inclusion criteria, variables to be collected and analyzed include, but are not limited to, those listed below.

- Demographic information – will be reviewed to address tertiary outcome of association between patient characteristics and positive microbial growth
  - Dates needed to calculate age
  - Gender
  - Height and weight for BMI
  - Comorbidities
  - Allergies
  - Scoliosis etiology
- Curvature characteristics- will be reviewed to address tertiary outcome of association between curve characteristics and positive microbial growth
  - Radiographic curve classification (Lenke type)
  - Coronal curve magnitude (Cobb angle)
  - Thoracic kyphosis magnitude
- Surgical treatment characteristics- will be reviewed to address tertiary outcome of association between surgical variables and positive microbial growth
  - Prophylactic antibiotics
  - Vertebral fusion levels (length of fusion)
  - Estimated blood loss
  - Operative time
  - Intra- and post-operative prophylactic antibiotic regimen
  - Intraoperative complications (i.e. Neurologic, etc.)
  - Length of hospital admission
- Complications- will be reviewed to address secondary outcome of complications associated with povidone-iodine application.
  - Allergic reactions (i.e. contact dermatitis)
  - Surgical site infections
  - Postoperative complications (i.e. poor wound healing, infection, severe pain, etc.)
  - Readmissions/ reoperations

- The following elements of PHI will be accessed and/or collected:

  ☒ Names

  ☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death

  ☒ Medical record numbers

E. Consent, Privacy and Confidentiality

- All investigators and study team members will meet Akron Children's IRB human research subject protection certification requirements. An investigator or research associate will invite parents and children meeting inclusion criteria to learn about study participation. Once the prospective parent or legal guardian expresses interest in study participation, the study team member will begin the informed consent/assent process using the IRB-approved form. After the parent/legal guardian reads the informed consent document, the study team member will solicit and answer all questions or concerns that parents raise. When the parent/legal guardian expresses satisfaction with the study team member's explanations and has no further questions, the study team member will reiterate all consent form content. The parent/legal guardian may then sign the informed consent document indicating a commitment to participate. As noted above, the same communication process will apply to children and adolescents requiring informed assent.
- We request a waiver of HIPAA authorization for screening purposes, as the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals. All electronic data will be stored on a password-protected institutional network drive, and any hard data will be stored in a locked filing cabinet in the principal investigator's work office. Once enrollment is complete, patient identifiers will be removed and replaced with a unique identifying number. The protected health information will not be reused or disclosed to any other person or entity, except as required by law. Access to and use of the protected health information is necessary to screen patients, as patients will be identified from their procedural codes, and their PHI will be utilized to identify their medical record. This could not practicably be conducted without the waiver as we would be unable to accurately identify patients' medical records to ensure accuracy.
- This study involves Protected Health Information (PHI). Authorization is obtained by a (Consent and Assent) Authorization Document and data used is a limited data set. Data collected will be a limited data set, specifically the only PHI utilized will be dates and MRN.
- The Eswabs will be managed according to standard microbacterial lab protocols: the Eswabs will be stored and refrigerated for 3 days after receiving the specimen. Following this time frame the specimen will be discarded. Any aerobic organism reported to the patient's chart is held at room temperature for 5 days before disposal, while anerobic organisms are frozen upon recovery and stored at-70C in the laboratory for approximately 2 years according to standard microbiology laboratory protocol. Disposal of all specimens and isolates is done as regulated medical waste to ensure proper control of biohazards and secure destruction of PHI that may be on labels.

- All electronic data will be stored on a password-protected institutional network drive, and any hard data will be stored in a locked filing cabinet. The enrollment log and linking log (to connect subject and the subject's unique identifying number) with patient identifiers will be kept separately. Information will not be disclosed to anyone outside of the research study. Once data abstraction is complete, the patient identifiers and linking log will be destroyed. The protected health information will not be reused or disclosed to any other person or entity, except as required by law.

F. Potential Risks/Benefits

- Povidone-iodine is an over-the-counter topical antiseptic that is FDA approved in pediatric and adult patients. It is considered safe and effective to reduce the number of bacteria on the skin prior to surgery. Therefore, it is widely utilized across multiple healthcare settings as an antiseptic with low risks. In addition to use as a topical surgical skin antiseptic, povidone-iodine can also be utilized within spinal wounds, with prior studies demonstrating lower rates of infection in pediatric deformity surgery when used as a wound irrigant.[15] Further, 10% povidone-iodine paint is commonly utilized for application directly onto the skin, subdermis, and deeper wound tissue in the setting of an open fracture when alcohol-based solutions are typically avoided due to potential for tissue toxicity.[16]
- Allergic or hypersensitivity reaction can rarely occur.[17] Allergic contact dermatitis (type-IV hypersensitivity reaction) is poorly described despite widespread use of this product, with prior studies demonstrating a prevalence of 0.04% - 0.4%.[17] One study reported 2 cases of allergic contact dermatitis in 5000 patients in whom a skin preparation solution was utilized (0.04%)[18], while a more recent study demonstrated a 0.4% incidence on formal patch testing, as recruited from a patch-testing clinic.[19] Recent literature has supported the safety of povidone-iodine even in patients with shellfish allergy, but should only be avoided in the setting of true iodine allergy confirmed by patch testing.[17] Other contraindication to povidone-iodine use include comorbidity such as hyperthyroidism or other thyroid disease after treatment with radioiodine.[12]
- Type-1 allergic reactions leading to anaphylaxis resulting from povidone-iodine exposure is exceedingly rare, though could result in anaphylactic shock which can be life-threatening.[20] This risk will be minimized by asking patients about allergy to povidone-iodine at time of consent. While the risk of previously undiagnosed allergy cannot be completely avoided, it is exceedingly rare.
- Another potential risk to participants is loss of patient confidentiality through their data being accessed and included as part of this study. However, the risk of invasion of privacy is no greater than would occur in the physician reviewing their records in normal clinical care. This risk will be minimized by taking precautions as detailed in Section E above.
- Participation in this surgery may slightly prolong surgery. We anticipate that obtaining each culture and the application of the povidone-iodine will each take about 10-20 seconds, so the total duration for study participation should be less than 2 minutes of additional time under anesthesia.
- The potential benefit of povidone-iodine as an antiseptic in the dermal layer could directly benefit the patient by reducing bacterial burden and decreasing risk of surgical site infection, which is one of the most common risks of spinal fusion surgery. This study also has the potential widespread benefit to others by improving methods of reducing the burden of SSI in all surgical wounds with potential applications beyond spinal fusion. Therefore, it is felt that the potential benefits outweigh the risks, given that povidone-iodine is widely accepted by the FDA and across health-care institutions (including our own) as a safe antiseptic for use in routine patient care.

G. Statistical Methods

- This is a repeated measures study design with one repeated factor, Location/Condition (skin, subdermal before treatment, subdermal after treatment, deep wound immediately after exposure, and deep wound just before closure) and one grouping factor, Treatment (test, control). The test treatment is povidone-iodine; the control treatment is saline. In both treatment groups, there will be five measurements per patient at different locations or under different conditions. Each swab will be analyzed for presence/absence of bacteria. For each location/condition the outcome measure is the percentage of patients with positive bacteria cultures.

- Comparisons among locations/conditions and between treatment groups will be conducted in a generalized linear mixed model (GLMM) framework with a binomial distribution and a logit link function. Locations/conditions, treatments, and their interaction will be assessed and multiple comparisons among locations/conditions will be conducted as appropriate.

- Sample size determination for GLMMs is an open question in statistical research. Methods that have been proposed are extremely complex, involving simulations, and are difficult to implement. For this study, we focus the power analysis on three comparisons that are of primary interest.

    - First, we will compare the percentage of patients with positive bacteria cultures in the subdermal layer of each treatment group before application of the treatment vs. after treatment. For this, McNemar's test of marginal homogeneity is appropriate. Based on previous research, we estimate that about 32% of patients will have bacteria present before treatment with povidone-iodine and about 3% will be positive after treatment. Under these conditions, the power for a one-tailed test at the 0.05 level of significance would be between 86% and 88% for n=30 patients in the test group, depending on the correlation of positive bacterial growth between the before and after measures.
    - The second comparison will be the percentage of patients with positive bacteria cultures in the deep wound at exposure in the povidone-iodine group vs. the control group. For this, a z-test for the equality of independent proportions is appropriate. From previous research, we estimate that about 17% of patients in the control group will have bacteria present in the deep wound and about 1.6% will be positive in the povidone-iodine group. For this comparison, the optimal sample size allocation is n=30 patients in the test treatment group and n=30 patients in the control group. With this allocation, a one-tailed test at the 0.05 level of significance would have 69% power.
    - The third comparison will be the percentage of patients with positive bacteria cultures in the deep wound at just before closure in the povidone-iodine group vs. the control group. Once again, a z-test for the equality of independent proportions is appropriate. From previous research, we estimate that about 40% of patients in the control group will have bacteria present in the deep wound before closure and about 4% will be positive in the povidone-iodine group. For n=30 patients in the test treatment group, n=30 patients in the control group, and a one-tailed test at the 0.05 level of significance the power would be 98%.

H. Data and Safety Monitoring

- This study poses minimal risk to the participant. The only differences from standard of care protocol for spinal fusion includes:
    - Performing cultures with a swab. This does not require removal of patient tissue and is considered minimal risk.
    - Application of povidone-iodine versus saline. While povidone-iodine has not been evaluated for this specific purpose, povidone-iodine is FDA approved in children, available over-the-counter, and is already widely utilized at our institution as a topical antiseptic, including for surgical skin preparation of open wound.
- Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable. Akron Children's Hospital Regulatory Compliance Specialists will monitor regulatory compliance, including processes for screening, consent, enrollment, and documentation. This will be done after the first 10 patients enrolled, 6 months after the start of the study and after the completion of enrollment. Data collection is the responsibility of the study staff at the site under the supervision of the site investigator, and the PI will personally review and verify data for accuracy and completeness, legibility, and timeliness of the data reported. All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data. The Data Management Specialist will monitor the data after the first 10 patients are enrolled, 6 months after the study start date and at the completion of the study. 100% of the data collected will be reviewed to that date to ensure that data are accurate, complete, and verifiable.
- The data safety monitor, Dr. Eric Robinette, will review the documented data by the study staff and monitor for any relationship between positive cultures every and SSI, if any, every 10 patients. If any relationship is noted, the data safety monitor will be report as necessary in the Adverse Event Log and notify all investigators. The data safety monitor and investigators will consider whether there is a reasonable possibility that the study intervention caused the event, whether there is potential harm by not treating a positive study culture, and/or if the study needs redesigned or discontinued.

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