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Intraoperative chlorhexidine irrigation to prevent infection in total hip and knee arthroplasty

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ABSTRACT

Background: Surgical site irrigation during total hip (THA) and total knee (TKA) arthroplasty is a routine practice among orthopaedic surgeons to prevent periprosthetic joint infection. The purpose of this study was to evaluate the effect of chlorhexidine gluconate (CHG) irrigation on infection rates following THA and TKA.

Methods: Arthroplasties performed before September 2014 served as controls. THA performed before September 2014 (N = 253) underwent intraoperative irrigation with 0.9% saline followed by a 2-minute soak with <2% dilute povidone-iodine. TKA (N = 411) patients underwent only intraoperative saline irrigation. After October 2014, all patients (248 TKA and 138 THA) received intraoperative irrigation with 0.9% saline and periodic 0.05% CHG solution followed by a final 1-minute soak in CHG with immediate closure afterward.

Results: In this 2:1 comparison of consecutive patients, there were no differences in patient demographics between the 2 groups. No difference was noted in wound healing concerns subjectively, and no statistically significant association in nonsurgical site infections, superficial surgical site infection, and deep surgical site infection rates between the 2 groups (nonsurgical site infections [THA: $P = .244$, TKA: $P = .125$]; superficial surgical site infection [THA: $P = .555$, TKA: $P = .913$]; and deep surgical site infection [THA: $P = .302$, TKA: $P = .534$]).

Conclusions: We were unable to discern a difference in infection rates between chlorhexidine irrigation and our prior protocols using dilute Betadine for THA and 0.9% saline for TKA. The theoretic advantages of dilute CHG retention during closure appear to be safe without infectious concerns.

Introduction

There is little standardization pertaining to wound irrigation to prevent surgical site infection [1]. Infections continue to be a dreadful and costly complication in total joint arthroplasty (TJA). The estimated cost of periprosthetic joint infections (PJIs) due to sensitive organisms is known to be over $60,000 dollars [2] and over $100,000 dollars for methicillin-resistant organisms [3] per case. Despite our best efforts, PJI occurs in approximately 0.8%-1.9% of total knee arthroplasty (TKA) and 0.3%-1.7% of total hip arthroplasty (THA) [4]. PJI after TKA is the single leading cause of early revision, accounting for 25.4% of revisions within the first 2 years after surgery and 7.8% thereafter [5]. THA infections are the third leading cause of revision accounting for up to 14.8% of revision surgeries [4,5]. The demand for TKA and THA is projected to increase by 137% and 601%, respectively, from 2005 to 2030 [6]. As the demand increases, the cumulative associated cost of TJA is projected to exceed $1 billion dollars this year [7].

Preventative measures of joint infection in TJA are constantly evolving [8]. Currently, the use of perioperative systemic antibiotics is the standard of care in joint replacement. It is also the only

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consensus recommendation by international authorities. Other methods to decrease the rate of infection are still under investigation, such as operating room ventilation, body exhaust suits, preoperative patient optimization, intraoperative temperature management, and perioperative skin preparation and wound management. Wound irrigation during arthroplasty is a routine practice among orthopaedic surgeons to prevent PJI. Several potential solutions have been proposed including the use of 0.9% saline, castile soap, antibiotic solutions, and antiseptics like povidone-iodine or hydrogen peroxide, yet no consensus has been reached due to a lack of convincing evidence and a paucity of studies. A majority of surgeons favor 0.9% saline, although studies have shown potential advantages to antibiotic and soap solutions [9-11]. Much of the theoretic advantages have not been borne out in clinical studies.

Given the lack of clinical studies on the topic, a "gold standard" is still missing [12]. The purpose of this study was to determine the effect of chlorhexidine irrigation on infection rates following THA and TKA. Chlorhexidine gluconate (CHG) has advantages of being a potent antiseptic with broad-spectrum efficacy while still being gentle on native tissue [13,14]. This study is the first to our knowledge to directly examine intraoperative wound irrigation with chlorohexidine in TJA.

Material and methods

We reviewed our first year of experience with a chlorhexidine irrigation with a contemporary 2:1 match of the preceding historical controls. We performed a retrospective review of a prospectively collected database containing 1050 consecutive TJA patients who had undergone primary TKA or THA by a single surgeon at our institution from February 2012 to October 2015. After excluding patients with incomplete data, a total of 906 patients were ultimately included for analysis. Arthroplasties performed before September 2014 served as controls, as chlorhexidine irrigation was not used before this date. There were 411 TKA and 253 THA patients in the control group whereas 248 TKA and 138 THA patients in the chlorhexidine irrigation group.

All surgeries were performed under spinal anesthesia unless otherwise contraindicated. Cementless THA via a modified posterior approach and standard (nonantibiotic) cemented TKA was used in all patients. Skin preparation consisted of 2% chlorhexidine and 70% isopropyl alcohol (ChloraPrep, Carefusion, San Diego, CA) followed by a double-prep with iodine povacrylex in isopropyl alcohol (DuraPrep, 3M, St. Paul, MN) after draping, following by coverage by an iodophor-impregnated incise drape (Ioban 2, 3M, St. Paul, MN). THA performed before September 2014 (N = 664) underwent intraoperative irrigation with 0.9% saline followed by a 2-minute soak with <2% dilute povidone-iodine which was washed out entirely before closure. TKA patients underwent intraoperative irrigation with 0.9% saline as the sole treatment. After October 2014, all TJA (N = 386) patients received intraoperative irrigation with 0.9% saline and periodic 0.05% CHG solution (Irrisept, Irrimax Corporation, Innovation Technologies, Inc., Lawrenceville, GA) followed by a final 1-minute soak in CHG with immediate closure afterward.

All patients were placed on standard joints protocol postoperatively. Preoperative antibiotics were administered within 1 hour of the skin incision, using a single dose of 1-1.5 g of vancomycin and 1-2 g of cefazolin. Only those with anaphylactic allergy to cefazolin were switched to gentamicin. Postoperatively, cefazolin was given for 2 doses to be discontinued within 24 hours. Physical and occupational therapy was initiated on postoperative day 1 and continued until discharge. Although we currently mobilize the day of surgery, at the time of this study period patients would only dangle legs at bedside. Wound healing was assessed daily while patients were in the hospital and again upon follow-up clinical visits. Routine deep venous thrombus prophylaxis was started on postoperative day 1 and continued for 2-5 weeks postoperatively. During the time of this study, patients received aspirin 81 mg twice daily beginning the night of surgery for chemoprophylaxis. Those on more aggressive anticoagulation before surgery were alternatively restarted on their prior regimen. Minimum length of follow-up was 1 year.

Patient demographics including age, body mass index, gender, surgery, and transfusion were included. Nonsurgical site infections (NSSI), superficial surgical site infection (SSSI), and deep surgical site infection (DSSI) rates between the 2 groups were compared. We defined DSSI according to the Musculoskeletal Infection Society guidelines [15]. Statistical analysis was performed using adjusted odds ratios at a 95% confidence interval (CI) and univariate repeated-measures logistic regression models ($P < .05$). Parameters were compared between treatment groups using t-tests. Some patients appear up to 3 times in the dataset due to repeat surgeries and/or surgeries on both knees, so a generalized estimating equations approach was taken to account for the lack of independence in these measurements. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

A total of 906 patients undergoing TJAs were analyzed. Table 1 shows demographic characteristics of the study cohort and controls. There were no statistical differences between the 2 groups. The mean age of the controls was 65.3 vs 66.5 years in the study cohort. Mean body mass index was 32.0 in each group. Two patients were excluded from the chlorhexidine irrigation group due to traumatic knee injury associated with a significant direct fall at home requiring operative debridement and repeat closure.

A post hoc power analysis was calculated given the low infection rate seen in TJA and found that a 2-group chi-square test with a 0.05 two-sided significance level will have 80% power to detect a difference in proportions of 0.01054 (7/664, preintervention) and 0.00777 (3/386 postintervention) when the sample sizes are 25,629 and 14,901, respectively. This would require a study population of over 40,000. This analysis underscores the difficulty in finding statistically significant differences with the rates of infection in TJA.

There was no statistically significant association in overall infection rates between control and chlorhexidine irrigation solutions. Overall odds ratio and 95% CIs between controls and treatment groups were 1.97 ([0.97, 3.97], $P = .059$); 1.75 ([0.35, 8.70], $P = .494$); and 1.36 ([0.35, 5.29], $P = .6757$) for NSSI, SSSI, and DSSI, respectively.

The prevalence of infections in control groups for TKA was 24 (5.8%), 3 (0.7%), and 3 (0.7%) for NSSI, SSSI, and DSSI, respectively. In the TKA study group, there were 8 (3.2%), 2 (0.8%), and 3 (1.2%) infections for NSSI, SSSI, and DSSI, respectively. Odds ratio and 95% CIs between TKA treatment groups were 1.86 ([0.84, 4.11], $P = .125$) and 0.9 ([0.15, 5.42], $P = .913$) for NSSI and SSSI, respectively

Table 1
Demographic characteristics.

Characteristic	Control (N = 664)	Chlorhexidine (N = 386)	P value
Age (y)	65.3	66.5	.065
Blood transfusion rate	10%	0%	
Body mass index (kg/m^2)	32.0	32.0	.996
Right side	356 (54%)	194 (50%)	.268
Female	400 (60%)	231 (60%)	.904

Table 2
Infection rates: TKA.

Infection	Control (N = 411)	Chlorhexidine (N = 248)	Odds ratio (95% CI)	*P* value
NSSI	24 (5.8%)	8 (3.2%)	1.86 (0.84, 4.11)	.125
SSSI	3 (0.7%)	2 (0.8%)	0.90 (0.15, 5.42)	.913
DSSI	3 (0.7%)	3 (1.2%)	0.60 (0.12, 3.0)	.534

(Table 2). The TKA DSSI group had an odds ratio of 0.6 ([0.12, 3.0], $P = .6757$). The prevalence of infections in control groups for THA was 9 (3.6%), 3 (1.2%), and 4 (1.6%) for NSSI, SSSI, and DSSI, respectively (Table 3). There were 2 nonsurgical site infections (1.6%) in the THA study group. NSSI odds ratio for THA was 2.51 ([0.53, 11.79], $P = .244$). There were no incidences of SSSI or DSSI in the THA chlorhexidine treatment groups.

Discussion

Chlorhexidine is currently used routinely in several healthcare applications due to its broad-spectrum activity and quick onset of action. At various concentrations, it is used in skin preparation, oral [16] and hand hygiene, wound and catheter site dressings and is impregnated in several brand of vascular access catheters and surgical meshes. It is even increasingly added as a preservative to cosmetics and other personal care products [17]. In addition, chlorhexidine has a faster onset of action than povidone-iodine [18] against a wide variety of microorganisms yet is safe for healthy tissue [19-22]. Although other antiseptics such as povidone-iodine and hydrogen peroxide have been reported to be beneficial, concerns remain regarding the safety profile of these agents [23-25]. CHG also has a unique strong affinity for binding to skin and mucous membranes, which could theoretically enhance the efficacy for prevention of surgical site infections [26]. Despite its wide array of uses elsewhere, it has only recently had attention as a routine irrigant intraoperatively, after it was packaged and Food and Drug Administration–cleared as Irrisept 0.05% CHG in 0.9% saline.

Chlorhexidine has been commonly used as a disinfectant and antiseptic. It is a bactericidal [22] agent, acting primarily through cell membrane disruption [27]. Several animal studies have demonstrated its efficacy and safety. Severyns et al. [28] studied the effect of different wound irrigants on femoral artery and veins in a rat model and found that 0.05%, 0.02%, and 0.001% chlorhexidine solutions had a very low toxicity, comparable to the toxicity of physiological saline. Chlorhexidine has also been shown to be comparable to normal saline in regard to its effect on wound healing. Brennan et al. [29] reported no difference between saline and chlorhexidine on collagen production or appearance on histologic slides in a rat model. In terms of chlorhexidine's effect on tendon mechanical properties, Han et al. found that disinfection of bovine digital flexor tendons using 3 L of 2% chlorhexidine irrigation did not affect tendon ultimate failure load, stress, or stiffness [19].

Several animal studies have validated the safety of chlorhexidine for use on wounds, and its potential use for wound lavage has been demonstrated by the studies on prevention of infection in humans. Perioperative chlorhexidine rinses in patient's receiving dental implants decreased the infectious complications to 4.1% vs 8.7% in the saline control group [20]. Smith et al. [12] showed that chlorhexidine has also demonstrated superior biofilm eradication compared to other solutions when used to scrub a methicillin-resistant staphylococcus aureus-coated titanium disc. In comparing cleansing agents in pin care for external fixation, Annette and Toksvig-Larsen [10] demonstrated that normal saline had a higher relative risk for positive bacterial cultures (1.7×) and *Staphylococcus aureus* presence (3.3×) compared to a 2 mg/mL chlorhexidine solution. Climo et al. reported that the use of 0.05% chlorhexidine with sterile water in wound irrigation resulted in 5-6 log reduction in gram-positive and gram-negative surgical isolates after 1 and 5 minutes (including methicillin-resistant *Staphylococcus aureus*). The same study found statistically significant reductions in the regrowth of bacteria on 4 biomedical devices when irrigated with 0.05% chlorhexidine and sterile water [11]. Although chlorhexidine does have proven antiseptic properties, there is a lack of evidence-based protocols in place for the use chlorhexidine for wound irrigation.

All irrigants have their advantages and weaknesses. Previous studies have evaluated the benefits of antiseptics, such as povidone-iodine, in irrigating solutions [21,30]. Brown et al. reported on infection rates in primary THA and TKA that underwent a 3-minute dilute Betadine lavage combined with painting of the skin with Betadine before surgical closure. They looked at 1862 patients using normal saline lavage and compared this to 688 patients using Betadine lavage and followed patients for 90 days postoperatively. They found an infection rate of 0.15% in the Betadine lavage and skin painting group vs 0.97% with normal saline lavage ($P = .018$). Their retrospective review had many of the similar limitations as ours given the evolution of the entire surgical episode over the last 5-10 years which often confounds causal relationships. Nevertheless, it was founded on sound principles and was a practice changer for many in our subspecialty. Similarly, Kokavec et al. [30] reported a decrease in postoperative infections when using a Betadine intraoperative lavage in hip and pelvis surgery in children. They looked at 89 patients using Betadine lavage compared to 73 patients using no Betadine lavage and found no infections in the Betadine group compared to 2 superficial infections without Betadine irrigation.

Although several studies have suggested the benefits of Betadine irrigation [21,31,32], concerns remain regarding the safe use of this irrigant. Betadine has been shown to have chondrotoxic effects on articular cartilage [9,33]. Specifically, von Keudell and Gomoll demonstrated statistically significant increased chondrocyte toxicity with longer exposure time to 0.35% povidone-iodine solution in freshly harvested calf knees. Ideally iodine should also be allowed to dry to reach its full antimicrobial potential, something skin preparation solutions emphasize. It is also inactivated by blood and serum, making its theoretic advantages inside a surgical wound less attractive [34]. CHG does not have this issue and brings the potential that it may hang around on tissues longer given its adhesive properties mentioned earlier. Its safety profile has been touted as well given its widespread use.

Sobel et al. [22] found that human patellar tendon allografts soaked in chlorhexidine for 30 minutes did not have any significant differences in terms of graft elongation, ultimate tensile load, or stiffness when compared to normal saline. Food and Drug Administration clearance dictates Irrisept CHG irrigation removal by repeat saline irrigation, because prolonged exposure and retention was not studied for approval process. We soaked the wound with CHG throughout the case to take advantage of adherence properties. After the final soak, we suctioned the bulk of the fluid but did not irrigate the CHG out. This potential chemotherapeutic advantage was chosen given theoretic similarities to recent studies showing

Table 3
Infection rates: THA.

Infection	Control (N = 253)	Chlorhexidine (N = 138)	Odds ratio (95% CI)	*P* value
NSSI	9 (3.6%)	2 (1.6%)	2.51 (0.53, 11.79)	.244
SSSI	3 (1.2%)	0 (0%)	N/A	.555
DSSI	4 (1.6%)	0 (0%)	N/A	.302

N/A, not applicable.

the benefit of vancomycin powder addition just before closure [35,36]. Our decision to leave it in was chosen given the low percentage dilution (0.05%) that only gets lower with bleeding as closure proceeds, along with its historic safety profile. We acknowledge that this risk/benefit decision is off-label but believe it does add to the relevant findings. The present study findings suggest that intraoperative CHG during TJA has a comparable infection rate to our prior protocols using Betadine in THA and 0.9% saline in TKA.

There are several limitations to this study. First, we are inherently limited by the retrospective nature of the study. Second, this was a single surgeon's experience, which may affect generalizability of the study. Given the multitude of variables with infection, we see the single surgeon design as a potential advantage given surgical variables such as approach and soft-tissue handling and surgical time can vary among surgeons. Even when isolating a single surgeon, there is a migration of surgical practices that happens over the years that limits anything but randomized prospective studies. Surgical nuances such as implant vendor changes, soft tissue retractors, assistant staffing, suturing technique and materials, blood management, and even postoperative dressings can have profound effects on infection potential. These are, however, difficult at best to quantify. We acknowledge that this is a small sample size and given the low prevalence of PJI, our study is underpowered. A post hoc power analysis illustrates the large number of patients required to reach significance given the low infection rates in TJA, which is a weak inference of equivalence of treatment effect in this present study population. Finally, we did not perform a cost analysis and one should be aware of the potential increase in cost associated with the use of commercially available CHG relative to other agents.

Conclusions

PJI continues to be one of the most devastating and costly complications after TJA. No consensus exists regarding the optimal solution for intraoperative wound irrigation. We were unable to discern a difference in infection rates between chlorhexidine irrigation and our prior protocols using dilute Betadine for THA and 0.9% saline for TKA. There are theoretical advantages, including antimicrobial benefits to sterilize the wound before closure, which may be further magnified as this has shown it to be safe to remain in the wound upon closure. Future research is needed to provide better insight into the utility of CHG for intraoperative wound irrigation in isolation for the prevention of PJI.

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