

Research Article

Novel Intra- Operative Wound Irrigation Solution to Manage Infection Prevention in Patients Undergoing Primary Joint Arthroplasty: Retrospective Review of a Case Series of 308 Patients

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Keywords: periprosthetic joint infection, total knee arthroplasty, total hip arthroplasty, polyhexanide betaine solution, biofilm, intra-operative infection prevention, intra-operative wound irrigation, total joint arthroplasty, polyhexanide, betaine, Prontosan

<https://doi.org/10.60118/001c.72787>

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He attended medical school at Ohio University and completed an orthopedic surgery residency at Doctors Hospital and Grant Medical Center in Columbus Ohio. He went on to complete a fellowship in adult reconstruction at the world-renowned Cleveland Clinic.

Dr. Jacob maintains a vibrant academic side to his practice and has an extensive background in clinical research. Dr. Jacob is the author of several Peer-reviewed journal articles and publications. He is the founding member of the Oklahoma Joint Reconstruction Institute and practices out of Oklahoma City, Oklahoma.

Dr. Jacob brings cutting edge techniques and technology to the Oklahoma City area. He has extensive training in minimally invasive, rapid recovery joint replacement as well as robotically assisted hip and knee replacement.

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She also serves as an instructor and Training Center faculty for the American

Heart Association. Mrs. Justice dedicates her time to being a community speaker for the US Bone and Joint Initiative and she sits on several academic and professional association boards. She is also an active volunteer in the Oklahoma City community, participating in medical mission trips and being a medical volunteer for Oklahoma Medical Reserve Corps.

Most recently, she served as the director of the Total Joint Program for the

Center of Excellence in Joint Replacement at HPI Community Hospital, where she helped to launch this program in 2014. Shortly after its launch, the government announced the Comprehensive Care for Joint Replacement program. She successfully led her team to multiple awards as a center of excellence in hip and knee replacements from various insurance providers.

She now serves as OJRI's Director of Clinical Research for the Oklahoma Joint Reconstruction Research Institute (OJR2I), which Dr. Paul Jacob and Elaine, successful launched in 2021. She maintains the duties as the Nurse Navigator for OJRI, and is honored to be the patient advocate for all aspects of the pre-op and post-op patient experience.

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Journal of Orthopaedic Experience & Innovation

Vol. 4, Issue 1, 2023

Introduction

Periprosthetic joint infection (PJI) after total hip and total knee arthroplasty is a devastating complication that is known to be associated with costly, resource-intensive interventions that place a significant burden on the US healthcare system. Estimated average hospital costs to treat female patients with PJI after total knee arthroplasty (TKA) or total hip arthroplasty (THA) in 2018 was \$27,307, and \$32,956 respectively. While the average costs to treat male patients with PJI after TKA or THA was \$27,097 and \$33,090 respectively. One strategy aimed at preventing PJI after total joint arthroplasty is the use of an intra-operative wound irrigation with an antiseptic solution. This retrospective case review was conducted to assess the incidence of PJI after using a novel wound antiseptic irrigation solution in patients undergoing primary TKA and THA.

Methods

The CDC defines surgical site infections, (SSI) as infections that occur after the surgery. The infections are further categorized as superficial involving the skin, or deep tissue. These infections are then divided into; superficial incisional SSI, deep incisional SSI, and organ-space SSI. In a study by Kannan et al., SSIs are more commonly seen in patients with more comorbidities. A consecutive series of 308 high-risk patients undergoing primary TKA or THA between January 4, 2021 and August 30, 2021, in whom Prontosan® Wound Irrigation Solution (B. Braun Medical Inc./ Innovice LLC), containing 0.1% Betaine, a surfactant, and 0.1% Polyhexanide (PHMB) was added to the intra-operative procedure, were evaluated for its impact on the incidence of PJI. The CDC's Surgical Care Improvement Project, (SCIP) guidelines are standard of care and followed with each surgical procedure. The CDC recommends using antimicrobial prophylaxis at a time before skin incision such that the antibiotic concentration reaches the minimum bactericidal concentration at the time of skin incision, Berríos-Torres SI, et al. All data were prospectively submitted to the American Joint Replacement Registry (AJRR) was retrospectively analyzed to measure the incidence of postoperative infection.

Results

Primary TJA was performed on 308 patients; of these 10 patients were bilateral TKA (205 TKA procedures and 113 THA procedures). The use of Prontosan® Wound Irrigation Solution was associated with zero (0%) incidence of postoperative infection in this population of patients during a 90-day episode of care, nor at any time postoperatively. CMS defines total joint arthroplasty codes as a major surgery, and encounters or procedures within 90 days of the initiating procedure are included in the 90-day episode of care. No patients were lost to follow-up.

Conclusion

There was no incidence of PJI uncovered in this retrospective analysis. Adding Prontosan® Wound Irrigation Solution to the intra-operative protocol, contributed to the absence of PJI in this population and potentially avoided 1.74 female and 1.34 male TKA as well as .95 female and .75 THA resulting in total hospital-avoided costs of \$83,824 and \$56,126, respectively totaling \$139,950.

INTRODUCTION

The incidence of prosthetic joint infection (PJI) remains problematic, with studies estimating that approximately 1-2% of total joint arthroplasty (TJA) patients develop this devastating complication (Premkumar et al. 2021). These infections can have severe consequences for a patient with significant morbidity of treatment and high mortality rates. It has been shown that PJI may be associated with a 5-year mortality rate that is higher than breast cancer, melanoma,

and Hodgkin's lymphoma (Kurtz et al. 2018). PJIs are also associated with costly, resource-intensive interventions that place a significant burden on both patients and the US healthcare system. In a recent sample analysis by Premkumar et al. (2021), 238,133 total knee arthroplasty (TKA) and 127,191 total hip arthroplasty (THA) inpatients were treated for PJIs in the US between January 1, 2002, and December 31, 2017. The mean average inpatient cost to treat these TKA and THA infections was reported to be \$27,158 and \$33,285, respectively. While the average cost to treat

individual TKA and THA PJI patients remained relatively stable during the 16-year study period, the total cost to treat TKA and THA PJIs nationally more than doubled from \$372 million in 2002 to \$902 million in 2017 due to the increasing volume of TJAs. Using Poisson regression models, the authors projected that total TKA/THA annual PJI volumes would reach 40,096 cases by 2030. Further, they estimated that the combined hospital inpatient PJI treatment costs associated with these procedures would be \$1.85 billion by 2030 unless efficacious preventative strategies for reducing rates of PJI after TKA and THA were adopted.

Multidrug antimicrobial resistance of nosocomial pathogens such as *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* is increasing in hospital settings (Bashyal et al. 2022; Berríos-Torres et al. 2017; Machuca et al. 2019). In addition, biofilms can adhere to orthopedic implants which form a protective barrier that can increase pathogen antimicrobial resistance 1,000-fold (Bashyal et al. 2022). Further, there is evidence that the most likely time for seeding of a wound is intraoperatively, with the risk of wound contamination increasing as the duration of the procedure increases. Reducing the colony forming units (CFU) of bacteria present in the wound both during and at the conclusion of the procedure is an important strategy to interrupt the progression of a contaminated wound to a frank PJI. Subsequently, interest in using adjuvant intra-operative wound irrigation (IOWI) solutions has increased in orthopedic surgery, and there is evidence that this strategy can decrease the risk of PJI after TKA and THA. An ideal IOWI for orthopedic surgery would have several characteristics. It would eradicate planktonic bacteria and the biofilm they produce (Bashyal et al. 2022), have a rapid onset of action, be effective in decreasing CFUs across a broad spectrum of bacterial species, have a low side effect profile and be non-toxic to human tissue (Kramer et al. 2019).

A novel intra-operative wound irrigation solution, Prontosan® Wound Irrigation Solution (B. Braun Medical Inc. / Innovive LLC), containing 0.1% Betaine, and 0.1% Polyhexanide (PHMB) meets the criteria for an ideal IOWI. Betaine is a mild amphoteric alkaloid surfactant that has a lower surface tension than water. The resulting low surface tension supports the physical removal of debris and bacteria (Andriessen and Eberlein 2008). Betaine also interferes with the production of homoserine lactone, a signaling molecule used in the cell-to-cell communication of biofilms (known as quorum sensing), which play a role in biofilm pathogenicity (Pinzon-Gamez 2009). PHMB is an antimicrobial with broad-spectrum activity against bacteria, fungi, yeasts, and viruses with a high therapeutic index (Chindera et al. 2016). The positively charged molecule binds to bacterial cell membranes and induces cell lysis by destroying membrane integrity. Additionally, PHMB can enter bacterial cells, arrest cell division and condense chromosomes, resulting in intracellular foci of DNA (Chindera et al. 2016). Because the surfactant/antimicrobial solution is comprised of non-cytotoxic ingredients, it does not need to be rinsed out of the wound and can be expected to con-

tinue to inhibit SSIs beyond the procedure itself (Kramer et al. 2019).

The purpose of this study was to evaluate whether the addition of Prontosan® Wound Irrigation Solution to the existing intra-operative protocol would further reduce the incidence of periprosthetic joint infection (PJI) in high-risk patients undergoing primary TKA and THA in a high-volume joint replacement practice. An international group of arthroplasty surgeons completed a survey consisting of 20 single and multiple response questions focused on PJI prevention strategies at three perioperative periods: preoperatively, intraoperatively, and postoperatively. Francesco Indelli, et al used the responses to develop recommendations for PJI prevention. The recommendations were used to update the practice's preoperative optimization protocol for risk stratifying patients according to modifiable and non-modifiable risk factors. Data from the American Joint Replacement Registry (AJRR) was used to retrospectively analyze the incidence of post-operative infection (PJI), between January 4, 2021 and August 30, 2021.

MATERIALS AND METHODS

A consecutive cohort of high-risk joint replacement patients was evaluated for this study. The existing intra-operative protocol was supplemented with the addition of a 1,000 mL solution, Prontosan® Wound Irrigation Solution (B. Braun Medical Inc./Innovive LLC) for both primary cementless and cemented TJA ([Table 1](#)). High-risk patients were defined as those patients who had one or more risk factors associated with postoperative infection risk, including BMI >35, diabetes mellitus, tobacco use, history of ETOH abuse, autoimmune disease, active cancer, history of MRSA/+ preoperative MRSA nasal swab, history of surgical site infection, hepatitis, anemia, HIV and chronic kidney disease. Practice antibiotic prophylaxis, Ancef for most unless the patient reports anaphylactic to penicillin. If severe penicillin allergy, alternative is clindamycin. Vancomycin is added to Ancef IV, if the patient swabs positive for MRSA during pre-op testing. The addition of Prontosan did not increase the OR time, as the irrigation solution was changed, however the overall surgical procedure process was not. All procedures were performed by a single surgeon at a single hospital in South Central United States, with the same surgical team and existing care protocols.

RESULTS

There were 308 patients included in this study who had primary total joint replacement, with 10 patients having bilateral total knees for a total of 318 primary TJR, with 205 TKA procedures and 113 THA procedures. ([Table 2](#)). There were more women than men for the total primary procedures (64.5%) cohorts. All patients who were included were found to have at least one risk factor known to predispose to the development of a PJI, with a wide array of comorbidity conditions. The most common comorbidity conditions were cardiovascular disease, diabetes, obesity, and autoimmune disorders. Further, we found that 15.5% TKA/3.2 %



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Table 1. IOWI Protocol for Primary Cementless and Cemented Total Joint Arthroplasty

Cementless	Cemented
1. Prepare 1 L of Prontosan® 2. Irrigate all bony and soft tissue surfaces with approximately 250 mL of Prontosan, soak 3 minutes with a mechanical scrub 3. Irrigate with 3 L of sterile saline to remove wound debris (i.e. bone fragments) 4. Place final implants 5. Final irrigation is with remaining Prontosan with a 3-minute soak and mechanical scrub – leave remaining Prontosan in the wound (Do not rinse) 6. Close surgical wound	1. Prepare 1 L of Prontosan 2. Irrigate all bony and soft tissue surfaces with approximately 250 mL of Prontosan (Do not rinse) 3. Irrigate with 3 L of sterile saline to remove wound debris (i.e. bone fragments) 4. Dry all bony and soft tissue surfaces with a dry surgical sponge 5. Cement the final components in the usual fashion and allow cement to set up 6. Once the cement has dried, perform a final irrigation with the remaining Prontosan with a 3-minute soak and mechanical scrub – leave remaining Prontosan in the wound (Do not rinse) 7. Close surgical wound

Table 2. Patient demographics and clinical characteristic (n = 318 procedures)

Primary TJA procedures n = 318	TKA n (%) 205 (64.5%)	THA n (%) 113 (35.5%)
Female	116 (56.6%)	63 (55.8%)
Male	89 (43.4%)	50 (44.2%)

Primary TJA was performed on 308 patients. Of these, 10 patients were bilateral TKA (205 TKA procedures and 113 THA procedures).

THA of the female patient population and 18.6% TKA/10% THA of the male patient population had three comorbidities considered high risk (Table 3). No patients developed a PJI. This patient population has a minimum length of follow up of 18 months with no one in this group developing a PJI to date.

DISCUSSION

In this study, we investigated the impact of adding a commercially available wound irrigation solution to the intra-operative total joint replacement protocol on the incidence of PJI in a high-risk population. Our findings of a complete absence of PJI in this cohort were encouraging and serve as preliminary evidence of the potential impact of this approach. If the findings of this initial high-risk cohort hold true for additional patients, and at additional centers, this would have the potential to significantly impact the incidence of PJI following total joint replacement.

From 2014 to 2030, the number of total hip arthroplasty and total knee arthroplasty procedures is projected to double to 2 million cases per year in the United States. Despite this demand, and the improvement in surgical techniques

that enable improved outcomes and rapid recovery, surgical site infection remains an unsolved problem, with the incidence of 1-2% largely unchanged over the past decade. It continues to represent one of the most common surgical complications in the US healthcare system for all surgical specialties, and among the most devastating for patients. In addition to the toll on patients' health, this complication presents an overwhelming cost burden to the US healthcare system. These cases result in a significant increase in readmission rate, ICU admission, mortality and morbidity with per case costs exceeding \$20,000 and likely, in many cases, 2-3 times that amount. The cost of treating acute periprosthetic joint infections (PJI), after primary joint replacement in the United States is projected to exceed \$1.85 billion by 2030.

Another significant concern for the US healthcare system is the emergence and rapid proliferation of multidrug-resistant organisms (MDROs). Antibiotic stewardship can help slow the spread of these superbugs and is an essential part of the practice of surgical medicine. There is increasing awareness that the development of methods to prevent and control infections that do not rely on antibiotics will become increasingly important.

The continued concern over the rate of PJI, along with the search for new methods to prevent them has brought about a resurgence of interest in intra-operative wound irrigation (IOWI) solutions over the past several years. Evidence is emerging on the importance of continuous and terminal wound decontamination as part of a surgical protocol and a number of potential agents have emerged to address this need. However, there does not seem to be a consensus as to the best IOWI solutions to use nor the protocols for their use. While some surgeons have adopted an approach that involves multiple agents, there has been recent concern that combining these IOWI solutions in the

Table 3. Patient High Risk Profile

	Female		Male	
	TKA n = 116 (56.6%)	THA n = 63 (55.8%)	TKA n = 86 (43.4%)	THA n = 50 (44.2%)
BMI>35	37 (31.9%)	16 (25.3%)	40 (46.5%)	17 (34%)
Diabetes Mellitus	62 (53.4%)	18 (28.6%)	54 (62.3%)	21 (42%)
Nicotine	6 (5.2%)	6 (9.5)	15 (17.4%)	6 (12%)
ETOH	1 (.09%)	8 (12.7%)	1 (1.2%)	11 (22%)
Autoimmune Deficiency	43 (37.1%)	20 (31.7%)	11 (12.8%)	7 (14%)
MRSA	0	0	0	0
SSI	1 (.09%)	0	0	0
Hepatitis	2 (1.7%)	2 (3.2%)	3 (3.5%)	2 (4%)
Anemia	2 (1.7%)	2 (3.2%)	1 (1.2%)	0
HIV	0	0	1 (1.2%)	0
CKD	2 (1.7%)	2 (3.2%)	4 (4.7%)	4 (8%)
CV Disease	66 (56.9%)	20 (31.7)	68 (79.1%)	31 (62%)
Obesity	41 (35.3%)	24 (38.1%)	44 (51.2%)	17 (34%)
DM CV Obesity	18 (15.5%)	2 (3.2%)	16 (18.6%)	5 (10%)

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wrong order can lead to deleterious and unforeseen consequences if done incorrectly.

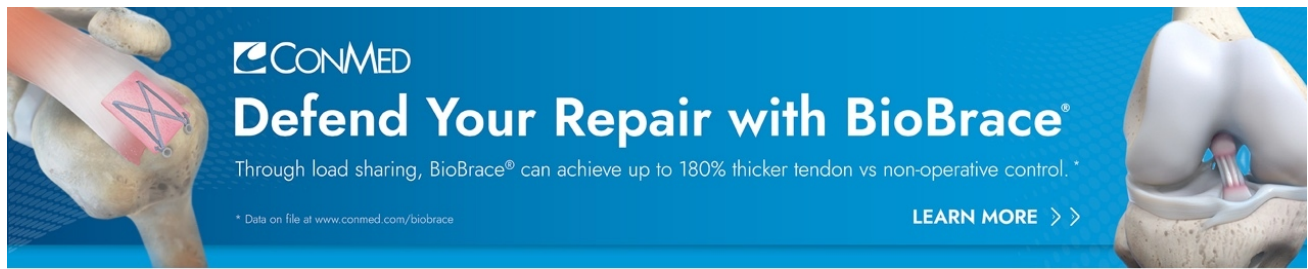
There is emerging consensus in the literature regarding the essential attributes that an effective intra-operative wound irrigation should exhibit.

- It must be able to effectively reduce the number of CFUs (both planktonic and biofilm sources) in the wound and on orthopedic implant material surfaces at a rapid pace.
- It must inhibit regrowth of bacteria for a sustained period
- It should be unaffected by the environment of its use (presence of blood, proteins, bioburden etc.)
- It must be effective against existing biofilms
- It should be safe for host tissue and not pose a risk of delayed wound healing
- It must not be susceptible to bacterial resistance
- It must not damage surgical implants (bone cement, cobalt chrome, titanium, polyethylene)

In this study, we chose to study a recently introduced wound irrigation solution that we felt exhibited all these characteristics. Prontosan® Wound Irrigation Solution,

contains two ingredients which are both known to be highly effective against a wide array of microorganisms without any known resistance. As it contains a surfactant (Betaine) as well as an antiseptic (PHMB), it is effective against both planktonic and biofilm resident organisms. Further, from a practical standpoint, for a busy surgical practice, it is ready to be used immediately out of either a sterile handheld bottle or a pulse lavage setup as was used in this study. Importantly, because of its well documented safety profile, has no requirement to be rinsed out of the wound, and so, the solution can be utilized routinely during the procedure and prior to closure. It also has broad-spectrum coverage against gram-negative and gram-positive bacteria. The solution is noted to be highly efficacious in a short period of time, even in the face of high loads of blood albumin. Prontosan noticeably improves wound healing and is non-toxic to viable cells.

After gaining experience with Prontosan, and the protocol that was developed for IOWI, we believe this early evidence suggests that this approach may contribute to improved outcomes for patients. This protocol gives the surgeon the ability to implement infection control mea-



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tures for the duration of the surgical procedure without the limitation of short dwell times required of other antiseptic solutions.

LIMITATIONS

This study represents the initial work and evaluation of this product in a specific patient population and in one center and one surgeon's practice, and like any study of this type, extrapolating the findings more broadly will require additional data from other surgeons and centers. As such, our results may not be generalizable to other surgical populations, or practices that do not adhere to the same risk stratification and surgical protocols of the study surgeon. In addition, further follow-up of this cohort is ongoing, and while no infections have emerged in the intermediate follow-up of this group, it is possible that further study will reveal different findings. Nonetheless, the striking findings of the absence of wound infection in this notoriously problematic group of patients compelled us to submit these findings for early review at this time. In addition, we felt it might be of use to other surgeons to publish our protocols on use of this product as they consider which irrigation solution best fits their practice and how best to apply it.

CONCLUSION

Periprosthetic joint infection (PJI) remains a vexing problem for total joint replacement surgeons and their patients. New methods are needed to reduce the incidence and may include important advances in wound antisepsis through intraoperative irrigation aimed at reducing or eliminating wound contamination. The selection of a proper wound irrigation solution is emerging as an important consideration for surgeons, and the literature, safety and efficacy is just being developed. In this study, we present compelling evidence on this promising multi-ingredient solution that in a high-risk cohort of patients undergoing total joint arthroplasty, eliminated the incidence of PJI. While this data is compelling and promising, further study is required to validate these outcomes to demonstrate the benefit of Pron-tosan on additional patient populations. Should these outcomes hold up in under further study, the potential benefit for patients is substantial.

Submitted: December 27, 2022 EDT, Accepted: March 05, 2023 EDT



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