Intra-Incisional Prophylactic Antibiotics for Dermatologic Surgery

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**Objective:** To determine the efficacy of intra-incisional antibiotics in decreasing the risk of wound infections in cutaneous surgery.

**Design:** Prospective, blinded, randomized, placebo-controlled trial conducted during an 8-month period.

**Setting:** A private practice Mohs micrographic surgery referral center.

**Patients:** Seven hundred ninety consecutive patients referred for Mohs surgery or other dermatologic surgery were randomized to receive anesthesia either with study compound or placebo. The 2 groups were equivalent with respect to age and sex distribution and the lesions treated were similar in character. No patients were withdrawn for adverse effects.

**Interventions:** Patients received local anesthesia before surgery with either buffered lidocaine hydrochloride or a solution consisting of nafcillin sodium in buffered lidocaine.

**Main Outcome Measures:** All surgical wounds were evaluated in a blinded fashion at the time of suture removal (5-7 days) and scored according to a standardized assessment chart based on erythema, edema, and the presence of purulent discharge.

**Results:** Seven hundred ninety consecutive patients with 908 surgical wounds were enrolled in this study. A total of 12 wound infections were recorded. Eleven (2.5%) of these occurred in the control group, while only 1 (0.2%) occurred in the nafcillin group. This difference was highly significant ($P = .003$). Observers were blinded to patient groupings particularly for surgical wound scoring.

**Conclusions:** This study offers strong supporting data for the use of a single intra-incisional dose of an antibiotic administered immediately before dermatologic surgery. The use of nafcillin and buffered lidocaine solution is inexpensive, safe, convenient, and effective.

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**POSTOPERATIVE wound infections are serious complications of cutaneous surgery. They cause pain, delay healing, and most important, they result in noticeable scarring. For these reasons, prophylactic antibiotics are often used in cutaneous surgery, particularly for facial reconstruction.**

No guidelines exist for the use of prophylactic antibiotics in dermatologic surgery. For the prevention of endocarditis, bacteremia may be minimized by the use of oral antibiotics 1 hour before surgery or intravenous (IV) antibiotics. Wound infections in head and neck or general surgery may be reduced by the use of IV antibiotics 1 hour before surgery, but neither oral nor IV antibiotics have been well tested for preventing infections in cutaneous surgery. Furthermore, both IV administration and a 1-hour delay from the time of administering oral antibiotics to the beginning of surgery are significant inconveniences for elective office-based surgery. Therefore, these regimens are rarely used, and instead a common practice is to prescribe postoperative antibiotics when the patient is discharged from the office, or alternatively administering oral antibiotics within minutes of beginning surgery. The efficacy of these practices in decreasing wound infection is unknown. The purpose of this article is to report the efficacy of intra-incisional antibiotics for decreasing the risk of wound infections in cutaneous surgery. This route of administration should immediately achieve high antibiotic levels in tissue and is easily incorporated into an office-based surgical setting.

**RESULTS**

A total of 397 patients with 461 wounds received nafcillin as intra-incisional pro-

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PATIENTS, MATERIALS, AND METHODS

A prospective, blinded, randomized, placebo-controlled study was conducted during an 8-month period from October 25, 1995, to June 30, 1996. A total of 790 consecutive patients (411 males and 379 females) with 908 surgical wounds were enrolled in this study. Patients were randomly allocated to 2 groups. The control group (393 patients) received local anesthesia injected approximately 15 minutes before surgery by infiltration into the dermis and subcutaneous tissues, with 1% buffered lidocaine hydrochloride with epinephrine 1:100 000. The treatment group (397 patients) received local infiltration of anesthesia with a solution consisting of 0.5 mg of nafcillin sodium per milliliter of 1% buffered lidocaine hydrochloride with epinephrine 1:100 000.

The surgical procedures performed in this study included the reconstruction following Mohs micrographic excisions using complex linear closure, flaps, and skin grafts; the second stage of any staged repair; and excision and repair of benign dermatologic neoplasms. Preoperative skin preparation was performed using antiseptic scrub (Technicare, Care Tech Laboratories, St Louis, Mo) (3.0% chloroxylenol and 3.0% cocamidopropyl PG-dimonium chloride phosphate). All linear closures and flaps were sutured in 2 or more layers. Deep subcutaneous suturing was performed with absorbable materials (either polyglactin 910 or monofilament polyglyconate), and superficial suturing was performed using either rapidly absorbable plain gut or nylon sutures.

All surgical procedures were performed using sterile techniques in a licensed ambulatory surgical facility operating room. Patients who had received any systemic antibiotic within 2 weeks before surgery were excluded from the study; no prophylactic perioperative systemic antibiotics were administered. Patients with a known history of allergy to penicillin were assigned to the control group.

MATERIALS

The nafcillin sodium in buffered lidocaine solution used in this study was prepared as follows: 5 mL of sodium bicarbonate (84 mg/mL) was injected into a 50-mL vial of 1% lidocaine hydrochloride with epinephrine 1:100 000; 4.15 mL of the buffered lidocaine solution was used to reconstitute the vial containing 1 g of nafcillin sodium for injection; 0.1 mL of the reconstituted nafcillin solution was withdrawn from the vial and injected into the 50-mL vial of buffered lidocaine with epinephrine; the remainder of the vial of reconstituted nafcillin was placed in a freezer and kept frozen for later use. The 5-mL syringes were filled from the 50-mL vial of the preparation and kept refrigerated for use in the study as needed; any syringe not used within 48 hours of refrigeration was discarded.

We tested our nafcillin lidocaine study solution against laboratory strains of penicillinase-producing Staphylococcus aureus by incubation of equal volumes of Mueller Hinton broth inoculated with bacteria in concentrations of $10^7$ organisms per milliliter and the drug mixture at 4 different ratios of drug-to-bacteria broth (1:1, 1:2, 1:4, and 1:8). The inoculated test tubes were incubated at 35°C for 24 hours. The presence of growth was determined visually by a microbiologist. Any tube found to exhibit bacterial growth by 48 hours was considered positive, any without growth was considered negative.

We found complete and consistent bactericidal activity of all dilutions of the drug mixture as follows: after 11 days under refrigeration, after 60 days frozen, and after 7 days at room temperature. The drug mixture demonstrated no antibacterial effect in identical experiments after being stored at room temperature for 20 days, thus demonstrating some chemical instability of the solution. The control solution exhibited no antimicrobial activity by identical broth inoculation experiments.

WOUND SCORING

We enlisted the use of a recently published scoring system for assessment of the postoperative wound condition (Table 1). All surgical wounds were evaluated in a blinded fashion at the time of suture removal (5-7 days) and scored by the physician or nurse according to this assessment chart. A score of 4 or higher was classified as a wound infection. Specimens were obtained for culture from all infected surgical wounds, as well as from those with equivocal evidence of infection (wound scores ≥3). Wounds with scores of 3 that demonstrated heavy culture growth of a single pathogenic bacterium were also considered infections. All isolates recovered were identified by standardized methods of subculturing.

4.15 mL; nafcillin, 4.09 mL); this volume corresponds to the size of the defect repaired.

Wound scores were higher in the control group (average, 0.62) compared with the nafcillin group (average, 0.37) (Table 4). There were no allergic reactions or complications attributable to the use of nafcillin.

A total of 12 wound infections were recorded. Eleven (2.5%) of these occurred in the control group, while only 1 (0.2%) occurred in the nafcillin group. This difference was highly significant ($P = .003$).

All infections in the control group were caused by S aureus. None of these patients were assigned to the control group because of a penicillin allergy. Five of these infections occurred on the nose, 2 on the ear, 2 on the...
In this study we have shown that a single intra-incisional dose of a local anesthetic preparation containing nafcillin can lower the rate of postoperative wound infections compared with local anesthetic alone. The difference in infection rates between the treatment group (0.2%) and the control group (2.5%) was highly significant (P = .003). The rate of infection in our treatment group compares favorably with the lowest published rates for cutaneous surgery (range, 0.70%-43%).

**COMMENT**

Our study also provides the first data on wound infection rates in Mohs surgery without prophylaxis followed by various reconstructive procedures. Our infection rate for the 447 procedures performed in the control group was 2.5%, compared with the only other published rate of 4.3% for cutaneous surgery without prophylaxis. This 2.5% infection rate is nearly identical to the previously published rate of 2.29% for Mohs surgery and excisions that included the use of prophylactic perioperative antibiotics for selected high-risk wounds.

The intra-incisional delivery of antibiotics offers the advantage of immediate achievement of effective levels in tissue. Conversely, IV, intramuscular, or oral administration requires a significant delay to attain effective levels of an antimicrobial in tissue. Intravenous prophylactic antibiotics for surgical wound infections have been shown to be most effective when administered within the 2 hours before surgery, and are commonly given within 30 minutes of an operation. The optimal timing for intramuscular or oral administration for wound infection prophylaxis is not as clear; no data exist to support the common recommendation of administering oral prophylaxis 1 or 2 hours before a procedure. The translation of the timing recommendations of oral antibiotics for endocarditis prophylaxis to cutaneous surgery is complicated by the associated variabilities in absorption, dis-
caine hydrochloride, wide availability, and low cost.18 cutaneous administration, chemical stability in lido-
coccus pyogenes microbials.13 Although their use does not appear to be
facilitate the persistence, and augment the transmission
These include factors that encourage the development,
development of bacterial resistance to antimicrobials.
phylaxis. However, the risk for anaphylaxis should not
phylaxis in our study (an average of 2 mg per patient)
sorption of the small amount of nafcillin required for pro-
these theoretical benefits, even complete systemic ab-
absorption; secondary yeast or bacterial overgrowth com-
other medications; gastrointestinal intolerance; variable
toxic and some allergic adverse effects; interactions with
sites to antibiotics. These could include reduced risks for
vantages associated with reducing exposure of other body
Nafcillin was chosen for this study because of its
strain. Among these is the use of anti-
microbials.13 Although their use does not appear to be the
major cause of the development of resistant bacte-
rional mutants (these are most likely to develop through
spontaneous genetic mutations or transfer of genetic
material from one resistant species to another),12,14,15 the
selective pressures associated with antimicrobial
use creates ideal environments for resistant strains to
multiply. Correspondingly, their use is the predominant
cause of the proliferation of resistant strains, and has
led to the rapidly increasing prevalence of multidrug-
resistant pathogens.10,17 Therefore, it is intuitive that by
minimizing the number of ideal environments created for
resistant bacteria to multiply, their proliferation
should be diminished. The administration of an anti-
microbial agent only to the desired site of infection
prophylaxis removes the exposure of common body
sites that harbor bacteria (nasopharynx, respiratory
tract, gastrointestinal tract, and genitourinary tract),
and may decrease the proliferation or development of
these strains.
Nafcillin was chosen for this study because of its
spectrum of activity (coverage for S aureus and Strepto-
coccus pyogenes), suitability for intracutaneous and sub-
cutaneous administration, chemical stability in lido-
caine hydrochloride, wide availability, and low cost.18 Unpublished trials conducted by Wyeth Laboratories,
Philadelphia, Pa (oral communication, September 15,
1995) have shown sustained antimicrobial activity of an
unbuffered solution of reconstituted nafcillin in lido-
caine for up to 48 hours under refrigeration and 14
days frozen.1 However, our in vitro studies clearly
demonstrate chemical stability for much longer peri-
ods. It would be safe to keep refrigerated solutions for
up to 1 week, frozen solution for 1 month, and solution
may be stored at room temperature for up to 3
days, if necessary.
The dosage of nafcillin used in this study was based on
peak serum levels associated with IV administration of
500 mg of nafcillin sodium. To achieve similar concen-
trations in a lidocaine solution, 0.0022 mL of the
reconstituted nafcillin sodium solution mixed with 50
mL of lidocaine would be required. This minuscule vol-
ume of solution was believed to be impractical for clini-
cal use. It was determined that 0.1 mL was the minimal
volume of solution practical for precisely withdrawing
from the vial of reconstituted nafcillin sodium. This
volume, when diluted in 50 mL of buffered lidocaine,
produces a concentration of 0.5 mg of nafcillin sodium
per milliliter of lidocaine, which is 45 times the peak
serum levels obtained after IV administration of 500 mg
of nafcillin sodium. This was the concentration used for
this study.
The monetary cost of the nafcillin used in this
study was minimal. Our cost for ten 1-g vials of nafcil-
lin sodium for injection was $39.75; $3.98 per gram.
When reconstituted, each 1-g vial is capable of formu-
lating 40 separate 50-mL vials of our nafcillin-buffered
lidocaine solution. The average cost of nafcillin per
study case was less than 1 cent. The labor cost of for-
mulating and administering our nafcillin-lidocaine solu-
tion was also minimal. The additional time required for
preparation of the study solution was insignificant com-
pared with that for the standard (control) buffered lido-
caine solution.
The routine use of antibiotic prophylaxis for cuta-
necous surgery is controversial. Some Mohs surgeons have
reported the use of prophylactic antibiotics in up to 77%
of patients, and many use prophylaxis for all repairs of
facial defects.10 We have demonstrated the effectiveness of
a single intra-incisional dose of an antibiotic formulation
administered immediately before the repair of de-
fects following Mohs surgery; this method of prophy-
laxis may prove to be a better alternative for other high-
risk wounds.
In conclusion, we have found the use of nafcillin
and buffered lidocaine solution to be inexpensive, safe,
convenient, and effective. Because there are scenarios in
which antimicrobials should be administered for
wound infection prophylaxis, we believe that their local
administration is sensible, practical, and in this era of
cost containment and increasing drug resistance, it is
responsible.

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REFERENCES


