Clindamycin for Intracisional Antibiotic Prophylaxis in Dermatologic Surgery

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Objective: To assess the efficacy of intracisional clindamycin therapy as an alternative to nafcillin treatment in decreasing the risk of postoperative wound infections in dermatologic surgery.

Design: Prospective, double-blinded, randomized, placebo-controlled trial conducted over a 7-month period.

Setting: Three private practice Mohs micrographic surgery referral centers.

Patients: A total of 1030 consecutive patients who underwent Mohs micrographic surgery with subsequent reconstruction.

Interventions: Prior to reconstruction, patients were randomly assigned to receive either intracisional buffered lidocaine with epinephrine containing clindamycin or buffered lidocaine with epinephrine without clindamycin. Nurses and physicians who scored the wound at follow-up were blinded to the treatment conditions.

Main Outcome Measures: Surgical wounds evaluated at the time of suture removal were scored according to a standardized assessment based on erythema, edema, and the presence of purulent discharge. Wounds scored 4 or higher were considered to be infected. Bacterial cultures obtained when indicated were also compared.

Results: Of the 1172 surgical wounds included in the study, 29 had wound scores of 4 or higher, 6 in the study group and 23 in the control group (P=.001, Fisher exact test). Of these 29, 18 had culture-positive infections. Four of these occurred in the study group, and 14 occurred in the control group (P=.02, Fisher exact test).

Conclusions: The results of this study further support the efficacy of single-dose preoperative intracisional antibiotic treatment for dermatologic surgery. With the relatively high prevalence of patient-reported penicillin allergies, buffered lidocaine containing clindamycin offers an inexpensive, safe, convenient, and effective alternative.

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Postoperative surgical wound infections can have a significant effect on the outcome of a dermatologic surgical procedure, including the final appearance of the wound. In many cases, patients are given preoperative or postoperative systemic antibiotics in an effort to decrease morbidity, despite the low estimated incidence of postoperative wound infections. Unfortunately, giving either oral or intravenous antibiotics prior to surgery is not only inconvenient and cumbersome, but the efficacy of such procedures is largely unstudied in dermatologic surgery.

A report by 2 of us has shown that intracisional nafcillin treatment prior to skin surgery resulted in a statistically significant reduction in the occurrence of postoperative wound infections. Unfortunately, there are many patients with a potential or documented allergy to penicillin or the penicillin class of antibiotics. For these patients, use of nafcillin is contraindicated, and an alternative antibiotic for intracisional prophylaxis would be desirable.

Given the spectrum of antimicrobial effects of nonpenicillin-type antibiotics, several candidates for use in skin surgery may be appropriate, but the macrolide clindamycin offers the most appropriate antimicrobial activity against the most common pathogens in cutaneous wound infections. Other injectable drugs that were considered (vancomycin and ciprofloxacin) had limitations such as restricted use recommendations or less appropriate antimicrobial coverage. The purpose of this study is to examine the efficacy of a single dose of preoperative intracisional clin-
Clindamycin in preventing postoperative wound infections in dermatologic surgery.

METHODS

A prospective, blinded, randomized, placebo-controlled study was conducted in our 3 private practice offices from February 12, 1998, to September 18, 1998. Consecutive patients undergoing Mohs micrographic surgery in whom reconstruction was to be performed (primary closure, local or fasciocutaneous pedicle flap, or skin graft) and who did not meet any exclusion criteria were included in the study. Exclusion criteria included history of allergic reaction to clindamycin or other macrolide, concurrent or perioperative use of systemic antibiotics, or inability to return for follow-up evaluation. Informed consent was obtained.

CLINDAMYCIN SOLUTION

The concentration of clindamycin used in the study solution was determined by extrapolation from published data. With intravenous administration of standard doses of clindamycin, serum levels of 7 to 14 µg/mL are achieved at steady-state dosing.4 Also, after standard intravenous dosing of clindamycin, steady-state wound fluid concentrations of 4 to 5 µg/mL are achieved and maintained within 1 to 5 hours.4 However, taking into account dilution among interstitial tissue fluid after injection, and to avoid the inaccuracies of delivering very small volumes when mixing the solutions, we decided to investigate concentrations that were much higher than the standards described above. Varying concentrations of clindamycin (272 µg/mL, 408 µg/mL, and 544 µg/mL) were tested. Using Mueller-Hinton broth inoculated with laboratory strains of nonpenicillinase Staphylococcus aureus bacteria in concentrations of 10⁶ organisms per milliliter, we diluted the study mixtures to 4 different ratios of solution-to-bacteria broth (1:1, 1:2, 1:4, and 1:8). Incubation of the sequential dilutions was done at 35°C and was performed and interpreted by a microbiologist who assessed growth at 24 and 48 hours. The 272-µg/mL concentration allowed growth of bacteria at 48 hours when tested 7 days after mixing the study solution at a dilution of 1:8. Further testing of this dilution was not pursued. At concentrations of 408 µg/mL and 544 µg/mL, no growth of bacteria occurred at 48-hour culture assessment in any dilution when tested up to 30 days after mixing.

Storage methods of the study solution were then tested and compared for bactericidal activity. There was complete bactericidal activity for all dilutions of preparations (408 µg/mL and 544 µg/mL) that were stored at room temperature, refrigerated, or frozen for up to 30 days after mixing the study solutions. In an attempt to avoid the potential tissue irritancy of higher concentrations, the 408-µg/mL concentration was selected as the lowest effective concentration for the current study. Our study solution, at a concentration of 408 µg/mL, is 29 to 58 times the standard steady-state serum concentration of clindamycin administered by intravenous injection.

PROCEDURE

Patients eligible for the study were randomized to receive local anesthetic with or without clindamycin. The anesthetic solutions were injected into the dermis and subcutaneous tissue following tumor extirpation, approximately 15 minutes prior to reconstruction. The volume of the preparations injected was that required to achieve adequate local anesthesia. After injection, the skin was treated with a preoperative antiseptic scrub containing 3.0% chloroxylenol and 3.0% cocamidopropyl PG-dimonium chloride phosphate (Technicare; Care Tech Laboratories, St Louis, Mo) prior to skin incision. Superficial, rapidly absorbable plain gut suture or nylon was used in each closure with buried interrupted absorbable suture used where appropriate in layered closures.

Syringes with study medications were made each week. They contained either 1% lidocaine with 1:10000 epinephrine buffered with sodium bicarbonate (control) or 1% lidocaine with 1:10000 epinephrine buffered with sodium bicarbonate containing clindamycin (408 µg/mL). Both solutions were prepared by adding 5 mL of 8.4% sodium bicarbonate (50 mEq/mL) to a 50-ML vial of 1% lidocaine with 1:100000 epinephrine. For the clindamycin solution, 0.15 mL of 150-mg/mL clindamycin phosphate injection was also added to yield a clindamycin concentration of 408 µg/mL. The 2 types of syringes were then stored in separate bins, and the medical staff selected one as each consecutive patient was ready for anesthesia. No note was made in the patient chart that indicated which solution was used. To facilitate approximately equal patients in each group, medical staff were instructed to use syringes from alternating bins.

WOUND SCORING AND ASSESSMENT

Patients were assessed at their follow-up visit for suture removal (5-8 days). At this visit, the wound appearance was scored by a physician or a nurse blind to the treatment group using a standardized wound scoring scale (Table 1). Patients were also questioned regarding cutaneous and systemic allergic reactions and bowel symptoms including nausea, vomiting, and diarrhea. When patients had multiple wounds, each wound was assessed individually and given a separate wound score. A wound was considered infected if a wound score of 4 or higher was obtained as the lowest effective concentration for the current study. If infection was suspected, the wound was cultured, and empiric antibiotics were prescribed, if clinically indicated, and logged. One patient, who had 2 tumors removed from her nose, was thought to have tissue necrosis at the wound edges at follow-up. Culture showed Escherichia coli, but owing to the clinical impression of wound edge necrosis, antibiotics were not prescribed, and the erythema resolved without sequelae. Analyses with and without this patient included yield-equivalent results.

ANALYSIS

Comparisons between the 2 study groups on demographic and wound characteristics were done using the Huber-White sandwich estimators for SEs because some participants contributed multiple observations. Comparisons between the 2 study
groups on the outcome variables were done with exact tests because of the low frequency of infections. The Fisher exact test was used for dichotomous outcomes and the Freeman-Halton extension of the Fisher exact test for the 8-level wound score.

### RESULTS

The 1172 wounds eligible for the study represented 93.5% of the 1253 wounds assessed for inclusion. Of the 1030 patients enrolled in the study, 910 had a single observation, 94 had multiple observations in which all wounds received either drug or control, and 26 patients had observations in both drug and control categories (treatment was obtained at different visits).

The patients in the 2 groups had similar demographic characteristics, and the lesions treated in each group were similar in character (Table 2). The mean defect diameter following Mohs micrographic surgery was similar for both groups (study, 1.80 cm; control, 1.72 cm). The mean volume of anesthetic solution injected was similar for both groups (study, 4.25 mL; control, 4.10 mL) and correlated with lesion size. There were no statistically significant differences between the 2 groups in demographic characteristics, number of non-Mohs micrographic surgery cases, Mohs stages, location of lesions, or type of reconstruction. A total of 452 patients with 598 surgical wounds received the clindamycin study solution for intraincisional antibiotic prophylaxis while 458 patients with 574 surgical wounds received the control solution.

Wound scores were lower in the clindamycin group (mean, 0.19) than in the control group (mean, 0.35) (P = .20; Mann-Whitney U). Six wounds (1.0%) in the clindamycin group and 23 wounds (4.0%) in the control group had wound scores of 4 or higher (P = .001, Fisher exact test) (Table 3).

Culture-positive wound infections were less frequent in the clindamycin group (4 wounds) than in the control group (14 wounds) (P = .02, Fisher exact test). The 4 organisms cultured from the study group grew *S aureus*. All of these infected wounds were on the face and were closed primarily. Twelve of the wound infections in the control group were *S aureus* infections, 1 was methicillin-resistant *S aureus*, and 1 was mixed *S aureus* and *Enterococcus*. Of the infected wounds in this group, 6 occurred on the face (other than the nose), 4 on the nose, 2 on the trunk, and 1 on the scalp. Twelve of these wounds were closed primarily, and 2 were closed by local flaps.

No allergic reactions (drug eruption or anaphylactoid reactions) were noted in either group. Gastrointestinal symptoms were recorded in both groups. In the clindamycin group, 4 patients noted postoperative nausea. In the control group, 1 patient noted postoperative cramping. No vomiting or diarrhea was reported in either group.

### COMMENT

This study further supports the efficacy of treatment with intracisional antibiotics to prevent postoperative wound infections in dermatologic surgery. In this study, local anesthetic administered with clindamycin prior to surgery decreased the incidence of clinical signs of wound infections and decreased the number of culture-proven postoperative wound infections when compared with placebo.

These findings concur with previous reports showing that intraincisional nafcillin treatment resulted in fewer postoperative wound infections. Our findings suggest that an alternative antibiotic, clindamycin, is also effective in preventing postoperative wound infections, thus providing an alternative antibiotic for penicillin-sensitive patients. While several penicillin alternatives were considered during study design, clindamycin was chosen primarily...
because of its antimicrobial activity against the most common skin pathogens, gram-positive cocci. It was also selected for its easy availability, low cost (pennies per 3-mL syringe of anesthetic), suitability for subcutaneous injection, and stability. Vancomycin was considered but was excluded owing to issues of use restriction and concern over promoting resistance to this “last chance” antibiotic. Ciprofloxacin was also considered, but despite adequate activity against *S. aureus*, it has less activity against *Streptococcus* species.

The potential benefits of intraincisional antibiotic prophylaxis include immediate delivery to the site where it is needed, ease of use, enhanced compliance, and low cost compared with other routes of delivery. There are also theoretically decreased potentials for resistance, drug interactions, intolerance, and bacterial or fungal overgrowth because miniscule quantities are delivered into a localized site. Though some of these potential benefits have been questioned, given the potential morbidity of surgical wound infections (despite their low 2%-4% incidence), the benefits appear to far outweigh the risks based on information currently available.

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REFERENCES


News and Notes

The 14th International Symposium on Contact Dermatitis and the 7th Asia-Pacific Environmental and Occupational Dermatology Symposium will be held together, September 19-21, 2003, in Seoul, Korea. The 2003 International Federation of Societies of Cosmetic Chemists Conference will be held immediately thereafter, September 22-24, 2003, in Seoul. It will be a good opportunity for dermatologists interested in contact dermatitis as well as cosmetic chemists to exchange scientific ideas and visit the Far East. For information, please contact Prof Hee Chul Eun, Department of Dermatology, Seoul National University College of Medicine, 28 Chongno-gu Yungon-dong Seoul, 110-744 Korea (phone: 82-2-760-2415; fax: 82-2-745-5934; e-mail: hceun@snu.ac.kr; Web site: www.iscd2003.com).