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Research Article

Novel Irrigation Reduces Prosthetic Joint Infection Rates: Meta-analysis of 3 clinical studies

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Prosthetic joint infection (PJI) in the setting of total joint arthroplasty represents significant morbidity and economic burden to patients and the healthcare system. We analyzed a non-toxic, no-rinse intraoperative antimicrobial irrigation solution (AIS) that was designed to combat infection. In this meta-analysis of three studies, the AIS rate of PJI was 0.727 per 1000 surgeries (95% CI: [0.041, 3.19]), which was significantly less than the standard of care (SOC) rate of infection of 4.854 per 1000 (95% CI: [1.178, 27.73]) (p=0.045). This corresponds to a reduction of 85% in the odds of PJI (p = 0.045, 95% CI: [24%, 99%]). When compared to the American Association of Hip and Knee Surgeons (AAHKS) estimate of 1 infection per 100 surgeries, the AIS rate of infection was significantly less (p=0.004). The use of this AIS intraoperatively represents an efficient and effective technique to combat PJI in the setting of total joint arthroplasty.

INTRODUCTION

For patient undergoing Total Knee Arthroplasty (TKA) and Total Hip Arthroplasty (THA) procedures, prosthetic joint infection (PJI) remains a daunting and formidable complication. PJI affects approximately 1-2% of patients undergoing elective joint replacements and represents a large financial burden, with estimated expenditures approaching $1.85 billion by 2030 (Premkumar et al. 2021; American Association of Hip and Knee Surgeons, n.d.). Despite attempts to elucidate risk factors, mitigation techniques, and prophylactic methods to reduce PJI incidence, rates have remained unchanged for decades ("Proceedings of the Second International Consensus Meeting on Musculoskeletal Infection," n.d.; McMaster Arthroplasty Collective 2020).

Pre-operative and post-operative antibiotics remain a mainstay of infection prevention efforts in THA and TKA procedures. Several guidelines support the use of prophylactic pre-operative antibiotics (Berríos-Torres et al. 2017; Leaper and Edmiston 2017; Anderson et al. 2014; Parvizi, Gehrke, and Chen 2013). Post-operative intravenous antibiotics are oftentimes utilized, however, their efficacy in infection prevention is yet to be fully supported (Tan et al. 2019). Extended post-operative oral antibiotics have demonstrated reduction in short-term infection rates (Inabathula et al. 2018). Despite the efficacy of antibiotics, concerns remain regarding systemic toxicity and antibiotic stewardship.

Clinicians have begun employing various intraoperative irrigation solutions in an attempt to decrease PJI incidence. One such formation is Xperience (XP) (Next Science, LLC, Jacksonville, FL). XP is a nontoxic, no-rinse intraoperative antimicrobial irrigation solution (AIS) cleared for use by the United State Food and Drug Administration. It is comprised citric acid, sodium citrate, and sodium lauryl sulfate in water.

Previous *in vitro* testing has shown that XP is highly effective against planktonic bacteria and their biofilm superstructures that are responsible for PJI (Bashyal et al. 2022). Three recent retrospective clinical studies have investigated the use of XP in primary joint arthroplasty (Vatti et al. 2024; Singer 2024; Williams and Harris 2024). The aim of this meta-analysis is to pool the clinical studies together to evaluate the efficacy of this specific AIS on reducing PJI rates in the setting of primary hip and knee arthroplasty.

METHODS

The three studies included total hip and knee arthroplasty procedures performed by different orthopedic surgeons at each institution (Vatti et al. 2024; Singer 2024; Williams and Harris 2024). Intraoperative protocols varied, however, in each case, the solution was used to irrigate the surgical wound during various stages of the arthroplasty procedure and/or at the end. XP is comprised of of 32.5 g/L citric acid, 31.3 g/L sodium citrate, and 1.00 g/L sodium lauryl sulfate in water. Given the lack of cytotoxicity of the solution, there was no secondary rinse required. Pre-operative and post-operative antibiotic protocols were not standardized across the three studies. Two of the studies lacked matched control groups, while the third study compared to historical data at their institution on PJI rates with the use of a povidone-iodine wash (Vatti et al. 2024). The primary outcome was 90-day PJI rate. The studies and treatment groups are summarized in Table 1. Given the lack of standardized control groups, 90-day PJI rates were compared to infection rates in a Standard of Care (SOC) group. Patients in the SOC group were treated with an intraoperative diluted (0.35%) topical povidone iodine soak for at least 3 minutes, followed up a pulsatile lavage rinse with normal saline.

To compare the AIS group with the SOC, a meta-analysis was applied to pool all three studies in Table 1. Further analysis was performed comparing the pooled AIS rate of PJI to a conservative national mean (Zeng et al. 2023; Ebrahimzadeh et al. 2023; Kobayashi et al. 2021). The meta-analysis was performed using a mixed effects logistic regression model with study as a random effect and group as a fixed effect (Papadimitropoulou et al. 2019). The two groups were compared using a 1-sided Wald test and 1-sided likelihood profile 95% CI of the odds ratio. Two-sided likelihood profile 95% CIs were generated for the rate of infection for each group. The statistical software R v4.4.1 package lme4 was used for all statistical calculations (R Core Team, n.d.; Bates et al. 2015).

RESULTS

Pooled across the 3 studies, a meta-analysis showed that the AIS rate of PJI was 0.727 per 1000 surgeries (95% CI: [0.041, 3.19]), which was statistically significantly less than the standard of care (SOC) rate of infection of 4.854 per 1000 (95% CI: [1.178, 27.73]) (p=0.045).

Table 1. Treatment Groups Across Studies and Corresponding PJI Incidence

Study	Treatment	Number of Surgeries	Number of PJI
Singer et al	AIS	524	1
Williams and Harris	AIS	381	0
Bashyal et al	AIS	471	0
Bashyal et al	SOC	824	4

This corresponds to a statistically significant reduction of 85% in the odds of PJI (p = 0.045, 95% CI: [24%, 99%]).

DISCUSSION

In this meta-analysis of total joint arthroplasties performed using a novel no-rinse irrigation solution, we found the PJI rate was significantly lower in the AIS group compared to a SOC group (p=0.045). This corresponded to an 85% reduction in the odds of PJI development (p=0.045). Despite the already relatively low PJI rate in the SOC group (0.48%), the use of this AIS still had enough efficacy as to result in a statistically significant reduction.

The number of elective total joint arthroplasties is only expected to rise in the coming years, with the annual THA and TKA numbers expected to be 652,000 and 1,272,000 in 2025, respectively[21]. It has been shown that the average cost for an infected THA and TKA is $88,623 and $116,383, respectively (Singh et al. 2019). Those values are substantially higher than the valued of non-infected THA and TKA counterparts, which are estimated to cost $25,659 and $28,249. Given the patient morbidity and economic burden PJI presents to the healthcare system, there is need to develop effective and novel practices for infection prevention.

The American Association of Hip and Knee Surgeons estimates the risk of prosthetic joint infection in hip and knee arthroplasty procedures at 1-2% (American Association of Hip and Knee Surgeons, n.d.). When compared to the lower threshold AAHKS estimate of 1 infection per 100 surgeries, the AIS rate of infection was significantly less (p=0.004). A more conservative estimate of national PJI rates is 0.5% (Zeng et al. 2023; Ebrahimzadeh et al. 2023; Kobayashi et al. 2021). When compared to this, the AIS rate of infection was still significantly decreased (p=0.027).

According to the National Institute of Health (NIH), a significant number of microbial infections are attributable to the formation of biofilm (Kapadia et al. 2016). Biofilm production is paramount to the development and pathogenesis of PJI ("NIH Guide: Research on Microbial Biofilms," n.d.). Any existing microbial presence can colonize intraoperative prosthesis and result in rapid formation of biofilm. Biofilm consist of bacteria as well as host parts that are created by fibrin, polymorphonuclear neutrophils, erythrocytes, fibroblasts, and other constituents (Khatoon et al. 2018). After maturing, biofilm can exhibit various defense mechanisms such as resistance to antibacterial treatments and host immune defenses (Buret et al. 1991).

This AIS was designed to cleanse and remove debris from surgical wounds, including microorganisms. Its design is based on patented technology aimed to prevent the formation of biofilm, as well as treat and remove matured biofilm. The irrigation solution incorporates a buffered pH modifier and surfactant, which work in combination to break down biofilm. The antimicrobial efficacy of the AIS was studied *in vitro* by Bashyal et al (Bashyal et al. 2022). After irrigating for 5 minutes, they showed high efficacy (at least a 6-log reduction) against planktonic bacteria (*Pseudomonas aeruginosa*, *Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli*, *Enterococcus faecalis, Enterobacter cloacae*). Furthermore, there was at least a 3-log reduction against yeast (*Candida albicans, Candida tropicalis*). This *in vitro* study also showed efficacy against biofilm bacteria, with at least a 2-log reduction of *S. epidermidis, Pseudomonas* and *Cutibacterium acnes* after 1 hour of irrigation, and a 4-log reduction of *S. aureus* after 30 minutes of irrigation. This study also showed persistent inhibition of biofilm regrowth from 5 minutes to 5 hours after AIS exposure. As highlighted previously, this AIS is a no-rinse solution. A contributing factor to the lower infection rate in the experimental group may stem from its long-lasting presence, even after wound closure.

There are several limitations to this analysis. First, surgical techniques were not standardized across the three retrospective studies and thus the AIS was used at different times throughout the procedure. Although this represents variation in surgical protocol, it shows that the use of the AIS at any point during the procedure can be beneficial. Second, two of the studies did not have control groups. To combat this, we compared PJI rates in the pooled AIS group to the PJI rate of the SOC from one of the included studies, which was 0.48%. This SOC PJI rate is similar to conservative national estimates (Zeng et al. 2023; Ebrahimzadeh et al. 2023; Kobayashi et al. 2021).

In conclusion, in a pooled meta-analysis of three studies using the AIS irrigation solution, we found that the use of this AIS was associated with a significantly lower PJI rate as compared to a SOC group. Compared to the AAHKS estimate and even more conservative national means, the AIS treatment group had decreased rates of PJI. As efforts are continuously made to prevent PJI and optimize total joint arthroplasty, the use of this AIS represents a meaningful development in infection prevention strategy.

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