IVYSPRING INTERNATIONAL PUBLISHER

Journal of Bone and Joint Infection

2017; 2(1): 10-14. doi: 10.7150/jbji.16448

Review

Treatment of Periprosthetic Joint Infection Using Antimicrobials: Dilute Povidone-Iodine Lavage

John A. Ruder[1], Bryan D. Springer[2]✉

1. Carolinas Medical Center, Department of Orthopaedics;
2. OrthoCarolina Hip and Knee Center, Charlotte, NC 28207.

✉ Corresponding author: Bryan D. Springer, bryan.springer@orthocarolina.com

Published: 2017.01.01

Abstract

Periprosthetic joint infections (PJI) remain a challenge for the orthopaedic surgeon to treat and remain a leading cause of failure of both primary and revision total joint arthroplasty. Once a PJI develops, surgical treatment is generally indicated and includes an aggressive irrigation and debridement. One component of the irrigation and debridement involves the use of an antiseptic irrigating solution. In primary and revision TJA, dilute povidone-iodine lavage can be performed prior to wound closure. Approximately 17.5mL of 10% povidone-iodine is diluted with 500-1000cc of normal saline. The wound is then irrigated with the dilute povidone-iodine for 3 minutes. The dilute povidone-iodine is then thoroughly irrigated and washed out of the wound with normal saline prior to wound closure. The use of dilute povidone-iodine lavage prior to wound closure has been shown to reduce the risk of deep surgical site infection in multiple surgical specialties. In primary TJA, it has been demonstrated to reduce the risk of infection, without any associated adverse effects. It is also included in multiple protocols for the surgical treatment of PJI. Dilute povidone-iodine lavage provides a safe and inexpensive method to reduce the rate of PJI in TJA.

Key words: Periprosthetic joint infections, antimicrobials

1. Introduction

Periprosthetic joint infections (PJIs) remain a challenge for orthopaedic surgeons to treat, and remain a leading cause of failure of both primary and revision total joint arthroplasty (TJA). [1] With a reported incidence of 0.5%-7.0%, PJI is associated with a high morbidity and a mortality rate ranging from 2.7%-18.0%.[1,2] Infection is devastating to the patient physically and financially.[3] The treatment of PJI can cost up to five times that of a primary TJA.[4] This is not only a financial strain on the patient, but also on the health-care system as a whole.[5] As the number of TJAs being performed has increased, the incidence of infections has also doubled between 1990 and 2004.[6] By 2030, the number of primary total knee arthroplasties (TKA) and total hip arthroplasties (THA) is projected to increase by 673% and 174%, respectively.[1] Even if the incidence of PJI remains the same, we will be faced with an increasing number of patients with PJI.

Because of the significant impact on the patient and the health-care system, there is continuous research aimed at identifying at-risk patients and methods to prevent PJIs.[7] These are often aimed at reducing the burden of and exposure to the most common causative organisms, including methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), and coagulase-negative *Staphylococci*.[8] Preventative measures are generally categorized as preoperative, intraoperative, or postoperative.[9] Preoperative preventative measures include the use of perioperative antibiotics, nutritionally optimizing the patient, and managing blood glucose levels in diabetic patients. Intraoperative measures include adequate

skin preparation before surgical incision, shorter surgical time, frequent glove changes, antibiotic-impregnated cement, and antiseptic irrigation prior to closure. Postoperative preventative measures include continuing antibiotics no more than 24 hours after surgery, and minimizing allogenic blood transfusions.

Once a PJI develops, surgical treatment is generally indicated and includes an aggressive irrigation and debridement.[10] One component of the irrigation and debridement involves the use of an antiseptic irrigating solution. This article will focus on the intraoperative use of antiseptic irrigation in TJA. Specifically, it will focus on the use of a dilute povidone-iodine lavage.

2. The rationale for antimicrobial irrigation in total joint arthroplasty

Bacterial contamination of the wound during surgery is a leading cause of PJI.[11] Because of this, multiple interventions have been directed at reducing bacterial contamination of the wound while in the operating room.[12,13] Despite these efforts, it is impossible to completely eliminate the risk of wound contamination. Therefore, efforts are made to sterilize the wound prior to closure. One such technique is the use of various irrigation solutions prior to wound closure.

Identifying the optimal agent to use for irrigation remains challenging. Irrigating solutions can contain antiseptics, antibiotics, or surfactants.[14] Irrigating solutions that contain antibiotics have frequently been used, but their efficacy has not been proven and they can potentially promote antibiotic resistance.[15] Antiseptic solutions negate this risk because they are not susceptible to antibiotic resistance.[16] However, they are cytotoxic, which can damage local tissue and lead to wound complications.[17] Commonly used antiseptic solutions include chlorhexidine digluconate, hydrogen peroxide, sodium hypochlorite (Dakin's solution), and povidone-iodine (Betadine).[18]

The ideal antiseptic solution has minimal cytotoxicity at its minimal bactericidal concentration (MBC), which is defined as the concentration required to diminish the bacterial load by 99.9%.[18] In general, the concentration of the active component in these solutions can be adjusted to minimize cytotoxicity, but maintaining its bactericidal activity. Povidone-iodine is commercially available at 100 g/L (10%), which is both bactericidal and cytotoxic.[18] Different concentrations of povidone-iodine have been tested against various organisms to determine their bactericidal activity, and to determine if they permit cell viability.[16,19] In a study where human cells were exposed to both *S. aureus* and *S. epidermidis*, povidone-iodine demonstrated a steep dose-response curve.[18] Of the antiseptics tested, only povidone-iodine permitted cell viability at its MBC, which was 1.32 g/L (1.32%).

3. Basic science of Povidone-iodine

Povidone-iodine is an antiseptic solution consisting of polyvinylpyrrolidone and 1% available iodine.[16] Iodine has great bactericidal activity but has very low solubility in aqueous environments.[19] To combat this, it is conjugated to polyvinylpyrrolidone, which is hydrophilic and able to deliver free iodine directly to the cell surface.[20,21]

Once iodine reaches the cell surface, it is able to enter the cell and oxidize various components of the cytoplasmic membrane and molecules in the cytoplasm.[19] This results in their inactivation. [22] Therefore, the cytotoxicity of povidone-iodine is proportional to its iodine concentration delivered to the cell wall.[23]

4. Historical use of dilute povidone-iodine in surgery

Povidone-iodine has been shown in multiple surgical specialties to reduce the rate of surgical site infection when used as an irrigation solution, including orthopaedic, urologic, cardiovascular, and general surgery.[24] One of the earliest studies to look at the use of povidone-iodine as an irrigation solution was in 1977 and evaluated 500 patients undergoing abdominal, gastrointestinal, and genitourinary procedures.[25] Patients either had their subcutaneous tissue irrigated with 10% povidone-iodine or normal saline for 60 seconds. The infection rate for patients who received povidone-iodine had an infection rate of 2.9%, and those who receive normal saline had an infection rate of 15.1%.

More recently, there have been two randomized controlled trials in the orthopaedic literature highlighting the benefits of povidone-iodine irrigation during spinal surgery.[26,27] In a series of 414 patients undergoing spinal decompression, discectomy, pedicle screw fixation, or tumor resection, povidone-iodine lavage was found to reduce the incidence of postoperative infection.[26] Patients were randomized to either have their surgical wound soaked with 3.5% povidone-iodine for 3 minutes or normal saline prior to closure. There was no difference in the superficial infection rate between the groups; however, the deep infection rate in the povidone-iodine group was significantly lower than those who were only irrigated with normal saline.

In an additional study of 244 patients undergoing lumbosacral posterolateral fusion, the safety and efficacy of a 3 minute, dilute

povidone-iodine lavage was demonstrated.[27] The infection rate was again shown to be significantly lower when the surgical wound was irrigated with 3.5% povidone-iodine prior to closure than with normal saline. There were no deep infections (0.0%) in patients who received the povidone-iodine lavage and 6 deep infections (4.8%) in patients only irrigated with normal saline. There was no difference in wound complication or rate of bony union between the two groups.

5. Results of dilute povidone-iodine in TJA

Dilute povidone-iodine lavage is frequently used during both primary and revision TJA cases.[28,29] Because of the difficulty in isolating a single variable and the overall low incidence of PJIs, there have been no randomized controlled trials evaluating its efficacy in the treatment of PJIs. Most of the evidence supporting its use in the surgical management of PJIs is derived from animal and basic science studies, and primary TJA literature.[18,28,30]

For the treatment of acute PJIs, a rabbit knee infection model was used to determine if irrigation and debridement with component retention using a dilute povidone-iodine lavage could successfully be completed.[30] A stainless steel screw and polyethylene washer were placed into the lateral femoral condyle and inoculated with MSSA. Seven days after the initial procedure, half of the animals underwent a 90 second lavage with 3.5% povidone-iodine, and half of the animals were irrigated with normal saline. Povidone-iodine lavage was shown to significantly reduce the bacterial burden on both the screw and polyethylene washer.

The use of dilute povidone-iodine lavage in primary TJA is supported by a single study.[28] The study evaluated 2,250 consecutive primary THAs and TKAs to determine the efficacy of a dilute povidone-iodine lavage at reducing the incidence of PJIs.[28] Patients either had their wound irrigated with normal saline alone or had a dilute povidone-iodine soak prior to closure. The 0.35% povidone-iodine solution was allowed to soak in the wound for 3 minutes, and then the wound was irrigated with 1 L of normal saline using pulsatile lavage. The addition of the dilute povidone-iodine lavage to the surgical procedure resulted in a significant reduction in the postoperative infection rate, dropping from 0.97% to 0.15%. There were no reported complications from the use of dilute povidone-iodine lavage and the authors deemed it a safe and inexpensive method to reduce the rate of PJIs.

Multiple institutions have now included the dilute povidone-iodine lavage as part of a comprehensive approach to reduce the rate of PJI following primary and revision TJA.[29,31] A seven-item checklist was created aimed at reducing the incidence of PJI. Dilute povidone-iodine lavage was one of three intraoperative measures on the checklist.[32] Dilute povidone-iodine lavage has also been described in multiple studies as part a comprehensive approach to the treatment of PJIs.[10,29] It has been utilized for the treatment of acute infections treated with irrigation and debridement and exchange of modular components.[33] It has also become part of multiple treatment protocols for the treatment of chronic infections undergoing either single or two-stage component exchange.[10]

Critics of dilute povidone-iodine lavage raise concerns over the possible negative effects on the bone-cement interface and deleterious effects on articular cartilage.[34,35] In a cadaveric animal model, different irrigation solutions were evaluated on their ability to cleanse bone prior to cement application.[34] They found superior cement fixation following hydrogen peroxide irrigation compared to povidone-iodine and normal saline solution. This highlights a potential benefit of hydrogen peroxide, not necessarily a deleterious effect of povidone-iodine. Also, clinically, the dilute povidone-iodine lavage is performed following implant insertion and therefore should not affect the bone-cement interface. However, if performing single-stage revision, this should be considered. An additional cadaveric animal model evaluated the effect of dilute povidone-iodine lavage on articular cartilage.[35] The 3.5% concentration was found to be chondrotoxic to the superficial cartilage layer when used for longer than one minute. This is certainly an effect that should be considered during articular cartilage retaining procedures, such as unicompartmental knee arthroplasty. However, this deleterious effect is negated during TJA where articular cartilage is not retained.

6. Algorithm and Surgical technique for use of dilute povidone-iodine lavage in the operating room

In primary and revision TJA, dilute povidone-iodine lavage can be performed prior to wound closure. Approximately 17.5mL of 10% povidone-iodine is diluted with 500-1000cc of normal saline. The wound is then irrigated with the dilute povidone-iodine for 3 minutes. The dilute povidone-iodine is then thoroughly irrigated and washed out of the wound with normal saline prior to wound closure.

In the setting of PJI, the same formulation of dilute povidone-iodine lavage is utilized as during

primary TJA. When irrigation, debridement and polyethylene exchange is performed, the authors prefer to use dilute povidone-iodine lavage following aggressive debridement and allow the povidone-iodine to soak against the retained components for 3 minutes prior to irrigating with normal saline. When performing a resection arthroplasty and placement of antibiotic spacer, the authors prefer to soak the wound with dilute povidone-iodine following removal of the components and aggressive debridement and prior to insertion of the antibiotic spacer.

7. Contraindications/concerns about using povidone-iodine

There are no studies directly evaluating the safety of dilute povidone-iodine lavage in TJA patients with iodine allergies. Although the preparation used in TJA contains a low concentration of free iodine, when an allergic reaction does occur, it can be severe.[36] The incidence of reported allergic reactions to iodine containing antiseptics is low.[37] Only two allergic reactions were reported in 5000 patients when polyvinylpyrrolidone-iodine was applied locally on intact skin or mucosa.[37] In 500 patients with known allergies to iodine-containing compounds, including fish, only two allergic reactions occurred.[38] While the risk is low, topical use of povidone-iodine has been shown to cause contact dermatitis, iododerma, and anaphylactic shock in multiple surgical specialties.[36,39] For this reason, the authors do not recommend the use of povidone-iodine in patients with a reported allergy to iodine.

A second commonly encountered clinical scenario is the concurrent use of povidone-iodine and liposomal bupivacaine. Povidone-iodine will cause rupture of the liposome containing bupivacaine, releasing the free bupivacaine from its liposome and negating the slow release. It is recommended that if an orthopaedic surgeon uses liposomal bupivacaine with povidone-iodine, the povidone-iodine should be used first, followed by thorough lavaging with normal saline, followed by application of the liposomal bupivacaine to keep the liposomes intact.[40]

8. Conclusions

The use of dilute povidone-iodine lavage prior to wound closure has been shown to reduce the risk of deep surgical site infection in multiple surgical specialties. In primary TJA, it has been demonstrated to reduce the risk of infection, without any associated adverse effects. It is also included in multiple protocols for the surgical treatment of PJI. Dilute povidone-iodine lavage provides a safe and inexpensive method to reduce the rate of PJI in TJA.

Competing Interests

The authors have declared that no competing interest exists.

References

1. Bozic KJ, Kurtz SM, Lau E, et al. The epidemiology of revision total knee arthroplasty in the United States. *Clin Orthop Relat Res.* 2010;468(1):45-51.
2. Illingworth KD, Mihalko WM, Parvizi J, et al. How to minimize infection and thereby maximize patient outcomes in total joint arthroplasty: a multicenter approach: AAOS exhibit selection. *J Bone Joint Surg Am.* 2013;95(8):e50.
3. Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. *Clin Orthop Relat Res.* 2010;468(1):52-56.
4. Waddell BS, Briski DC, Meyer MS, Ochsner JL, Jr., Chimento GF. Financial Analysis of Treating Periprosthetic Joint Infections at a Tertiary Referral Center. *J Arthroplasty.* 2016;31(5):952-956.
5. Matar WY, Jafari SM, Restrepo C, Austin M, Purtill JJ, Parvizi J. Preventing infection in total joint arthroplasty. *J Bone Joint Surg Am.* 2010;92 Suppl 2:36-46.
6. Kurtz SM, Ong KL, Schmier J, Zhao K, Mowat F, Lau E. Primary and revision arthroplasty surgery caseloads in the United States from 1990 to 2004. *J Arthroplasty.* 2009;24(2):195-203.
7. Fletcher N, Sofianos D, Berkes MB, Obremskey WT. Prevention of perioperative infection. *J Bone Joint Surg Am.* 2007;89(7):1605-1618.
8. Berrios-Torres SI, Yi SH, Bratzler DW, et al. Activity of commonly used antimicrobial prophylaxis regimens against pathogens causing coronary artery bypass graft and arthroplasty surgical site infections in the United States, 2006-2009. *Infect Control Hosp Epidemiol.* 2014;35(3):231-239.
9. Daines BK, Dennis DA, Amann S. Infection prevention in total knee arthroplasty. *J Am Acad Orthop Surg.* 2015;23(6):356-364.
10. Haddad FS, Sukeik M, Alazzawi S. Is single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? *Clin Orthop Relat Res.* 2015;473(1):8-14.
11. Charnley J. Postoperative infection after total hip replacement with special reference to air contamination in the operating room. *Clin Orthop Relat Res.* 1972;87:167-187.
12. Moyad TF, Thornhill T, Estok D. Evaluation and management of the infected total hip and knee. *Orthopedics.* 2008;31(6):581-588; quiz 589-590.
13. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med.* 2004;351(16):1645-1654.
14. Anglen JO, Apostoles S, Christensen G, Gainor B. The efficacy of various irrigation solutions in removing slime-producing Staphylococcus. *J Orthop Trauma.* 1994;8(5):390-396.
15. Harkaway KS, McGinley KJ, Foglia AN, et al. Antibiotic resistance patterns in coagulase-negative staphylococci after treatment with topical erythromycin, benzoyl peroxide, and combination therapy. *Br J Dermatol.* 1992;126(6):586-590.
16. Zamora JL. Chemical and microbiologic characteristics and toxicity of povidone-iodine solutions. *Am J Surg.* 1986;151(3):400-406.
17. Russell AD. Introduction of biocides into clinical practice and the impact on antibiotic-resistant bacteria. *J Appl Microbiol.* 2002;92 Suppl:121S-135S.
18. van Meurs SJ, Gawlitta D, Heemstra KA, Poolman RW, Vogely HC, Kruyt MC. Selection of an optimal antiseptic solution for intraoperative irrigation: an in vitro study. *J Bone Joint Surg Am.* 2014;96(4):285-291.
19. Rodeheaver G, Bellamy W, Kody M, et al. Bactericidal activity and toxicity of iodine-containing solutions in wounds. *Arch Surg.* 1982;117(2):181-186.
20. Gershenfeld L, Flagg WB, Witlin B. Iodine as a tuberculocidal agent. *Mil Surg.* 1954;114(3):172-183.
21. Oduwole KO, Glynn AA, Molony DC, et al. Anti-biofilm activity of sub-inhibitory povidone-iodine concentrations against Staphylococcus epidermidis and Staphylococcus aureus. *J Orthop Res.* 2010;28(9):1252-1256.
22. Alexander NM. Reaction of povidone-iodine with amino acids and other important biological compounds. In: Degenes G, ed. Proceedings of the Internations Symposium on Povidone. Lexington, KY: University of Kentucky. 1983:274-288.
23. Rutherford JM. Reaction of povidone-iodine with amino acids and other important biological compounds. In: Degenes G, ed. Proceedings of the Internations Symposium on Povidone. Lexington, KY: University of Kentucky. 1983:217-221.
24. Chundamala J, Wright JG. The efficacy and risks of using povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. *Can J Surg.* 2007;50(6):473-481.
25. Sindelar WF, Mason GR. Efficacy of povidone-iodine irrigation in prevention of surgical wound infections. *Surg Forum.* 1977;28:48-51.
26. Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine (Phila Pa 1976).* 2005;30(15):1689-1693.

27. Chang FY, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? *Eur Spine J.* 2006;15(6):1005-1014.
28. Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty.* 2012;27(1):27-30.
29. Jiranek WA, Waligora AC, Hess SR, Golladay GL. Surgical Treatment of Prosthetic Joint Infections of the Hip and Knee: Changing Paradigms? *J Arthroplasty.* 2015;30(6):912-918.
30. Gilotra M, Nguyen T, Jaffe D, Sterling R. Dilute betadine lavage reduces implant-related bacterial burden in a rabbit knee prosthetic infection model. *Am J Orthop (Belle Mead NJ).* 2015;44(2):E38-41.
31. Matsen Ko LJ, Yoo JY, Maltenfort M, Hughes A, Smith EB, Sharkey PF. The Effect of Implementing a Multimodal Approach on the Rates of Periprosthetic Joint Infection After Total Joint Arthroplasty. *J Arthroplasty.* 2016;31(2):451-455.
32. Heller S, Rezapoor M, Parvizi J. Minimising the risk of infection: a peri-operative checklist. *Bone Joint J.* 2016;98B(1 Suppl A):18-22.
33. Sukeik M, Patel S, Haddad FS. Aggressive early debridement for treatment of acutely infected cemented total hip arthroplasty. *Clin Orthop Relat Res.* 2012;470(11):3164-3170.
34. Howells RJ, Salmon JM, McCullough KG. The effect of irrigating solutions on the strength of the cement-bone interface. *Aust N Z J Surg.* 1992;62(3):215-218.
35. von Keudell A, Canseco JA, Gomoll AH. Deleterious Effects of Diluted Povidone–Iodine on Articular Cartilage. *The Journal of arthroplasty.* 2013;28(6):918-921.
36. Rahimi S, Lazarou G. Late-onset allergic reaction to povidone-iodine resulting in vulvar edema and urinary retention. *Obstet Gynecol.* 2010;116 Suppl 2:562-564.
37. Bogash RC. A three year observation of a new topical germicide. *Bull Am J Hosp Pharm.* 1956;42:201-204.
38. Dungeman H, Rakoski J. Iodine allergy, facts and phantoms. Proceedings of the World Congress on Antisepsis. Lund, Germany: Mundipharma Gmbh Limburg. 1978:21-23.
39. Adachi A, Fukunaga A, Hayashi K, Kunisada M, Horikawa T. Anaphylaxis to polyvinylpyrrolidone after vaginal application of povidone-iodine. *Contact Dermatitis.* 2003;48(3):133-136.
40. Pacira Pharmaceuticals Inc. Exparel (bupivacaine liposome extended-release injectable suspenssion [prescribing information]. San Diego, CA: Pacira Pharmaceuticals Inc. 2011.