Cosmetic Special Topic

Optimizing Breast-Pocket Irrigation: The Post-Betadine Era

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The practice of breast-pocket irrigation with various antibiotic solutions is supported by good literature and extensive clinical practice among most plastic surgeons. Unfortunately, recent restrictions on the use of Betadine (povidone-iodine) for breast-pocket irrigation have left many plastic surgeons confused regarding their surgical protocol for aesthetic and reconstructive breast surgery. The purpose of this study was to examine the in vitro efficacy of alternative non–Betadine-containing solutions for breast-pocket irrigation and to subsequently provide recommendations for breast-pocket irrigation in the "post-Betadine era." Bacitracin, cefazolin, gentamicin, and vancomycin were tested as single agents and in combination against organisms that have been most commonly cultured around breast implants and implicated in capsular contracture and peri-procedural infection. An established in vitro method was used for this testing. The single antibiotic agents were ineffective at controlling many of the bacteria tested. The combinations of bacitracin, cefazolin, and gentamicin, and vancomycin, cefazolin, and gentamicin both demonstrated excellent control of all the bacteria, except for allowing a 9 percent and a 6 percent growth of *Pseudomonas,* respectively. It was concluded that a combination breast irrigant of bacitracin, cefazolin, and gentamicin is an effective alternative to Betadine-containing breast irrigants and is recommended for clinical practice. Clinical implications are discussed in greater detail in the study. (*Plast. Reconstr. Surg.* 107: 1596, 2001.)

Breast-pocket irrigation has been a common practice of plastic surgeons for many years. The etiology of implant complications such as capsular contracture has not yet been fully defined; however, good data exist to support the use of breast-pocket irrigation to minimize the risks of contracture and peri-procedural infection.[1–6] Although the practice of breast-pocket irrigation has been a relatively ill-defined procedure, recent data have served to identify the most effective in vitro solution and concentrations in an attempt to make this practice more standardized and, hopefully, provide better clinical results.[7]

Unfortunately, the spring of 2000 proved to be a confusing time in our specialty, with the recent dictums issued by the Food and Drug Administration (FDA) stating that contact of any breast implant with povidone-iodine (Betadine, Purdue Frederick, Stamford, Conn.) is contraindicated. This decision has been troublesome for many surgeons who have used some form of Betadine as their breast-pocket irrigant with no apparent ill effect. We concur with the use of Betadine-containing breast irrigants on the basis of previous study data which reported that a 10% Betadine, gentamicin, and cefazolin (Ancef) solution provided optimal antimicrobial spectrum coverage while minimizing any potential cytotoxic effects of Betadine.[7]

The basis for the recent FDA decision regarding Betadine is somewhat turbid; however, it potentially places plastic surgeons who continue using breast-pocket irrigation solutions containing Betadine at medicolegal risk. The purpose of this study was to examine the in vitro efficacy of alternate non–Betadine-containing solutions for breast-pocket irrigation and, subsequently, provide recommendations for breast-pocket irrigation in the "post-Betadine era."

Materials and Methods

The study design was based on our laboratory's previous in vitro experiments with breast irrigation solutions.[7] We began with cultures of the following bacteria: *Escherichia coli*, *Staphylo-*

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coccus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, and *Propionibacterium acnes.*

Cultures were grown in standard Lauri Bertani liquid media and incubated at 37°C for 48 hours to obtain cultures that were in the logarithmic phase of growth. Irrigation solutions were prepared using a sterile technique in an enclosed tissue-culture hood. Ten 500-ml solutions were prepared as follows: (1) 50,000 U of bacitracin, (2) 100,000 U of bacitracin, (3) 50,000 U of bacitracin with 1 g of cefazolin, (4) 100,000 U of bacitracin with 1 g of cefazolin, (5) 50,000 U of bacitracin with 1 g of cefazolin and 80 mg of gentamicin, (6) 100,000 U of bacitracin with 1 g of cefazolin and 80 mg of gentamicin, (7) 1 g of vancomycin, (8) 1 g of vancomycin with 80 mg of gentamicin and 1 g of cefazolin, (9) 1 g of vancomycin with 80 mg of gentamicin and 50,000 U of bacitracin, and (10) 1 g of vancomycin with 50,000 U of bacitracin.

In experimental subgroups, 0.5 ml of bacterial culture and 0.5 ml of irrigation solution were mixed in 1-ml centrifuge vials and allowed to mix for 30 to 60 seconds. The solutions were then plated on sterile agar plates and incubated for 48 hours at 37°C. The control subgroup was produced by combining 0.5 ml of the bacteria with an equal volume of saline and mixing the solution for 30 to 60 seconds, then plating it on agar. At 24 and 48 hours, the plates were assessed by a laboratory technologist (who was blinded to the solutions) for the percentage growth of bacteria.

RESULTS

Table I summarizes the results for all solutions tested. All controls grew colonies to cover more than 90 percent of their respective plates, with the exception of *P. acnes,* which grew on 20 percent after 1 week. The bacitracin solutions alone were ineffective at controlling bacterial growth for all organisms tested. The most efficacious combinations were bacitracin/

TABLE I
Effectiveness of All Irrigation Solutions

Solutions	*Escherichia coli*	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Propionibacterium acnes*	*Pseudomonas aeruginosa*
50,000 U Bacitracin	– (60%)	– (62%)	– (67%)	– (1%)	– (90%)
100,000 U Bacitracin	– (72%)	– (35%)	– (70%)	+	– (85%)
50,000 U Bacitracin 1 g Cefazolin	+	+	– (1%)	+	– (90%)
100,000 U Bacitracin 1 g Cefazolin	+	+	+	+	– (82%)
50,000 U Bacitracin 1 g Cefazolin 80 mg Gentamicin	+	+	+	+	– (9%)
100,000 U Bacitracin 1 g Cefazolin 80 mg Gentamicin	+	+	+	+	– (5%)
1 g Vancomycin	– (98%)	+	+	+	– (87%)
1 g Vancomycin 80 mg Gentamicin 1 g Cefazolin	+	+	+	+	– (6%)
1 g Vancomycin 80 mg Gentamicin 50,000 U Bacitracin	– (42%)	+	– (3%)	+	– (17%)
1 g Vancomycin 50,000 U Bacitracin	– (85%)	– (2%)	+	+	– (87%)

+ implies zero bacterial growth or completely effective treatment.
– implies any level of growth or not completely effective treatment.
(##%) is the percentage of plate covered by bacteria.

cefazolin/gentamicin and vancomycin/cefazolin/gentamicin; both of these combination solutions were completely effective at controlling all organisms, except for a small amount of *Pseudomonas*.

Discussion

The events leading up to the FDA decision to restrict implants coming in contact with Betadine are confusing yet warrant review because of the extensive interest the issue has caused among all plastic surgeons.

In 1997, Mentor Corporation (Santa Barbara, Calif.) identified, via product-complaint reports, an association of implant delamination with the intraluminal use of Betadine. By the fall of 1997, Mentor had registered 94 complaints. It was confirmed that Betadine had been used in the majority (of these complaint cases) as a portion of the fill solution. These initial reports led Mentor to conduct a series of preclinical in vitro studies.[8] The methods and outcomes for the preclinical in vitro studies are summarized below.

In Vitro Study 1

Eight Siltex saline-filled mammary prostheses were filled with a 10% Betadine/90% normal saline solution and totally immersed in normal saline solution for 4 months. The devices were then evaluated for delamination at the joint areas.

Result. At 4 months, all eight devices demonstrated delamination of various components.

In Vitro Study 2

A total of 32 smooth and Siltex saline-filled mammary prostheses were filled with a 10% Betadine/90% saline solution or a 20% Betadine/80% saline solution, then totally immersed in saline for up to 7 weeks. Eight control devices were filled with saline and also immersed in saline for up to 7 weeks.

Result. All 32 devices filled with 10% or 20% Betadine experienced delamination within the 7 weeks. The control group of eight devices filled with saline and immersed in saline showed no evidence of delamination or loss of physical properties.

In Vitro Study 3

A total of 16 smooth and Siltex saline-filled mammary prostheses were filled with normal saline and then immersed in 100% Betadine for up to 7 days, with observations made at 15-minute intervals during the first 2 hours and daily thereafter.

Result. None of the 16 devices filled with saline and immersed in 100% Betadine experienced delamination or a loss of physical properties.

In Vitro Study 4

A total of 40 smooth and Siltex saline-filled mammary prostheses were filled with 20% Betadine/80% saline and adjusted to a pH of 7.4. In addition, citric acid adjusted to a pH of 3.95 to simulate the usual pH of a 20% Betadine/80% saline solution was used as a filler for comparison. All implants underwent a 5-week duration test.

Results. All devices filled with 20% Betadine and having a pH of 7.4 experienced delamination by 5 weeks. None of the citric acid–filled devices showed delamination by 5 weeks.

The results of all four of these in vitro tests were communicated to the FDA along with product-complaint information, in accordance with the administration's mandatory regulatory requirements. The FDA, after consultation with Mentor, made the ultimate decision and changed the product insert data sheet/package insert information regarding antibacterial compounds, specifically Betadine. The changes were incorporated into the product label in 1998 and read as follows:

> In vitro testing has determined that even low concentrations of Betadine solution placed within the breast implant will compromise implant integrity in the long term. Therefore, we recommend that no Betadine solution or other anti-bacterial, antiseptic, or cleaning agents be added to the injection media. If a cleaning agent is to be used within the implant space during surgery, a careful rinsing of the implant site to removal residual cleaning agent or cleaning solution is also recommended.

In March of 2000, the implant manufacturers (McGhan Medical Corp., Santa Barbara, Calif., and Mentor) underwent their final FDA presentation for the saline-implant premarket approval. During these hearings, one implant company (Mentor) presented data from their clinical study that indicated an increased rate of implant deflation with the use of Betadine as an intraoperative medication. These data (± Betadine) were not considered in the McGhan clinical studies. At the time of the hearing, the scientific panel of invited guests rejected the finding as not significant.[9] Despite the recommendations from the scientific panel, the FDA concluded that the findings were significant

and subsequently made their recommendations contraindicating Betadine usage.

A more detailed review of the methodology of the Mentor clinical study demonstrates that it was a 3-year, multicenter prospective clinical trial involving 1680 patients.[8] This work represented the primary study supporting the recent FDA approval of Mentor's PMA submission. The primary objective was to assess short-term incidents and complications including infection, deflation, and capsular contracture. A Cox proportional hazards analysis was performed to define the various baseline risk factors that may contribute to saline-implant complications. This type of analysis controls for other factors while evaluating the potential factor of interest. The baseline factors that were evaluated in the study included patient age, indication (cosmetic versus reconstructive), race, smoking status, surgical approach, unilateral versus bilateral implants, surgical placement of implants, incision size, implant surface type, valve type, Betadine use, implant shape, and clinical site. The collection of Betadine-usage information was obtained from an operative case report that included a section of intraoperative medications:

Intraoperative Medications	**Right**	**Left**
Pocket Irrigation	_____	_____
Steroids	_____	_____
Antibiotics	_____	_____
Betadine	_____	_____
Other	_____	

The results from the Cox regression analysis on factors that related significantly to implant deflation included[8] indication for surgery ($p = 0.007$), use of Betadine ($p = 0.005$), unilateral versus bilateral implants ($p = 0.04$), and average incision size ($p = 0.03$).

Specifically on a per patient basis among augmentation patients, 4.2 percent of the patients (24 of 574) in whom intraoperative Betadine was reported as an intraoperative medication experienced deflation, compared with 1.9 percent of the patients (13 of 690) who had not been treated with Betadine as an intraoperative medication. In the reconstruction subgroup, 8.1 percent of the patients (nine of 111) in whom Betadine was used as an intraoperative medication experienced deflation, compared with 6.2 percent of the patients (19 of 305) who were not treated with Betadine.

This study assessed the use of Betadine as an intraoperative medication. It was assumed that the intraoperative use of Betadine was only for breast-pocket irrigation; however, Mentor Corporation acknowledged that, on the basis of the reporting questionnaire design, the intraluminal use of Betadine among patients with deflations, in whom Betadine was reported as an intraoperative medication cannot be excluded.[8] Implants examined from the deflation subgroups in which Betadine was used as an intraoperative medication demonstrated implant delamination, which was consistent with in vitro preclinical studies performed by Mentor. Because delaminations were only seen in the intraluminal subgroup in Mentor in vitro studies, the deflations noted in the Mentor clinical study suggest that the implants that exhibited delamination may have come in contact with intraluminal Betadine as well.

On the basis of the data presented in the Mentor clinical study, we do not believe that a causal relationship between Betadine and implant deflation has been established. Since the study was not specifically designed to investigate Betadine, there are several flaws that question the validity of these findings. Specifically, the study design does not control for intraluminal versus extraluminal Betadine nor does it control for the concentration of Betadine. Furthermore, the results of the in vitro studies strongly suggest problems with intraluminal Betadine but no effects with extraluminal Betadine. It should also be noted that the conclusions drawn from these studies were not formulated by Mentor or organizations representing plastic surgeons but rather by the FDA and their agents.

Aside from this clinical study, there have been other excellent published and peer-reviewed studies that lend themselves to the examination of the effects of Betadine on implants. Burkhardt and Demas and Burkhardt and Eades performed similar trials in two studies, using implants from one major company in each study, to investigate the effects of Betadine pocket irrigation on capsular contracture.[10,11] The study design was a randomized blinded protocol in which one implant pocket was irrigated with a 50% Betadine solution and the other side was irrigated with saline as a control. The range in follow-up duration was 12 to 40 months (average, 21 months). Of the combined total of 188 implants for both studies, there was one deflation in the Betadine

group and one deflation in the saline control group, resulting in no differences in deflation.

Becker and Becker reported data that suggested an adverse effect of Betadine on the fill tubes of Spectrum (Mentor) adjustable saline-filled mammary prostheses.[12] In their brief communication, the breaking strengths of the silicone elastomer fill tubes in the Spectrum implants were found to be significantly reduced by 2 weeks' exposure to different concentrations of Betadine. Additionally, a color change from the normal clear to white upon exposure to the Betadine was noted.

The significance of these data is not clear; however, we have also had an extensive experience with the adjustable Spectrum and Becker implants and their associated fill tubes. Intraoperative combination Betadine irrigation was used in all of our cases, and we have never noted any fill-tube color change nor experienced any problems with premature or fill-tube breakage. The method used in this pilot study likely exposed the inside of the tubing to Betadine, which introduces other variables. Additionally, the vulcanization process of these fill tubes involves a peroxide cure technique that is completely separate from that used for the elastomer of the implant. (It is notable that the diaphragm valve used in standard saline implants also has a peroxide-cured component that is only exposed to the internal contents of the implant.) Thus, the concerns raised in this communication are interesting but not likely applicable to potential concerns regarding the effects of extraluminal Betadine on saline-filled prostheses.

The decision of the FDA to restrict Betadine usage seems peculiar when one looks at the available data. At this time, to our knowledge, the only data that could possibly implicate a detrimental effect of Betadine on implants are from the Mentor clinical premarket approval study; however, this study was not specifically designed to look at the effects of Betadine. As a result of this lack of control, it is our feeling that any absolute conclusions drawn from this study on the effects of Betadine on implants are potentially flawed.

Despite this and the large number of plastic surgeons who have used Betadine for many years with no untoward effects, the FDA has made its decision regarding Betadine. We are currently making plans to look again scientifically at the in vitro effects of extraluminal Betadine on implants to obtain more data on this subject; however, until more data exist, plastic surgeons will need to modify their practices accordingly with respect to Betadine usage in implants.

We have previously demonstrated that a combination breast-pocket irrigation solution provides more effective in vitro broad-spectrum coverage of bacteria that have been commonly cultured around breast implants and implicated in the formation of capsular contracture and peri-procedural infection. The most effective solution is a 10% Betadine, gentamicin, and Ancef solution. Because of the current restrictions on Betadine, we designed this study to scientifically consider an alternate non–Betadine-containing solution to again optimize breast-pocket irrigation.

The results of this study demonstrate a higher in vitro control of the tested bacteria with a combination antibiotic irrigation. The bacitracin/cefazolin/gentamicin and vancomycin/cefazolin/gentamicin solutions have a much better in vitro efficacy than do any of the single antibiotics alone; however, the solutions are not as universally effective against all the bacteria (especially *Pseudomonas*) as the originally recommended 10% Betadine/gentamicin/cefazolin solution was. The results of this study make sense, considering the mechanism of action of the various antibiotics. As mentioned in our previous studies, cefazolin and gentamicin can be used to create a synergistic rather than an additive response, because of the effect of cefazolin on the cell walls of replicating bacteria, permitting entrance of the gentamicin which acts intracellularly at the level of RNA translation. Although this combination is potentially very effective over long periods, its use is limited for breast-pocket irrigation because of the short time period in which any possible bacteria are exposed to the antibiotics during the washing period. In our previous study, Betadine greatly increased the effectiveness of the two antibiotics by directly attacking cellular membranes and allowing entrance of these antibiotics. In this study, we used bacitracin, which also attacks cellular membranes directly. Although it was not as effective as Betadine, it did allow for an increased efficacy of cefazolin and gentamicin.

Although the substitution of vancomycin for bacitracin in the triple combination did improve our results slightly, we would strongly caution against its use in an irrigation solution for breast implants. In most teaching centers,

the use of vancomycin has been greatly restricted to avoid the emergence of resistant bacteria, in many cases requiring approval by an infectious disease committee. Widespread use of this antibiotic as a prophylactic medication would most likely be considered inappropriate. If a Gram-positive organism were to survive irrigation with this antibiotic as a prophylaxis, the resulting infection may prove very difficult to treat.

Our clinical practice recommendations for breast-pocket irrigation in the post-Betadine era are as follows:

1. As an alternative to Betadine-containing solutions, a combination irrigant containing the following can be used:

   - 50,000 U of bacitracin
   - 1 g of Ancef
   - 80 mg of gentamicin
   - 500 cc of saline

   This solution may be used to soak the implant as well as to thoroughly irrigate the implant pocket without active evacuation. A pocket contact time of 5 minutes prior to implant placement is recommended.
2. The wording of the FDA policies restricts the contact of Betadine with implants. One alternative is to use a Betadine-containing breast irrigant. We would recommend a 10% Betadine/cefazolin/gentamicin solution, allowing the breast pocket to bathe in the solution for 5 minutes, then clearing it with sterile saline before the implant is placed. The Betadine solution should not be used to soak the implant before placement.
3. A Betadine-containing irrigant may be used in standard fashion with written and signed preoperative consent from the patient, who would need to be educated regarding all the issues that have been discussed in this study.

Despite this controversy, the onus is on all of us to ensure that our patients receive optimal care, allowing them the safest and best results possible. Breast-pocket irrigation has been a time-tested practice, and we strongly recommend its safe usage in patients undergoing aesthetic and reconstructive breast surgery.

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