Optimizing Breast Pocket Irrigation: An in Vitro Study and Clinical Implications

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Subclinical infections have been implicated in the etiology of capsular contracture. Intraoperatively, breast pocket irrigation with povidone-iodine or other antibiotic solutions has been popularized; however, detrimental effects on wound healing for these agents have been reported and their efficacy against common organisms found around breast implants has not been studied. The purpose of this study was to compare the in vitro efficacy of serial dilutions of povidone-iodine and two double antibiotic solutions DAB-1 (gentamicin/polymyxin B) and DAB-2 (gentamicin/cefazolin), against organisms most commonly found around breast implants. In phase I trials, serial dilutions of povidone-iodine and DAB were combined 1:1 with cultures of five common organisms found around implants. In phase II, povidone-iodine was serially diluted in DAB-1 rather than saline. In phase III, povidone-iodine was serially diluted with DAB-2. Efficacy for all phases was determined by plating the mixture onto agar plates and incubating at 37°C for 48 hours. Povidone-iodine was 100 percent effective at a dilution of 12.5% against *Staphylococcus epidermidis* and 25% against *Staphylococcus aureus* but relatively ineffective against *Escherichia coli* and *Pseudomonas*; DAB-1 was found to be ineffective against *S. epidermidis* but effective against *S. aureus, Propionibacterium acnes, E. coli,* and *Pseudomonas.* In phase II trials, a concentration of 12.5% povidone-iodine in DAB was effective at killing all experimental bacteria. In phase III trials, 10% povidone-iodine in DAB-2 was effective at killing all bacteria tested. In conclusion, to maximize bacterial control of common breast implant organisms and to minimize the detrimental effects on wound healing, 10% povidone-iodine in gentamycin/cefazolin may be used with excellent results and its use clinically may reduce the incidence of capsular contracture. (*Plast. Reconstr. Surg.* 105: 334, 2000.)

As the science of the aging breast implant becomes better defined in plastic surgery, we continue to optimize the use of breast implants. Nevertheless, capsular contracture remains a significant complication of aesthetic and reconstructive breast surgery, and despite clinical and basic science research, the etiology of this condition is unresolved. However, the infectious theory of capsular contracture, popularized by Burkhardt et al.,[1] implicates a subclinical bacterial infection, particularly *Staphylococcus epidermidis* as a possible cause, and has been substantiated by multiple other studies.[2,3]

To maximize sterility of implants, surgeons frequently irrigate implant pockets with diluted solutions of stock povidone-iodine (Betadine) or other antibiotic solutions before implantation. Although povidone-iodine is a commonly used and effective disinfectant for skin, its detrimental effects on wound healing have been well documented. In 1985, Lineaweaver reported the effects of antiseptics and antibiotics on wound healing in rats. They found that solutions of 0.05% povidone-iodine were significantly cytotoxic to fibroblasts in vitro. Furthermore, they demonstrated an adverse effect in vivo by demonstrating a lower tensile strength of healing wounds that had been irrigated with a 1% povidone-iodine solution.[4] The clinical effect in aesthetic and reconstructive breast surgery has yet to be defined; however, it is likely to be detrimental.

As an alternative to povidone-iodine, some surgeons have chosen to use combination antibiotic solutions to irrigate pockets. Although these solutions are likely to be less cytotoxic, the antimicrobial effectiveness of these solutions versus common breast implant organisms has not been reported, and thus, efficacy for prevention of capsular contracture is unproven.

The purpose of this study was to compare the effectiveness of povidone-iodine and dou-

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ble antibiotic solutions gentamicin/polymyxin B (DAB-1) and gentamicin/cefazolin (DAB-2) against organisms frequently cultured from implants, and to determine the minimal concentrations that were effective, thus minimizing adverse wound healing effects.

MATERIALS AND METHODS

The bacteria selected for the study were *S. epidermidis, Staphylococcus aureus* (batch 95-12), *Escherichia coli* (batch 92-04SV), *Pseudomonas aeruginosa* (batch 93-03), and *Propionibacterium acnes* (batch 90-02). Storage cultures were kept at 4°C in 50% glycerol and 50% Lauri-Bertani (LB) media. Bacteria were grown at 37°C in a solution of LB growth media. A new 15-ml vial of broth was incubated 24 to 48 hours before each experiment to obtain mid–log-phase growth bacteria.

Stock solutions consisted of povidone-iodine solutions (standard commercial concentration), double antibiotic solution-1 (DAB-1) (1 million units of polymyxin B + 160 mg of gentamicin in 500 ml of sterile saline), and double antibiotic solution-2 (DAB-2) (160 mg of gentamicin + 1 g of cefazolin in 500 ml of sterile saline). In the phase I trial, serial dilutions of these stock preparations were gently mixed for approximately 2 minutes with an equal volume (0.5 ml) of bacteria in LB in centrifuge tubes. Dilutions tested ranged from 100% stock to 1:15 (6.25%) stock:saline. Tubes were mixed by inversion, and then the bacteria were plated on appropriate agar culture plates by using sterile technique. Plates were incubated at 37°C and read at 24 and 48 hours. Volume-matched controls of pure bacterial culture and an equal mixture of bacteria and saline were also mixed and plated individually. All experimental procedures took place under a tissue culture hood to maintain a sterile environment. Culture plates were photographed at 24-hour intervals and independently read for the presence of bacterial growth by a research assistant blind to the protocol. Effective concentration was defined as the concentration resulting in no colony growth in the 48-hour interval.

In the phase II study, povidone-iodine was serially diluted in stock DAB-1, rather than in saline. Dilutions tested ranged from 1:1 povidone-iodine:DAB-1 to 1:31 povidone-iodine:DAB. Experiments were in a similar manner to phase I with volume-matched controls. Plates were again read at 24 and 48 hours by a research assistant blinded to the protocol.

In the phase III study, experiments were performed similar to phase II, with the exception that DAB-2 was used instead of DAB-1. Plates were prepared and read in exactly the same manner.

The phase IV study involved diluting DAB-2 in saline in a manner similar to the phase I study with DAB-1. The phase V study used the stock solution of cefazolin, which was serially diluted in saline.

RESULTS

Figure 1 demonstrates a representative control and experimental plates for dilutions of Betadine versus *S. epidermidis*.

Phase I. A summary of the results is presented in Table I. Minimal effective dilutions were defined as solutions that totally limited bacterial growth to 0 colonies on the agar plate. Povidone-iodine was effective at a concentration of 12.5% against *S. epidermidis,* yet required full undiluted stock strength to eliminate *Pseudomonas* and 50% concentration for *E. coli.* Undiluted DAB was generally effective but failed to kill *S. epidermidis* even at full stock strength.

Phase II. Dilution of the stock solution of povidone-iodine in DAB-1 to a solution of 1:15 (6.25%) was completely effective (0 observable growth) for all organisms except for *Pseudomonas.* At a concentration of 12.5%, no *Pseudomonas* colonies grew; whereas at 10%, two colonies were noted at 48 hours.

Phase III. A concentration of 10% povidone-iodine solution in DAB-2 was completely effective at controlling all microorganisms tested.

Phase IV. By using DAB-2 alone, no dilution used was fully effective against *Pseudomonas* or *S. epidermidis.*

Phase V. With serial dilutions of cefazolin, no dilution was effective against *Pseudomonas* or *S.*

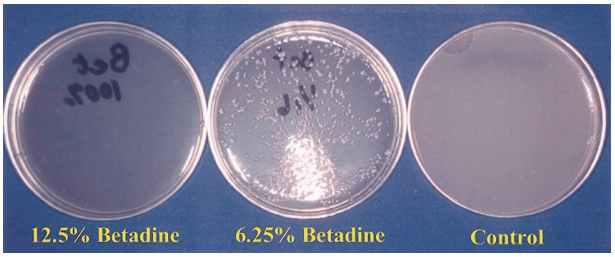

FIG. 1. Representative agar plates for Betadine versus *S. epidermidis,* demonstrating confluent bacterial growth (6.25% Betadine, *center*; control, *right*) and complete bacterial control with 12.5% Betadine (*left*).

TABLE I
Minimum Effective Concentrations of Breast Pocket Irrigation Solutions

Bacterium	Betadine Solution (%)	DAB-1 (%)	Betadine in DAB-1 (%)	Betadine in DAB-2 (%)	DAB-2 (%)	Cefazolin (%)
Staphylococcus epidermidis	12.5	Not effective	3	5	Not effective	Not effective
Staphylococcus aureus	25	Undiluted	5	5	5	10
Propionibacterium acnes	5	Undiluted	3	5	5	5
Escherichia coli	50	12.5	3	5	10	25
Pseudomonas aeruginosa	Undiluted	50	12.5	10	Not effective	Not effective

epidermidis. Figure 2 depicts a graphic summary of the minimal effective dilutions of the various solutions tested with regard to each specific organism.

Discussion

Capsular contracture remains an unresolved problem in aesthetic and reconstructive breast surgery. The infectious theory of capsular contracture implicates a subclinical infection with *S. epidermidis*, or other pathogens, in the etiology of symptomatic contracture and is supported by both basic science and clinical data. A report by Shah et al.[5] demonstrated that inoculation with bacteria led to an increase in the thickness of capsules formed around implants in a rabbit model. Clinical support for this theory is also provided by a study from Netscher and colleagues, who retrospectively reviewed 389 explanted implants that were removed for reasons other than clinical infection. Statistical analysis was used to identify a correlation between a positive implant culture and other variables to include implant rupture, type of implant, location of implant, and symptomatic capsular contracture. The only correlation detected in their study was between Baker class IV capsular contracture and positive culture.[6]

Although the importance of sterilizing breast pockets for prosthetic implants has been recognized, there is also concern that agents used to disinfect these pockets have detrimental effects on wound healing. A report by Lineaweaver et al. examined the effects of topical antimicrobials, including povidone-iodine, on fibroblasts in vitro and on wound healing in vivo (by measuring tensile strength). Evidence from these experiments demonstrated that povidone-iodine was cytotoxic to fibroblasts in vitro even at concentrations of 0.01% (standard Betadine diluted 1000-fold) and that wound irrigation with 1% povidone-iodine (1:10 of a stock dilution) adversely affected the tensile strength of wounds, especially during the first 24 hours.[4] The clinical implication of adverse effects on wound healing remains to be

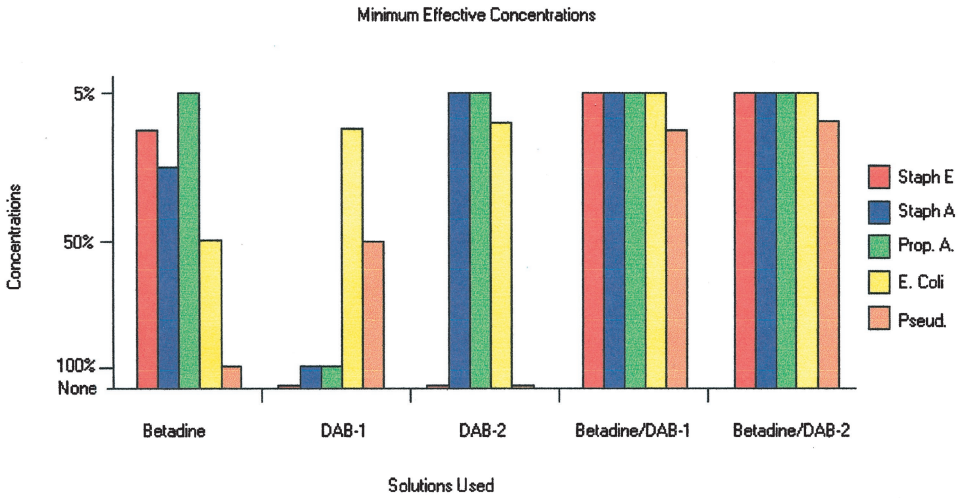

FIG. 2. Graphic depicting the minimal effective concentration for each tested solution versus different bacteria, demonstrating the best overall coverage and control with a combination solution of betadine/DAB-2.

fully elucidated; however, the usual effects of gravity on breast implants lead to unwanted "bottoming out," particularly with saline implants. This adverse effect may be minimized in an uninhibited wound bed; thus, wound healing implications of irrigating solutions are clinically relevant.

Concerns regarding the detrimental effects of povidone-iodine have prompted some surgeons to use an antibiotic solution for breast irrigation that would likely avoid adverse wound healing effects on fibroblasts; however, at the time of this study, the effectiveness of these antibiotic solutions had not been tested scientifically. Our study was designed to evaluate the concentrations of these solutions that would be effective at eliminating bacteria that are commonly found cultured around breast implants.

Ahn et al. reported commonly cultured organisms from 47 percent of 139 implants that had been removed. *P. acnes* (57.5 percent), *S. epidermidis* (41 percent), and *E. coli* (1.5 percent) were found on a significant number of implants.[7] Because these bacteria are the most commonly associated with breast implants, we included them in our study. In addition, *P. aeruginosa* and *S. aureus* were chosen in light of their tendency to cause serious nosocomial wound infections. We attempted to mimic "clinical" pocket irrigation by mixing the bacteria with the irrigant for 2 minutes, then allowing the solution to absorb into the agar, similar to the nonstandardized breast pocket irrigation clinically practiced by plastic surgeons.

Initially, our results demonstrated that neither of these agents was ideal for use of pocket irrigation. Although povidone-iodine was effective against most organisms, its efficacy was only at concentrations well above its cytotoxic threshold and its inability to control *Pseudomonas* casts doubt on its efficacy at dilute concentrations. DAB-1, DAB-2, and cefazolin were generally effective versus *P. acnes and E. coli.* However, none of the three controlled *S. epidermidis,* which is the most frequently implicated organism in the infectious theory of capsular contracture.

In phase II and III trial results, combinations of DAB-1 and DAB-2 with povidone-iodine were encouraging. Povidone-iodine and the antibiotic solutions appeared to work synergistically. DAB-1 and povidone-iodine effectively eliminated 100 percent of the organisms at a povidone-iodine concentration of 12.5% of stock solution strength. Even larger dilutions of povidone-iodine (1:15) in DAB-1 resulted in excellent control, yet still permitted limited growth of *Pseudomonas.* Results with DAB-2 were even more encouraging. A 10% solution completely controlled growth of all bacteria tested. Another advantage of the DAB-2 solution is that it uses cefazolin, which is more frequently stocked in hospital operating rooms.

Phase IV and V trials demonstrated that neither cefazolin nor DAB-2 is fully effective without povidone-iodine added, thus providing still more convincing evidence that povidone-iodine is a necessary adjunct to antibiotics. We believe that the synergy of these two antimicrobials is related to the disruption of bacterial membranes by povidone-iodine. Therefore, antibiotics such as gentamicin and cefazolin have greater access and are effective at smaller concentrations. However, future investigations would be required to examine this theory more critically.

We acknowledge the specific limitations in the study that include unpredictable correlation of in vitro activity with in vivo results. Nevertheless, the gold standard for antibiotic activity is in vitro activity versus specific organisms. We have no reason to suspect that the in vivo activity would not be similar given a competent immune system. Furthermore, the results in vitro do not mimic the in vivo setting that includes the presence of a foreign body (i.e., the implant). Additionally, it is impossible to devise a direct correlation of our in vitro method to the usual manner in which we irrigate our breast pocket in the clinical setting; however, the need to control potential pathogens while minimizing the negative effects on wound healing remains undisputed. Furthermore, our inclusion of *Pseudomonas* in the experimental group was done empirically; however, although we have demonstrated excellent control of *Pseudomonas,* its clinical relevance has yet to be realized, because we have not seen a clinical infection with *Pseudomonas.*

We conclude that neither povidone-iodine nor a polymyxin B/gentamicin antibiotic alone appears to be completely effective at eliminating all commonly cultured bacteria from a breast pocket; however, a combination of these two seems to work synergistically with excellent overall efficacy. This approach allows the use of a more dilute concentration of povidone-iodine, a substance that has been shown to be cytotoxic to fibroblasts and has adverse effects on wound healing. If subclinical breast implant colonization/infection is an important factor

in the development of capsular contracture, we would suggest that irrigation with random dilute povidone/iodine or other solutions is probably suboptimal; in fact, use of this solution does not optimize bacterial control or effectively reduce the detrimental effects on wound healing.

We recommend using 50 ml of povidone-iodine, 1 g of cefazolin, and 80 mg of gentamicin in 500 ml of sterile saline for irrigation of breast pockets. Copious pocket irrigation should be performed as well as purposeful incomplete evacuation of the irrigant before implant placement. It is our practice to close our wounds in three layers and apply Steri-strips externally. We are presently collecting data by using this new breast pocket irrigant solution and hope to eventually obtain long-term data on clinical capsular contracture.

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