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Brief Communication

Effect of 0.05% chlorhexidine gluconate in water on the hydrophilic inflatable penile prosthesis: biocompatibility, adherence, and dip time

Ryan Griggs, DO[1], Edward Karpman, MD[2], LeRoy Jones, MD[3], Carolyn Twomey, BSN[4], Gerard Henry, MD[1,*]

[1]Willis Knighton Advanced Urology, Bossier City, LA 71111, United States
[2]El Camino Health Urology, Mountain View, CA 94040, United States
[3]Urology San Antonio, San Antonio, TX 78229, United States
[4]Department of Medical Affairs and Research, Irrimax Corporation, Lawrenceville, GA 30043, United States

*Corresponding author: Willis Knighton Advanced Urology, 2300 Hospital Drive, Suite 460, Bossier City, LA 71111, United States. Email: gdhenry@hotmail.com

Abstract

Background: Rates of infection after inflatable penile prosthesis range from 1% to 3%; however, a new surgical irrigation solution is Food and Drug Administration cleared as antimicrobial wound lavage and appears to be safe for patients and noncaustic during hydrophilic inflatable penile prosthesis (hIPP) dipping and irrigation.

Aim: To evaluate if 0.05% chlorhexidine (CHG) lavage is caustic to the hIPP coating and if dip adherence is dependent on time.

Methods: Preconnected hIPP devices were tested at a Coloplast research and development laboratory. The devices were soaked in the 0.05% CHG lavage solution or normal saline for 1, 15, 30, and 60 minutes. Subsequently, all parts were dried for 15 minutes in a 35 °C oven. A Congo red dye test was performed following a Coloplast-validated and Food and Drug Administration–cleared test method to ensure product reliability. Implants were then visually inspected for deleterious effects as well as dip coverage. In addition, we evaluated 0.05% CHG lavage solution vs previously published hIPP dipping solutions.

Outcomes: 0.05% CHG lavage does not appear to damage the hIPP coating, and adherence of this solution is not dependent on dip time.

Results: All components of the preconnected hydrophilic IPPs were tested for coating adherence and defects. All tested IPPs achieved a "satisfactory" coating, meaning a uniform coat without flaking or clumping. Furthermore, there were no noticeable caustic effects or differences in coating adherence between the normal saline–soaked control and 0.05% CHG–coated arms with increasing dip time. A review of the literature for 0.05% CHG lavage solutions vs previously published hIPP dipping solutions revealed that it may have some advantages over previously reported antibiotic solutions.

Clinical Implications: This study serves as a foundation to introduce 0.05% CHG lavage to the urologic literature as a potentially new "magic bullet" irrigation.

Strengths and Limitations: Major strengths of the study are that it is the first study of its kind to address the question of what dip duration should be used and whether it is scientifically reproducible. A limitation is the in vitro model, thus needing validation in a clinical setting.

Conclusion: 0.05% CHG does not appear to negatively affect the hIPP coating or differ in adherence with increasing dip time; however, long-term device performance has not been verified.

Keywords: antiseptic; biofilm; irrigation; dip; penile prosthesis infection; replacement penile prosthesis..

Introduction

The penile prosthesis remains the gold standard in the treatment of medically refractory erectile dysfunction. In addition to numerous enhancements for mechanical reliability, infection prevention remains paramount. One key advancement was the development of a hydrophilic coating called hydroVantage (Coloplast). This coating is covalently bonded to the implant surface and composed of polyvinylpyrrolidone, which enables dipping and/or irrigation with any aqueous solution and reduces bacterial attachment.

Inflatable penile prosthesis (IPP) infection ranges from 1% to 3% and from 7% to 18% for virgin and revision cases, respectively.[1-3] Infection remains one of the most devastating and feared complications of penile prosthesis surgery due to medical and economic sequelae. To further prevent this complication, there have been recent investigations into novel dipping and irrigation solutions.

Despite numerous antimicrobial dip solutions for hydrophilic IPPs (hIPPs), the ideal combination and dip time have yet to be described.[4-6] Irrisept Antimicrobial Wound Lavage (Irrimax Corporation) is a Food and Drug Administration (FDA)–cleared class II medical device; it is an antimicrobial wound lavage with 2 designations: FQH jet lavage (FDA product code) and FRO wound, drug, and dressing (FDA subsequent product code). Irrisept consists of 0.05% chlorhexidine (CHG) in sterile water that is aseptically filled

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and then ethylene oxide sterilized. The 0.05% CHG acts as a preservative to help inhibit microbial growth in the solution.

Irrisept has been recently used in other surgical disciplines, such as orthopedic, colorectal, and breast reconstructive surgery with reduction in postoperative infections; however, there are no published studies relating to penile implants or within urology.[7-11] It is equipped with a tapered probe enabling up to 15 psi of sustained pressurized lavage to remove microorganisms and particulate debris. Its design is also ideal for intracorporal, pump, and reservoir implant spaces. CHG is a cation and covalently binds to the negatively charged cell wall phospholipid bilayers causing rupture. Per third-party testing (Bioscience Laboratories) using kinetic time-kill testing, it innately covers >99% of the bacteria, fungi, and even viruses tested, such as hepatitis B virus, hepatitis C virus, and human immunodeficiency virus.

No published studies exist regarding hIPP dipping time or biocompatibility of solutions. We sought to perform a novel study in the urologic literature evaluating 0.05% CHG adherence and dip time while assessing its biocompatibility with the hIPP coating. We exclusively use Irrisept for device dipping and intraoperative irrigation of the surgical field.

Methods

Eight preconnected hIPP components were tested in vitro at a Coloplast research and development laboratory. Four were soaked in 0.05% CHG and 4 in normal saline solution (NSS) for 1, 15, 30, or 60 minutes. All parts were subsequently dried for 15 minutes in a 35 °C oven. The devices were dipped in Congo red dye following a proprietary Coloplast-validated and FDA-cleared test method that ensures hydrophilic coating viability. Devices are first immersed in Congo red for a minimum of 30 seconds and up to 45 seconds. The components are rinsed with water to remove loosely bound dye. During rinsing, components are agitated with the technician's gloved thumb and index finger 3 or 4 times. Last, components are visually inspected for adequate adherence; that is, the coating did not flake or come off in clumps.

Results

All components of the preconnected hIPPs were tested with Congo red staining and achieved a uniform coating with NSS and 0.05% CHG without flaking or clumping. There were no caustic effects or differences in coating adherence between the arms with increasing dip time (Figure 1) after macro- and microscopic evaluation. A review of the literature for dilute CHG lavage vs previously published hIPP dipping solutions revealed that it may have some advantages over previously reported antibiotic solutions.

Discussion

IPPs are a well-established treatment for erectile dysfunction. Multiple product and technique enhancements in the last 40 years have resulted in a decrease in mechanical failure and infection rates. Yet, infection has remained a serious complication of penile prosthetic surgery. It is believed that most of these infections are associated with contamination of organisms introduced during primary implant surgery.[12,13] Moreover, the urologic literature has not demonstrated the ideal dipping solution or dip time for first-time or revision hIPPs.

In 1995, Licht et al reported that 43% of penile prostheses and 36% of artificial urinary sphincters cultured organisms from clinically uninfected devices during revision surgery.[2] Years later, Henry et al illustrated that culture-positive bacteria were found in 54 of 77 patients (70%) with clinically uninfected penile prostheses at reoperation and several of these patients had visible biofilm.[14] More recently, Gross et al described pathogenic microflora in IPP infection, which aided in directed antibiotic treatment for coverage.[15] Although the complete biofilm microbiome has yet to be identified, studies are underway using next-generation DNA sequencing in hopes of advancing infection prevention.[16]

Various irrigation concoctions of the implant space have been shown to be effective in cases of infected IPPs.[17] In 2011, Wilson et al investigated various antimicrobial dips for the hIPP. Every tested combination had better zone of inhibition (ZOI) vs InhibiZone (rifampin and minocycline). At that time, they concluded that injectable diluted trimethoprim-sulfamethoxazole was the ideal dip due to cost, availability, and ZOI.[4] Lokeshwar et al provided a review in 2019 as a guide to various recent antibiotic dips available during IPP implantation.[5] They identified rifampin + gentamycin as the most studied combination and cited an increased need for further gram-negative coverage. In addition, Pan et al reviewed 3 commonly used antiseptic solutions in the prevention and management of IPP infection. For prevention of infection in primary prosthetics and revisions without evidence of infection, irrigation of the scrotal pump site and corporal spaces with dilute povidone-iodine (PVI; 0.35%-3.5%) was conducted for no less than 3 minutes; followed by saline or antibiotic solution.[6] This was recommended because of hydrogen peroxide's cytotoxicity, adverse events, and lack of data evaluating CHG outside the orthopedic and colorectal studies reviewed. However, there are no published studies regarding the optimal dipping time for hIPPs in these aforementioned studies. Our study is the first of its kind, which illustrates that regardless of hIPP dip time, there are no deleterious effects to the hydrophilic coating or differences in dip adherence from 1 to 60 minutes.

Furthermore, there is no literature evaluating the hydrophilic device coating biocompatibility or adherence of any antibiotic dips. Yet, Mishra et al recently concluded that dipping hIPPs in antifungal and anesthetics did not decrease the efficacy of various antibiotic dips and that the drug elution capabilities of the hydrophilic coating last approximately 24 to 48 hours.[18] In their study, ZOI diameters are referenced as "wider or narrower." However, no specific breakpoints were identified to indicate that antibiotics are effective as a bacteriostatic agent on the hIPP. This points to the importance of our study, which indicates that there is no difference in coating or adherence between NSS and 0.05% CHG with increasing time from 1 to 60 minutes. There were no observed detrimental effects on the implant coating; thus, dipping the implant in 0.05% CHG seems to be as safe for the hIPP coating as NSS.

Over the years, CHG has acquired a central role in disinfection and infection prevention. Recent evidence suggests that CHG combined with alcohol may be superior to PVI skin preparation for surgical patients, which has incited a global shift in surgical practice.[19] CHG is a water-soluble cationic bisbiguanide that binds negatively charged bacterial cell walls and results in cell leakage and death. Combining

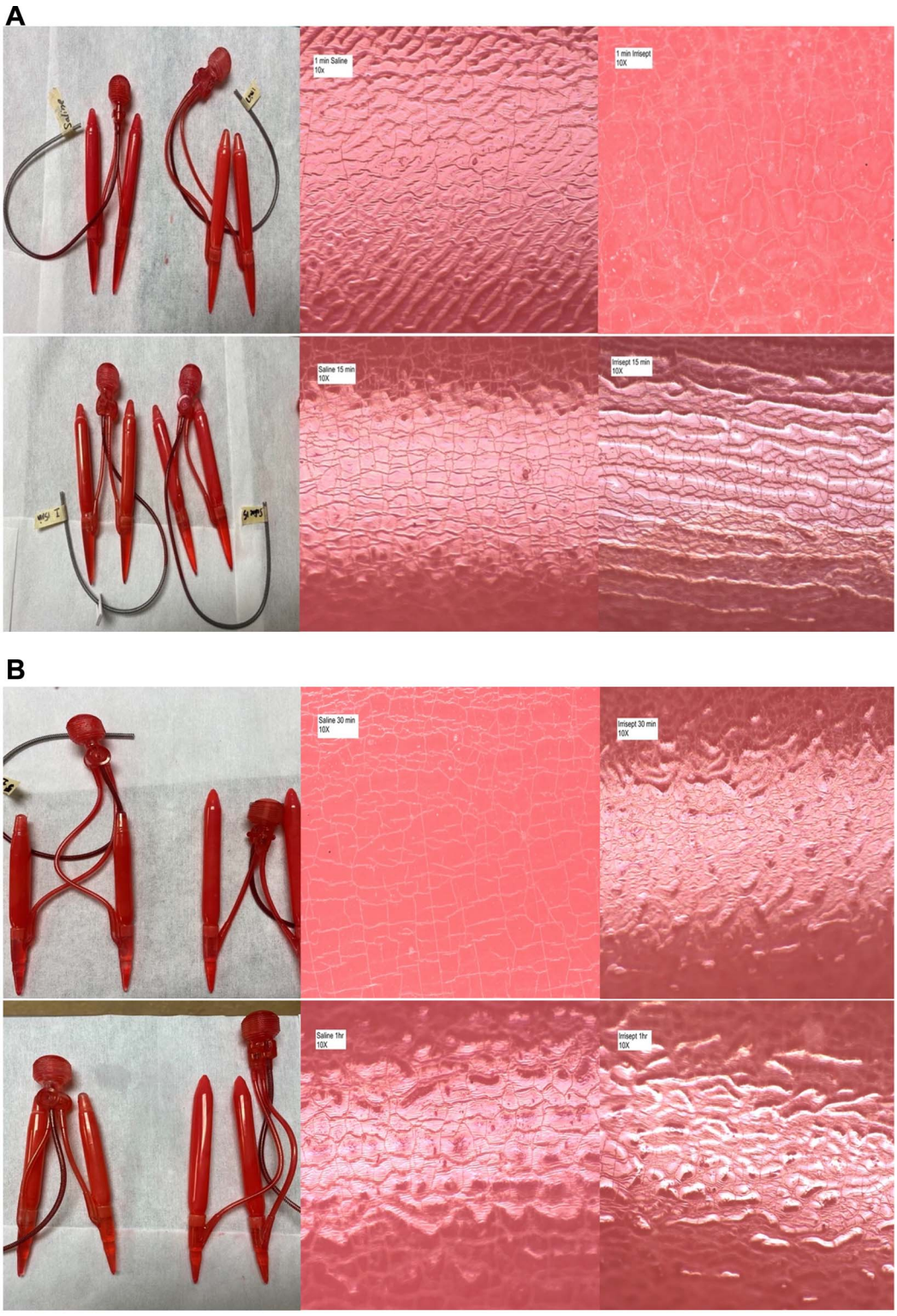

Figure 1. Hydrophilic inflatable penile prosthesis coating and adherence after Congo red staining and wash-off. Left, gross examination; middle, normal saline at 10×; end, Irrisept at 10×. (A) 1 minute (top) and 15 minutes (below). (B) 30 minutes (top) and 60 minutes (bottom).

CHG's innate antiseptic properties with mechanical lavage adds to its efficacy by creating pressures of up to 15 psi with the tapered Irriprobe tip (Irrimax Corporation) and is coincidentally well suited for irrigation of tight intracorporal, pump, and reservoir spaces. 0.05% CHG lavage is also off the shelf in sterile packaging, which obviates the need for pharmacy interference, mixing, and nurse transport. Consequently, this decreases operating room time and improves the health care economics associated with the procedure.

0.05% CHG has been extensively tested for cytotoxicity, skin irritation, and skin sensitization/immune allergic reactions and for infection reduction within in vivo

multiple-species animal models and in vitro settings.[7-11,19-20] In 2018, Goztok et al performed a prospective randomized study of 122 patients with NSS vs CHG to reduce surgical site infection in closure of temporary loop ileostomy. The authors found a significantly faster healing time and reduced infection rate in the CHG arm (4.8%) vs the NSS arm (31.6%).[7] A breast reconstruction study from Loskin et al at the Emory University School of Medicine in 2019 compared triple antibiotic solution with 0.05% CHG.[8] The triple antibiotic solution group underwent significantly more skin-sparing mastectomies, adjuvant chemotherapy/radiation, and less direct-to-implant reconstruction than the CHG group. The CHG group experienced a significantly lower incidence of total complications (22.4% vs 31.8%, $P = .006$), minor complications (8.7% vs 16.5%, $P = .003$), infection (6.4% vs 12.7%, $P = .006$), and seroma (2.6% vs 6.9%, $P = .011$). In 2019, Driesman et al from NYU Langone reported a retrospective study of prospectively collected data for patients who underwent unilateral primary total knee and hip arthroplasty.[9] Five thousand subjects were required for statistical significance; 2386 were recruited. Raw data revealed 14 infections in the PVI arm and 9 in the CHG arm, with prosthetic joint infection rates of 0.35% and 0.57% for the low-concentration CHG and PVI, respectively. However, in a nonrandomized trial, Frisch et al performed 138 total hip and 248 knee arthroplasties after 2014 with NSS irrigation + periodic 0.05% CHG intraoperative irrigation. In 2017, they compared this cohort with their retrospective data regarding dilute PVI for total hip arthroplasties and NSS for total knee arthroplasties. There were no significant differences in nonsurgical site, superficial surgical site, and deep surgical site infection rates between the groups.[10] Arslan et al in 2020 reported outcomes from their single-blind prospective pilonidal disease study.[11] There were 129 patients in the control group and 138 in the CHG group. Surgical site infection was seen in 35 patients (13.1%): 26 (20.2%) in the control group and 9 (6.5%) in the CHG group ($P = .001$). The primary healing rate was higher in the CHG group (n = 130, 94.2%) than in the control group (n = 104, 80.6%). Time to healing was 7.8 to 20.5 days in the control group and 4.3 to 16 in the CHG group ($P < .001$). Anecdotally, our 3 high-volume IPP implant authors have had no cases of patient intolerance or adverse reactions when solely using the 0.05% CHG lavage for irrigation and dipping.

This study will be a foundation for evidence for the use of dilute CHG in urology and will possibly serve as a new standard intraoperative irrigation and dip during hIPP implantation to prevent postoperative infections. However, further prospective randomized trials are needed prior to universal application. There is also a need for further studies investigating in vitro models that mimic an in vivo environment for hIPP infection prevention.

Conclusions

Soaking the hIPP in dilute CHG solution does not affect its coating when compared with NSS up to 1 hour, thus demonstrating hIPP biocompatibility. Also, there were no differences in adherence with increased dip time between the arms after 1 minute, indicating that clinically the surgeon can be confident that dipping the hIPP in Irrisept for >1 minute is unnecessary. However, long-term device functionality has yet to be determined.

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