Can We Approach a Zero Percent Infection Rate In Total Knee Arthroplasty? A Program To Achieve This Goal With Antimicrobial Agents

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ABSTRACT

Periprosthetic joint infections (PJIs) are one of the most feared complications in the realm of adult reconstruction due to the substantial morbidity and mortality associated with these cases. Advancements in arthroplasty have been made across a variety of areas of interest including implant surfaces, implant design, material science, etc., but a focus on infection prevention and treatment is of utmost importance. A new technology has been created that targets biofilm and aims to prevent infection in total joint arthroplasty. In this manuscript we aim to describe the benefits of this technology and describe the ideal use in a case scenario format. We believe that with this technology that we can approach the goal of a zero periprosthetic infection rate.

INTRODUCTION

The overall effect of periprosthetic joint infections (PJIs) on the healthcare system, including patients, surgeons, and their economic burden/cost, is enormous, and this continues to be the most common reason for revision after failed total knee arthroplasty.[1,2] Current incidences of PJIs are approximately 0.74 and 1.38%, at one and five years, respectively.[3] PJI has been shown to severely effect mortality rates with a recent meta-analysis finding a one-year mortality rate of 4.33% after total knee arthroplasty (TKA) PJI with an increase of 3.13% per year thereafter ($r=0.76$ [0.46, 0.90] $p<0.001$). Five-year mortality in this study was 21.64%.[4] This is similar to morality rates after various common cancers. Another study found that approximately 7% of patients died between the first and second stages of exchange arthroplasty highlighting the sobering reality of the effect of PJI on patient outcomes.[5] While we understand that advancing technologies in the treatment of PJIs are crucial, we also believe that prevention is the real end goal in total joint arthroplasty (TJA).

Currently many modes of infection prevention are used in the preoperative, intraoperative, and postoperative periods. Preoperative methods include patient optimization, antibiotic prophylaxis, skin preparations, and hand hygiene.[6–19] Intraoperative methods include decreasing room traffic, proper sterile technique, judicious draping method, and irrigation solutions (Fig. 1).[6,7,12–14] Postoperatively, surgeons use antibiotics, surgical dressings, negative pressure wound therapy, and other wound management regimens.[6,7,12–14] This list is not comprehensive, but emphasizes the array of prevention methods that are available for the surgeon and care team throughout a patient's TJA experience.[20]

Despite all the efforts of the orthopaedic community, infection continues to take its toll on the TJA population. An analysis by Parvizi et al., evaluating Medicare patients undergoing TJA from 2005 to 2015, showed no significant decrease in PJI rates over this period, though mortality rates due to PJI have decreased.[3] Another investigation performed by Springer et al. queried six separate international joint registries to determine trends in PJI over a six-year period from 2010 to 2015 and discovered that the global rates of infection have actually increased.[21] Other studies have demonstrated slightly better infection trends.[22–24] For example, Sodhi et al. studied the annual rates and trends in the United States of overall, deep, as well as superficial surgical site infections (SSIs) after TKAs and found downward trends for all three from 2012 to 2016.[24] However, this is still a problem. With the expected spike in TJA cases over the next several years, the prevention of infection is of utmost importance for improving patient outcomes and lessening the economic burden of this complication.

Figure 1. Proper sterile technique and judicious draping.

ANTIMICROBIALS BEING USED TO FIGHT PJIS

A new world of antimicrobial formulations is available for orthopaedic surgeons in our fight against PJIs. These different formulations are typically based upon surgeon preference with no current gold standard. Some commonly used formations used preoperatively include chlorhexidine (CHD) skin cleansing, povidone-iodine (PVI) skin cleansing, and surgeon scrubbing with either PVI or CHD (Fig. 2).[7,19] Intraoperatively, CHD irrigation solution, betadine irrigation, PVI irrigation, or acetic acid-based solutions are utilized.[25,26] Postoperatively, antimicrobials used include silver-impregnated dressings or wound-care techniques with additive antimicrobials in various forms (e.g., gels, dressings, etc.).[27,28]

As mentioned above, the preoperative period is a surgeon's first timepoint for intervention to try to prevent PJIs. Prior to surgery, it has become quite commonplace to recommend that patients perform skin cleansing prior to the date of surgery to decrease transient and resident microflora on the skin's surface. Various CHD wipes are easy for patients to use,[7–9,15,19] and they have led to excellent results with decreased PJIs. Iodine-based washes have also produced favorable results in reducing skin colonization,[29,30] although some studies in the literature have shown a potential superiority of CHD compared to PVI scrubs.[31] Two application methods of the CHD scrubs are currently available as either a scrub and rinse application or a cloth wipe. In a comparative study of 2% CHD-impregnated preoperative skin preparation cloths with 4% CHD scrub and rinse solution, it was found that the microbial reduction was significantly greater for the sites treated with the cloths at approximately six hours after preparation (3.64 vs. 3.15, $p<0.01$).[32] Another study looked at the effect of a CHD cloth skin decontamination protocol on surgical site infections (SSI) after TJA and found that for 709 patients, the 30-day SSI rate in the intervention group was significantly lower (1.1%) than the control group (3.8%) ($p=0.02$).[33] Cloth application is an easy-to-follow application for patients and may be more appropriate than a scrub and rinse solution. A recent review by Chen et al. determined that CHD cloths for prophylaxis during TKA and THA are both appropriate and effective.[7]

Intraoperatively, there has been literature that has shown the antiseptic effects of antimicrobials such as diluted povidone-iodine irrigation solution with use in TJA and its influence on infection rates.[34,35] In a systematic review by De Jonge et al., the authors showed that aqueous povidone-iodine irrigation significantly decreased the rates of SSIs by 50 per 1,000 procedures (p=0.007), but they were unable to find any differences in SSI rates between antibiotic irrigation, saline irrigation, and no irrigation (p=0.63).[36] Though some data on the reduction of infection with PVI irrigation has been promising,[35,37,38] some of these studies were flawed by smaller sample sizes or the addition of other ingredients in the irrigation solution and, as such, introduced confounding factors. A recent retrospective review of over 11,000 patients, found no protective effect of PVI irrigation against the reduction of infection at three months and one year following TKA or THA.[39] Other options include CHD irrigation solutions intraoperatively, which have also shown some promise at reducing PJIs in the literature.[40,41] For example, Frisch et al. found no subjective difference in wound healing of TJAs with intraoperative irrigation with 0.9% saline and periodic 0.05% CHD solution followed by a final one-minute soak in CHD with immediate closure afterward.[40] Therefore, they concluded that the theoretic advantages of retained dilute CHD during closure appear to be safe and effective. In summary, the search for the ideal irrigation solution is still underway and there exists no data to definitively state superiority of any solution in the literature.[42]

NOVEL INTRAOPERATIVE ANTIMICROBIAL

Recently, a new intraoperative antimicrobial irrigation solution (XPERIENCE®, Next Science LLC, Jacksonville, Florida) has been developed. It has just received United States Food and Drug Administration (FDA) approval. XPERIENCE® is a surgical lavage that contains acetic acid, sodium acetate, and sodium lauryl sulfate. It targets planktonic and biofilm bacteria after the implantation of prosthetic materials. The bacteria that are enveloped within the biofilm-disrupting formulation undergo cell lysis through a high-osmolarity imbalance produced by the sodium and citric acid distending the bacterial cell membranes and walls.

Figure 2. Preoperative skin cleansing.

XPERIENCE® is intended for use with both primary and revision arthroplasty cases. The irrigation solution is introduced through a pulsed lavage system into the joint intraoperatively after the prostheses have been implanted. After a thorough irrigation is performed, no subsequent saline rinse is required. The wound is then closed in the typical fashion depending on surgeon preference. It should not be used in patients who have a history of allergy to any of the ingredients (citric acid, sodium citrate, and sodium lauryl sulfate).

NOVEL POSTOPERATIVE ANTIMICROBIAL

Using similar biofilm-eradicating technology, another product SURGX® (Next Science LLC, Jacksonville, Florida) was created for use at the time of closure and subsequent wound care. SURGX® is a sterile wound gel technology that uses bactericidal properties with the ability to defend surgical incisions from biofilm formation. Simultaneous action of four key ingredients: (1) citric acid; (2) sodium citrate; (3) benzalkonium chloride; and (4) polyethylene glycol targets creates a high osmolarity, pH-controlled environment that prevents biofilm formation while destroying pathogens and promoting a moist environment for optimal wound healing.

SURGX® antimicrobial gel is applied directly to the closed incision site in the operating room using aseptic technique (Fig. 3). An optional applicator tip can be used to control gel dispersion and spread it evenly on the incision. This technology is approved for use with sutures, staples, steri-strips, and/or cyanoacrylate glue. It is compatible with commonly used surgical dressings, although it will deactivate the action of silver in silver-impregnated dressings. The wound gel protects against pathogens for up to five days after application,[43] and patients can apply it themselves at the time of dressing changes allowing for an extended period of protection.

HYPOTHETICAL CASE SCENARIO

In this section, we will outline some of the above infection prevention strategies based on current literature with emphasis on antimicrobial agents in an example case of a patient undergoing a

Figure 3. SURGX© antimicrobial gel application.

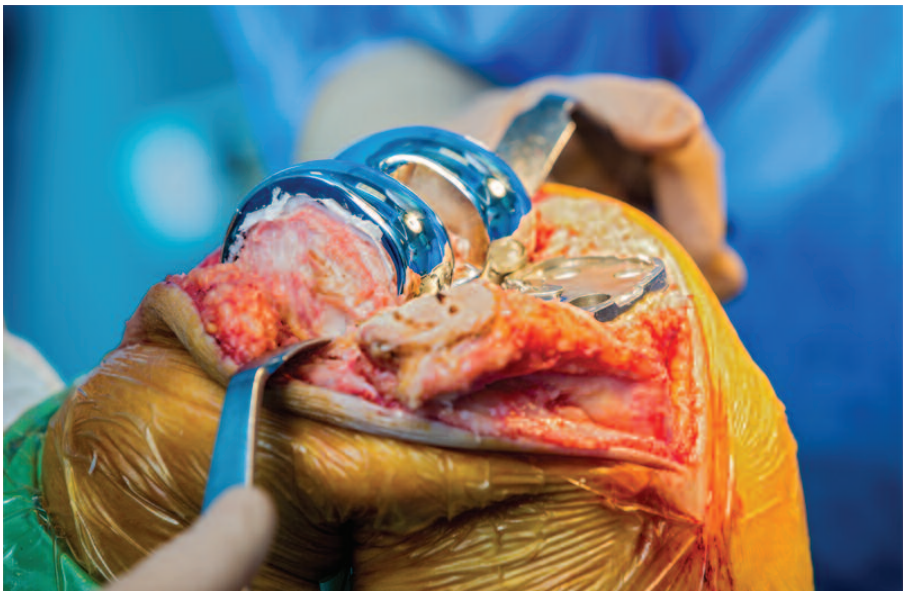

Figure 4. XPERIENCE® is used again after implantation of all components and prior to wound closure.

total knee arthroplasty that we believe may lead to an important decrease in infection rates.

First, we start preoperatively as the patient prepares for surgery. Depending on the patient's demographics and medical comorbidities, it is important to achieve optimization of diseases such as atrial fibrillation,[44,45] congestive heart failure,[46,47] peripheral vascular disease,[47] chronic pulmonary disease,[47] anemia,[47,48] renal disease,[49] and diabetes/glucose control,[46,50] as these have shown to affect outcomes and rates of postoperative infection. In this case, the patient has been optimized through a multi-disciplinary approach and deemed safe to proceed with his/her total knee arthroplasty. The night prior to surgery, the patient would be instructed to take a leisurely shower and use antimicrobial CHD wipes before bed. They would then apply the wipes again the next morning (the morning of their surgery). This protocol has been shown to be effective at reducing rates of surgical site infections by more than 70% when compared to an in-hospital skin preparation in a comparative study by Johnson et al.,[17] and again by Kapadia et al., where the rates of SSI was found to be 0.6% in patients using the CHD cloths and 2.2% in patients undergoing the in-hospital skin preparation.[10,19] These same authors conducted a prospective randomized study to better assess the effect of the CHD cloths on TJAs and found deep periprosthetic infection rates of 0.4% in the chlorhexidine group and 2.9% in the non-chlorhexidine group.[8]

When the patient arrives at the hospital, typical hospital protocol is followed including evaluation by the anesthesia team and the orthopaedic surgeon, followed by infusion of the appropriate antibiotic prophylaxis with operating room (OR) cleaning/preparation. Hair removal with electric clippers instead of razor blades[51] is performed as close to the time of surgery as possible.[52] Hospital protocol followed for skin preparation in an aseptic manner is done with either PVI or CHD by the operating room staff. The operating team undergoes meticulous hand hygiene in the sub-sterile area with the option for an alcohol-based cleanser which has shown promise[53] and was shown to reduce the rate of SSIs after TJA.[54] Draping is performed with disposable, non-woven drapes as these have been shown to be superior to woven, reusable drapes at blocking out bacterial contaminants.[55,56]

Following all preps, the arthroplasty is performed. XPERIENCE® is used prior to insertion of the tibial and femoral component when saline irrigation would typically be used on the joint and all bone surfaces. It is allowed to bathe the joint for one to five minutes until the implantation step. Implants are kept sterile right up until the time of implantation. After implantation of all components and prior to wound closure, XPERIENCE® is used again and allowed to sit in the joint space for five minutes, as no subsequent saline rinse is required (Fig. 4).

Routine multilayer wound closure is undertaken according to surgeon preference. Once the wound is closed with the typical skin closure, SURGX® sterile wound gel is applied over the surgical wound with care to spread it evenly across the entire incision. Two options are available for the application of SURGX®: 1) Sterile gauze is cut to the size of the incision and placed over the gel and a transparent film dressing is placed over the gauze. In this subset of patients, they are sent home with additional tubes of SURGX® and instructed to reapply it over the incision site every five days until the wound is fully healed; or 2) After wound gel is applied, the incision is covered with the preferred, compatible dressing choice and is left sealed for 12 days or until the first post-operative visit. At the time of the visit, the wound gel can be reapplied until the wound is fully healed. Patient receives antibiotic prophylaxis for 24 hours post-operatively and are sent home with all appropriate home-care instructions.

CONCLUSION

Prevention of PJIs and SSIs are crucial for improving outcomes after TKA. Despite all of the advances in technology, the threat of infection remains. This paper has outlined both current and future avenues for prevention of infection, including two new antimicrobial formulations of a recent technology that can be used intraoperatively and postoperatively. Our hope is that continued effort and research in infection prevention will lead to eradication of SSIs and PJIs after TKA. STI

AUTHORS' DISCLOSURES

Dr. Myntti receives stock and/or stock options from Next Science.

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