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Original Article

A Randomized, Clinical Trial of Preadmission Chlorhexidine Skin Preparation Following Lower Extremity Total Joint Arthroplasty

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ABSTRACT

Background: Periprosthetic infections are devastating postoperative complications of total joint arthroplasty (TJA), with native skin flora commonly identified as causative organisms. We compared 2% chlorhexidine gluconate–impregnated cloths to standard-of-care antiseptic bathing in patients before TJA, to evaluate periprosthetic infection risk at 1-year follow-up.

Methods: This was a prospective, randomized, controlled trial at a single institution of patients undergoing hip or knee arthroplasty. Chlorhexidine-treated patients (275 arthroplasties) applied 2% chlorhexidine gluconate–impregnated cloths the night before and morning of admission. The standard-of-care cohort (279 arthroplasties) bathed with soap and water preadmission. Patients were excluded according to the following: (1) unable to comply with study requirements, (2) pregnant, (3) <18 years, (4) medical history of immunosuppression or steroid use, (5) chronic hepatitis B/C infection, (6) had infection around joint requiring surgery, or (7) chose not to participate. A total of 539 patients (554 arthroplasties) were included in the final population. There were no significant differences in American Society of Anesthesiologists grade, cut time, risk scores, or diabetes and smoking prevalence between cohorts ($P > .05$).

Results: A lower periprosthetic infection rate was found in the chlorhexidine cohort (0.4%) when compared to standard-of-care cohorts (2.9%). The infection odds ratio was 8.15 (95% confidence interval = 1.01-65.6; $P = .049$) for the standard-of-care cohort compared to the chlorhexidine cohort. No differences in assessed risk factors were found between groups. No severe adverse events were observed.

Conclusions: Preoperative chlorhexidine cloth use decreased the risk of periprosthetic infection. This may be an appropriate antiseptic protocol to implement for patients undergoing lower extremity TJA.

Background

Lower extremity total joint arthroplasty (TJA) effectively increases function and reduces pain in patients with hip or knee osteoarthritis. However, periprosthetic infection is a common complication, with reported incidences of 0.7%-2.5% after hip arthroplasty and 1%-3% after knee arthroplasty [1-6]. These periprosthetic infections have serious consequences, including delayed recoveries, increased lifetime health care expenditures, multiple reoperations, and increased mortalities [7,8]. With the increased older aged population, the frequency of arthroplasty patients is expected to increase over the next decade [9], who will be at risk for periprosthetic infection. Therefore, there is a need to identify preventative methods to decrease this devastating complication [1].

Sources of wound contamination following arthroplasty include operating room air and native skin flora [10]. Protocols effective in decreasing airborne pathogen load include positive air pressure, laminar airflow, and reduced foot traffic [11-14]. To reduce native skin flora, bathing with antiseptic agents the evening before surgery is recommended by the Centers for Disease Control and Prevention and is the standard-of-care [1]. Chlorhexidine is a broad-spectrum biocide effective against Gram-positive and Gram-negative bacteria. It exerts its bactericidal effects through direct disruption of the organisms' membrane permeability [15]. Therefore, preoperative chlorhexidine showers may be an efficacious alternative to bathing to decrease postoperative infection risk [7,10,16]. However,

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maintaining bactericidal skin concentrations are challenging with bathing alone [17].

A 2% chlorhexidine gluconate–impregnated cloth was developed specifically to maintain bactericidal concentrations for skin preparation. This cloth allows for prolonged antisepsis, as chlorhexidine gluconate persists on skin [18-20]. The long-lasting antiseptic effect is attributed to chlorhexidine gluconate not being inactivated by blood or serum proteins [21]. Furthermore, significantly greater reductions in bacteria up to 6 hours following application have been found compared to standard chlorhexidine skin preparation [22].

Chlorhexidine gluconate–impregnated cloths have been shown to reduce infection risk; however, there is limited evidence in orthopedic-related prophylaxis. We, therefore, conducted a prospective, randomized, controlled study comparing chlorhexidine cloths to standard-of-care antiseptic bathing in patients before TJA, to evaluate any differences in periprosthetic infection risk. Secondary end points were factors that may affect infection risk and adverse event incidences. We anticipated that risk factors would be similar between groups, and this intervention would significantly decrease infection risk as an alternative to standard-of-care preoperative skin preparation. Primary and secondary end points followed Food and Drug Administration guidance as agreed on with Food and Drug Administration as part of a Special Protocol Assessment.

Methods

Study Oversight

This prospective, randomized, controlled trial was performed at a tertiary care center, after institutional review board approval. It was conducted in accordance with Declaration of Helsinki and current regulatory requirements and registered with Clinicaltrials.gov (NCT02469311). It was designed by all authors and supported by an educational grant from Sage Products, LLC (Cary, IL). Data management, trial monitoring, and statistical analysis were performed and supervised by the participating authors. Sage Products, LLC had the opportunity to review and provide comments before manuscript submission; however, they had no role in trial design, data collection or analysis, or the decision to submit. All authors assume responsibility for data, vouch for integrity and completeness of data and analyses, and assume responsibility for the fidelity of this report toward the study protocol.

Patient Enrollment

Patients were enrolled between March 1, 2012 and November 30, 2012. Consecutive patients undergoing a joint arthroplasty, specifically a total knee arthroplasty or total hip arthroplasty (total knee arthroplasty or total hip arthroplasty) were eligible. Patients were excluded according to the following: (1) unable to comply with study requirements (n = 18); (2) pregnant (n = 0); (3) under 18 years of age (n = 0); (4) medical history of immunosuppression, for example, human immunodeficiency virus, status-post organ transplantation, or received >10 milligrams prednisone equivalent for >10 days within 90 days of enrollment (n = 9); (5) chronic hepatitis B or C infection (n = 6); (6) had infection around joint requiring surgery (n = 6); or (7) chose not to participate (n = 32) (Fig. 1).

Study Design

Patients provided written informed consent before randomization. They were randomized via a computer-generated algorithm preoperatively to receive either advance preadmission chlorhexidine (treatment) or standard-of-care (soap bathing). Eight patient cohorts were formed; 4 each of the treatment and standard-of-care groups involving: (1) primary knee arthroplasty patients, (2) revision knee arthroplasty patients, (3) primary hip arthroplasty patients, and (4) revision hip arthroplasty patients.

Primary and revision arthroplasty patients randomized to standard-of-care received bathing instructions with antibacterial soap and water the night before surgical admission. Patients randomized to chlorhexidine were provided with 2 packets containing six 2% chlorhexidine gluconate–impregnated cloths (Sage Products LLC), along with instructions for use the night before and morning of surgery. Patients used one cloth at the following cutaneous sites: (1) neck, chest, and abdomen; (2) back; (3) left and right upper extremity; (4) left lower extremity; (5) right lower extremity; and (6) surgical site. The chlorhexidine protocol specified that if patients were to bathe or shower, they should wait for a minimum of 2 hours before cloth application. Following cloth use, patients were not allowed to shower, rinse, or apply any topical cream or powder.

To verify compliance, patients submitted adhesive stickers from packets at the time of application, which were collected in the preoperative waiting area. If patients used the first packet correctly, the second packet was administered in hospital. Patients were excluded from the study if one or both cloth packs were not used as indicated (n = 28).

Enrolled patients underwent standard infection control practices during admission. All patients had the same perioperative skin preparation and postoperative care protocol, as described in the following section. As per the CDC, intravenous antibiotic prophylaxis (1 gram cefazolin) was commenced 1 hour before surgery. The incision site was cleaned with alcohol using a scrub and paint technique. This was followed by skin preparation, using aniodine povacrylex and isopropyl alcohol solution (DuraPrep Surgical Solution, The 3M Company, Saint Paul, MN). Nonpermeable paper drapes were used during surgery, with surgical adhesive tapes. Postoperatively, prophylactic antibiotics were stopped within 24 hours.

End Points

The primary end point assessed the incidence of deep periprosthetic infection. Patients were followed for 1 year postoperatively, consistent with the susceptibility period defined by CDC [23]. Recently, this was redefined as within 30-90 days after operation [24]. Periprosthetic infections were identified using criteria as specified by the Musculoskeletal Infection Society [8]. Superficial infections, which involved the skin or subcutaneous site, were documented, but not considered deep infections, and were excluded from the study.

Secondary end points were the correlations between infections and American Society of Anesthesiologists (ASA) grade [25], diabetes and smoking prevalence, mean surgery time, and wound type (clean vs contaminated) in the cohorts. A National Healthcare Safety Network (NHSN) risk score was calculated to determine infection risk [23,26]. Patients were assigned points based on operation duration, wound class, and ASA score [23]. Zero points were low risk, 1 point was medium risk, and 2 or 3 points were high risk.

Overall, 1 (0.2%) arthroplasty had a contaminated wound type. Mean ASA grade was 2 (95% confidence interval [CI], 2.3-2.4), and 213 (38%) arthroplasties had patients with an ASA score of 3 or greater. Mean surgical time was 102 (95% CI, 97.7-105.7) minutes (149 [27%] >120 minutes). Overall mean NHSN risk score was 0.6 (95% CI, 0.6-0.7), with 271 (49%) low risk, 206 (37%) medium risk, and 77 (14%) high risk. Overall, these factors were found to be