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Research Article

The Use of a Novel Surgical Irrigant May Be Associated with Decreased Incidence of Surgical Site Infections

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Background

Periprosthetic joint infection (PJI) represents a formidable challenge to patients undergoing elective total hip arthroplasty (THA) and total knee arthroplasty (TKA). This investigation evaluated a novel antimicrobial surgical irrigation solution, XPerience (XP) (Next Science LLC, Jacksonville, FL), with proven high & persistent in-vivo efficacy against planktonic bacteria and biofilm. The primary objective of this investigation was to compare the incidence of PJI following TKA performed with use of XP versus a standard control rinse (povidone-iodine). The secondary outcome was an all-cause return to operating room (OR) rate.

Methods

A retrospective cohort study was conducted from 824 consecutive patients undergoing primary THA/TKA from 12/1/2019 - 11/30/2021 treated using povidone-iodine solution and 471 consecutive patients undergoing primary THA/TKA from 12/1/2021 - 12/30/2022 treated with XP at a single institution by the senior author. All surgeries in both groups followed largely identical preoperative, perioperative, and postoperative protocols. A total of 1,295 cases were analyzed. The groups shared largely analogous background characteristics pertaining to age, sex, BMI, and American Society of Anesthesiologists (ASA) class.

Results

The overall SSI rate was 0% (0/471) in the XP group and 0.49% (4/824) in the control group (P = 0.3). The overall return to OR rate was 0.21% (1/471) in the XP group and 0.85% (7/824) in the control group (P = 0.3). Control group cases returned to the OR for hematoma debridements, periprosthetic fracture fixation, and PJI revisions.

Conclusion

This investigation is the first to remark on the clinical efficacy of a novel surgical irrigant. There was no statistically significant difference in rates of PJI or return to OR with the irrigant versus without, though a trend towards lower rates was observed in the context of a low baseline infection rate. Limitations pertaining to a single-center experience and sample size may be addressed by further studies incorporating broader enrollments.

INTRODUCTION

Periprosthetic joint infection (PJI) represents a formidable burden in the form of morbidity to patients undergoing elective total hip arthroplasty (THA) and total knee arthroplasty (TKA). Affecting approximately 1-2% of patients undergoing such elective surgeries, PJI imposes economic catastrophe with estimates of $1.85 billion in hospital costs for related expenditure by the year 2030 (Premkumar et al. 2021). In addition to the financial burden, patient outcomes and well-being are dramatically worsened when faced with PJI. Accordingly, targeted adjuvant therapies to reduce this risk have been proposed most notably with various topical applications of antibiotics. The use of pre-operative antibiotics is supported as a prophylactic measure by several guidelines (Berríos-Torres et al. 2017; Leaper and Edmiston

2017; Anderson et al. 2014; Parvizi, Gehrke, and Chen 2013). While the use of local formulations of antibiotic medications within the surgical wound is occasionally practiced, evidence does not support corresponding statistically significant reductions in infection rates. Post-operatively, the utility of additional doses of intravenous antibiotics has not been fully supported by recent literature (Tan et al. 2019). Extended oral antibiotic protocols have, however, demonstrated reductions in 90-day infection rates (Inabathula et al. 2018). While antibiotics have proven successful as prophylactic measures in some applications, an inherent risk profile that includes systemic toxicity as well as concerns around antibiotic stewardship and development of resistance potentially limits their liberal use.

XPerience (XP) (Next Science LLC, Jacksonville, FL) is a nontoxic, no-rinse antimicrobial surgical irrigation cleared for use by the United States Food and Drug Administration. XP is comprised of 32.5 g/L citric acid, 31.3 g/L sodium citrate, and 1.00 g/L sodium lauryl sulfate in water. Early data has demonstrated high efficacy of the irrigant against planktonic bacteria and biofilm (Bashyal et al. 2022). The sodium lauryl sulfate in the solution is an antimicrobial surfactant, functioning by inciting lysis of bacterial cells as well as reduction of biofilm surface tension. As it does not require a post-application rinse, therapeutic effects may persist with residual solution within the surgical site. In-vivo use has shown strong anecdotal support in favor of infection risk reduction, though no present studies have examined its clinical efficacy.

This investigation was conducted with the primary objective of determining the incidence of PJI following use of XP during THA/TKA as compared to THA/TKA performed with a standard control rinse (betadine/saline). Secondary outcomes analyzed during this study were any other return to operating room rates for non-infectious causes.

The authors hypothesized that patients undergoing primary TKA or THA treated with the novel wound rinse intraoperatively would have demonstrably lower rates of PJI.

MATERIAL AND METHODS

After approval from the Institutional Review Board (IRB), a retrospective analysis was performed on a consecutive series of patients from the Northshore University Healthsystem Department of Orthopaedic Surgery. From December 1 2019 to November 30 2021, 824 consecutive patients undergoing primary TKA/THA were treated using a povidone-iodine (Betadine) solution soak in a standardized protocol. Unicompartmental knee arthroplasty and conversion arthroplasty of the hip or the knee were excluded. Starting December 1 2021 through December 30 2022, 471 consecutive patients undergoing primary TKA/THA were treated with the novel XPerience advanced surgical irrigation.

A chart review was performed for these included patients. Demographic data was collected on the following characteristics: age at time of index arthroplasty, sex, height and weight for calculation of body mass index (BMI), and American Society of Anesthesiology (ASA) class. In addition, type of arthroplasty (THA or TKA) was noted along with the method of anesthesia used during the procedure.

All TJA in both groups followed identical preoperative, perioperative, and postoperative protocols with regards to pain control, anesthesia, wound closure, postoperative wound care. All patients received dual antibiotic prophylaxis with vancomycin and cefazolin preoperatively followed by 2 doses of cefazolin postoperatively. If patients had a documented penicillin or cephalosporin allergy, aztreonam, clindamycin or gentamicin was administered in its place. Surgical helmets with body exhaust suits and iodophor-impregnated drapes were used for all cases. All procedures were performed by the senior author (RB). Prior to December 1 2021, the intraoperative protocol was to use a 3 liter bag of standard saline connected to pulse lavage for irrigation and visualization during the case, followed by a dilute betadine soak for up to 3 minutes, followed by further saline irrigation to remove the dilute betadine solution at the end of the case after implantation of final components and prior to closure. After December 1 2021, the intraoperative protocol was to use 500cc - 1000cc of the XPerience solution connected to pulse lavage in lieu of the saline irrigation throughout the case for irrigation and visualization. No additional separate soak time was used, and no separate saline rinse of the XPerience solution was required. For all cases in both groups, one gram of powdered Vancomycin was placed within the joint capsule prior to closure with sutures deep and skin staples superficially; a standard dressing with a silver impregnated strip (Acticoat Flex; Smith-Nephew, Memphis TN) covered with a negative pressure dressing (PICO; Smith-Nephew, Memphis TN) was placed.

Patients were assigned standardized follow-up in clinic at 3 weeks, 4 months, and 1 year. The negative pressure dressing and silver impregnant strip were removed on POD6, staples were removed on POD14, both by home health nursing care. Periprosthetic joint infections were defined in accordance with the definition set forth by Parvizi et al (Parvizi, Gehrke, and Chen 2013). In addition, any incidence of return to the operating room for reasons other than infection were recorded.

Data was analyzed with the use of Welch two sample t-testing for continuous variables and Fisher's exact testing or Pearson's chi-square test for categorical variables depending on number of categories.

A total of 1,295 cases were available for analysis following the application of inclusion criteria, with 824 cases in the control (betadine) group and 471 in the treatment (XP) group. As shown in Table 1, the groups shared largely analogous background characteristics for examined variables including age, sex, height, weight, BMI, ASA class. The XP group was noted to have a statistically higher rate of regional anesthesia use.

RESULTS

Examining the primary outcome of PJI incidence, no patients in the XP group developed an PJI within the duration of the study. As shown in Table 2, the incidence of PJI rate

Table 1. Patient Characteristics

	Control, N = 824[1]	Xperience, N = 471[1]	p-value[2]
Age	68 (9)	67 (10)	0.5
Sex			0.5
Female	493 / 824 (60%)	272 / 471 (58%)	
Male	331 / 824 (40%)	199 / 471 (42%)	
Height (in.)	66.6 (4.2)	66.7 (4.2)	0.7
Weight (lbs)	188 (42)	188 (45)	0.8
Body Mass Index	29.7 (5.4)	29.5 (5.5)	0.5
Type of Surgery			0.5
THA	391 / 824 (47%)	214 / 471 (45%)	
TKA	433 / 824 (53%)	257 / 471 (55%)	
ASA >2 or <=2			0.9
<=2	546 / 824 (66%)	310 / 471 (66%)	
>2	278 / 824 (34%)	161 / 471 (34%)	
Anesthesia Type			**0.009**
General	28 / 824 (3.4%)	20 / 471 (4.2%)	
Monitored Anesthesia Care	3 / 824 (0.4%)	0 / 471 (0%)	
Regional	51 / 824 (6.2%)	51 / 471 (11%)	
Spinal	742 / 824 (90%)	400 / 471 (85%)	

[1]Mean (SD); n / N (%)
[2]Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

Table 2. Patient Outcomes

	Control, N = 824[1]	Xperience, N = 471[1]	p-value[2]
Surgical Site Infection	4 / 824 (0.5%)	0 / 471 (0%)	0.3
Return to Operating Room			0.3
Did not return	817 / 824 (99%)	470 / 471 (99.8%)	
Returned to OR	7 / 824 (0.8%)	1 / 471 (0.2%)	
Reasons for OR return			
Hematoma I&D	2 / 824 (0.2%)	0 / 471 (0%)	
Peri-Prosthetic Fracture	1 / 824 (0.1%)	0 / 471 (0%)	
PJI	4 / 824 (0.5%)	0 / 471 (0%)	
Superficial Wound Dehiscence (culture negative)	0 / 824 (0%)	1 / 471 (0.2%)	

[1]n / N (%)
[2]Fisher's exact test

for our entire cohort of patients was 0.3% (4/1295). Between groups, the PJI rate was 0% (0/471) in the XP group and 0.5% (4/824) in the betadine group with a significance of *P = 0.3*. Of the four patients in the control group with PJI, all were noted to be patients that underwent TKA and were diagnosed within 4 weeks of the index arthroplasty; all underwent surgical debridement and exchange of the modular polyethylene component without further complication or additional return to OR.

As it pertains to the secondary outcomes, as shown in Table 2, the overall return to OR rate was 0.21% (1/471) in the XP group and 0.85% (7/824) in the control group (*P = 0.3*). One case in the XP group underwent return to the OR for the purpose of superficial wound irrigation and debridement (I&D) following an injury resulting in the skin superficially splitting and opening. In this case, all intraoperative cultures were negative at final analysis. Seven cases in the control group returned to the OR. Four cases of infection required re-operation. In addition to these cases for deep infection, three cases in the control betadine group required return to the OR for non-infectious causes; a hematoma I&D occurred in two cases and fixation of a periprosthetic femur fracture in one case. Both cases that required I&D for hematoma evacuation were noted to have negative intraoperative cultures at final analysis.

DISCUSSION

Our study is the first to show that use of a novel wound rinse, XPerience (XP) in patients undergoing primary THA/TKA signifies a trend towards lower incidence of PJI, though did not achieve statistical significance. 4 patients in the betadine group developed deep infections requiring return to the OR, whereas none in the XP group developed this complication during final follow-up. Statistical significance was unable to be achieved in the context of a low overall infection rate in a 1-year cohort; we believe this finding represents a meaningful trend that requires consideration and further investigation as it demonstrates a reduced incidence of infection when compared to published national averages (1-2%) (Premkumar et al. 2021). Additional investigation with expanded cohorts may further elucidate findings.

Various measures for PJI prophylaxis have previously been investigated. A retrospective cohort study by Inabathula et al in 2018 examining the effects of extended oral antibiotics (EOA) demonstrated a significantly lower rate of infection within 90 days for patients with 1 or more risk factors undergoing TKA (0.5% vs 2.1%, $P = 0.038$) & THA (1.1% vs 4.3%, $P = 0.034$). Overall 90-day infection rates were 2.2% and 1.0% after the THAs and TKAs, respectively (Inabathula et al. 2018). Similarly in 2021, Kheir et al found that the use of a 7-day course of EOA significantly reduced the risk of PJI in high risk patients (0.89% vs 2.64%, respectively; $P < .001$), with an overall 1-year infection rate of 1.40% (Kheir et al. 2021). Whereas there remains controversy in the widespread use of antibiotics for this purpose, their utility in infection prophylaxis for high-risk patients or in revision cases has been supported by several publications. Topical antibiotics, such as vancomycin, within the surgical wound affords an additional means by which surgeons may seek to control the incidence of PJI. A 2021 systematic review examining the use of topical vancomycin found that of 9 studies, only 1 found a lower risk of PJI with broad odds ratios ranging from 0.09 - 1.97 and concluded that there was an absence of evidence for its efficacy. Rates of PJI incidence in topical vancomycin groups ranged between 0.1% - 7.8% and 0.7% - 9.4% in control groups (Wong et al. 2021). An additional randomized trial comparing the ability of intrawound vancomycin powder to standard post-operative antibiotics was halted early due to a significantly greater proportion of patients receiving vancomycin powder developing a PJI. The overall incidence of PJI in this study was 4% (Abuzaiter et al. 2023). Further, the use of topical vancomycin has been associated with aseptic wound complications (Mulpur et al. 2023). Thus, there is currently limited evidence to support the use of topical antibiotics, either independent of or in lieu of standard post-operative antibiotics, in preventing PJI.

It has been estimated in prior studies that the rate of PJI in elective surgeries in the United States varies between 1-2% (Premkumar et al. 2021). In comparison to the aforementioned literature, our analysis showed a markedly lower PJI incidence of 0.3% across both cohorts of patients for this single-surgeon study. This represents a challenge in terms of necessary inclusion required to demonstrate a significant reduction of a narrow incidence. As such, the authors hold the belief that any delineation of statistical significance is limited by our current sample size. A higher rate of enrollment in both groups would be necessary for this metric, which remains outside the scope of this preliminary study.

As previously discussed, the cost of PJI diagnosis and treatment is high (Premkumar et al. 2021). Kapadia et al noted the average cost for the infected THA and TKA was $88,623 and $116,383 compared to that of non-infected THA and TKA $25,659 and $28,249 respectively (Kapadia et al. 2016). While individual institutional costs for XP may vary, we believe the marginal cost added with use of XP will be outweighed by its potential cost-savings benefit to the healthcare system by avoiding development of PJI. The cost of Xperience solution is estimated to be in-line with similar surgical irrigation solutions available on the market.

In analysis of our baseline characteristics, we found a significant difference between methods of anesthetic used between the two groups. The No XP group showed higher rates of spinal anesthetic use at 90% compared to 85% in the XP group. We do not believe this finding reflects a clinically meaningful difference between the groups and instead is attributable to a pattern of anesthesiologist preference during the study period.

Our results also showed there was no significant difference in return to OR rates between groups, with rates of was 0.21% (1/471) in the XP group and 0.85% (7/824) in the betadine control group ($P = 0.3$). In addition to the four patients that required reoperation due to PJI diagnosis in the betadine cohort, three patients required return to the OR for non-infectious causes. The periprosthetic femur fracture was due to the mechanical fall sustained by the patient and likely unrelated to any irrigation use. 2 patients developed hematomas and underwent I&D, both with negative intraoperative culture results.

This data builds upon a growing body of evidence regarding Xperience solution. A pilot clinical study performed by Battista et al reported statistically significant improvements in post-operative swelling, range-of-motion, and ambulatory assistive devices at measured intervals with the use of Xperience solution as compared to dilute povidone-iodine (Battista and Wickline 2023). This demonstrates the potential for lower rates of inflammation with use of the solution and stimulates discussion regarding effects on functional outcome.

Our study has several limitations. First and foremost, is the relatively rare nature of PJI in primary TKA/THA patients in this cohort. As previously discussed, the infection rate in our single-surgeon cohort limited our ability to perform an adequately powered cohort study. Second, this study was limited to a follow up of 6 months for the most recent patients in the XP group. While the majority of PJI occurs in the early postoperative period, a longer-term follow-up may provide more accurate long-term results, though we would expect that early infections due to seeding in the OR or external wound contamination prior to skin healing/epithelialization would have presented in

the first 6 months. Additionally, the utility of Xperience solution has not yet been investigated in alternative arthroplasty surgeries including unicompartmental knee arthroplasty (UKA). As any UKA cases which would've occurred during the study period would be sparce, the current study does not offer data regarding this. The solution is, however, not known to be chondrotoxic and UKA would not be considered a contraindication to use. The authors advocate for broader enrollments and continued investigation in future studies of the novel irrigant solution for further elucidation of the clinical & prophylactic benefit in prevention of PJI.

CONCLUSION

This investigation is the first to remark on the clinical efficacy of a novel surgical irrigant. There was no statistically significant difference in rates of PJI or return to OR with the irrigant versus without, though a trend towards lower rates was observed in the context of a low baseline infection rate. Limitations pertaining to a single-center experience and sample size may be addressed by further studies incorporating broader enrollments.

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