INTRANASAL MUPIROCIN TO PREVENT POSTOPERATIVE *STAPHYLOCOCCUS AUREUS* INFECTIONS

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ABSTRACT

Background Patients with nasal carriage of *Staphylococcus aureus* have an increased risk of surgical-site infections caused by that organism. Treatment with mupirocin ointment can reduce the rate of nasal carriage and may prevent postoperative *S. aureus* infections.

Methods We conducted a randomized, double-blind, placebo-controlled trial to determine whether intranasal treatment with mupirocin reduces the rate of *S. aureus* infections at surgical sites and prevents other nosocomial infections.

Results Of 4030 enrolled patients who underwent general, gynecologic, neurologic, or cardiothoracic surgery, 3864 were included in the intention-to-treat analysis. Overall, 2.3 percent of mupirocin recipients and 2.4 percent of placebo recipients had *S. aureus* infections at surgical sites. Of the 891 patients (23.1 percent of the 3864 who completed the study) who had *S. aureus* in their anterior nares, 444 received mupirocin and 447 received placebo. Among the patients with nasal carriage of *S. aureus,* 4.0 percent of those who received mupirocin had nosocomial *S. aureus* infections, as compared with 7.7 percent of those who received placebo (odds ratio for infection, 0.49; 95 percent confidence interval, 0.25 to 0.92; P=0.02).

Conclusions Prophylactic intranasal application of mupirocin did not significantly reduce the rate of *S. aureus* surgical-site infections overall, but it did significantly decrease the rate of all nosocomial *S. aureus* infections among the patients who were *S. aureus* carriers. (N Engl J Med 2002;346:1871-7.)

EACH year, more than 40 million patients undergo surgery in the United States,[1] and up to 20 percent of these patients acquire at least one nosocomial infection in the postoperative period.[2] Infections at surgical sites are the third most common nosocomial infections and complicate 1 to 10 percent of operations.[2] These infections are associated with substantial morbidity and mortality, double the length of hospitalization, and increase the cost of health care in the United States by $5 billion to $10 billion annually.[3-7]

Staphylococcus aureus causes 25 percent of nosocomial infections and contributes substantially to the complications and costs of hospitalization.[3] The ecologic niche of *S. aureus* is the anterior nares, and 25 to 30 percent of the population is colonized at a given time.[8-10] Patients who are carriers are at higher risk for staphylococcal infections after invasive medical or surgical procedures than are those who do not carry this organism.[8,10] Carriers of *S. aureus* are also two to nine times as likely as noncarriers to have surgical-site infections.[8,10]

Two percent mupirocin calcium ointment (Bactroban Nasal, GlaxoSmithKline) is a topical antibiotic that decolonizes the anterior nares.[11,12] Decolonization of the anterior nares appears to prevent *S. aureus* infections among patients who are receiving dialysis, thereby decreasing complications and costs.[13-16] Several studies have reported lower rates of surgical-site infection among patients who received mupirocin than among historical control subjects.[17-19] However, the efficacy of mupirocin has not been studied rigorously among surgical patients.

We conducted a clinical trial — the Mupirocin and the Risk of *Staphylococcus aureus* (MARS) Study — to determine whether preoperative intranasal application of mupirocin ointment would decrease the rate of *S. aureus* infections at surgical sites. In addition, we assessed whether mupirocin decreased the overall rate of nosocomial infections caused by *S. aureus.*

METHODS

Study Design and Patients

This randomized, double-blind, placebo-controlled clinical trial was approved by the institutional review board of the University of Iowa College of Medicine. The study evaluated adults who underwent elective and nonemergency cardiothoracic, general, oncologic, gynecologic, or neurologic surgical procedures at the University of Iowa Hospitals and Clinics and the Veterans Affairs Medical Center in Iowa City between April 1995 and December 1998.

All adult patients who provided written informed consent and met the study criteria were randomly assigned to receive either

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2 percent mupirocin calcium ointment or an identical-appearing placebo ointment. Randomization was stratified within each surgical service (general, gynecologic, cardiothoracic, and neurologic). A patient could be enrolled in the study only once. We excluded patients who were allergic to mupirocin or glycerin ester, patients who were pregnant or breast-feeding, patients who were participating in another clinical trial, patients who had had *S. aureus* infections within the previous month, those who had documented disruption of the nasal and facial bones, and those who were only having permanent central catheters inserted.

Study Medication and Follow-up

Cotton swabs were used by health care workers or the patient to apply the mupirocin or placebo to the interior of each anterior naris twice daily for up to five days before the operative procedure. Patients were monitored for a mean of 30 days (range, 25 to 35) after their operations to determine whether they acquired *S. aureus* infection. Study personnel examined hospitalized patients and reviewed their medical records every three to five days and telephoned discharged patients weekly during the follow-up period to determine whether the patients had signs or symptoms of infection. Patients who had signs of infection were asked to telephone the study personnel immediately.

To ascertain the patients' compliance, the study personnel reviewed medical records and diary cards listing the dates and times at which mupirocin or placebo was applied. In addition, study personnel asked patients whether they had had any side effects.

Surveillance and Definitions

Surveillance for nosocomial infections has been conducted continuously at both hospitals since 1976. The methods of surveillance have previously been validated.[20,21]

Nosocomial infections were identified with the use of definitions that were based on those of the Centers for Disease Control and Prevention.[22] A surgical-site infection was defined by the occurrence of one of the following within 30 days after the operation: the wound drained purulent material; the wound drained serosanguineous material, the edges of the wound and surrounding tissues were erythematous, and the wound culture yielded a pathogen; or a physician stated in the medical record that the surgical site was infected. Stitch abscesses were not considered surgical-site infections. Three physicians who were unaware of the patients' treatment assignments reviewed the records of all patients with *S. aureus* infections at surgical sites to ensure that the criteria for infection were met. We considered an infection to be caused by a specific pathogen, such as *S. aureus,* if the patient met the criteria for nosocomial infection at a particular site and if the organism was obtained from a cultured site.

The McCabe and Jackson score (nonfatal, ultimately fatal, or fatal)[23] and the Karnofsky performance status[24] were used to determine the severity of underlying illness. The risk index developed by the National Nosocomial Infections Surveillance System was used to predict risk, as described previously.[25] Scores can range from 0 to 3, and higher scores indicate a higher risk of infection.

Perioperative Care

Surgeons followed standard clinical practice and used standard prophylactic antimicrobial regimens when appropriate. Patients who were undergoing cardiac procedures showered with chlorhexidine the night before and the morning of the procedure. In the operating room, the site of each incision was cleansed with an iodophor-based product.

Microbiology

Nasal cultures were obtained by rubbing a premoistened Dacron swab in the anterior vestibule of each naris. Cultures were obtained from surgical sites when signs and symptoms of infection were observed. Standard microbiologic methods were used to identify *S. aureus.*[26] Isolates were saved in skim milk at −70°C.

In vitro susceptibility of the isolates to oxacillin was determined by disk-diffusion testing, performed according to methods specified by the National Committee for Clinical Laboratory Standards.[27] Susceptibility to mupirocin was determined with the E test (AB Biodisk), according to the manufacturer's instructions. An organism was considered resistant to mupirocin if the minimal inhibitory concentration exceeded 4 μg per milliliter.[28]

Pulsed-field gel electrophoresis was performed as previously described.[27] To be considered a match, the resulting patterns could not differ from each other by more than three bands.[29]

Statistical Analysis

We estimated that *S. aureus* infections would occur at surgical sites in 2.8 percent of patients. Overall, we calculated that 2023 patients were needed in each group to detect a 50 percent reduction in the rate of *S. aureus* surgical-site infections among patients who received intranasal mupirocin ointment (1.4 percent [28 patients] vs. 2.8 percent [57 patients]), given a two-tailed alpha level of 5 percent and a statistical power of 85 percent.

The rate of *S. aureus* infections at surgical sites was the primary end point. The secondary end points were the rates of surgical-site infections among patients with nasal carriage of *S. aureus,* the overall and site-specific rates of nosocomial infection, and the rates of nosocomial infection with *S. aureus.*

The two groups were compared with use of either Student's t-test or Wilcoxon's rank-sum test for continuous variables and Fisher's exact test for categorical variables. Variables that differed significantly between the groups were used as covariates in a logistic-regression analysis to evaluate the effect on the outcome of mupirocin as compared with that of placebo. Odds ratios and corresponding 95 percent confidence intervals were calculated. All tests were two-tailed, and a P value of less than 0.05 was considered to indicate statistical significance. Data were analyzed at the University of Iowa in the Department of Preventive Medicine, and the sponsor did not have control over the data or the analysis.

RESULTS

The team identified 5257 potential study participants, 4030 (76.7 percent) of whom were enrolled and underwent randomization (Fig. 1). Of these, 166 were excluded from the analysis, because they were not undergoing an eligible operation (49 in the mupirocin group and 48 in the placebo group), they received no study medication (22 and 26, respectively), or they met both exclusion criteria (8 and 13, respectively). Thus, 3864 patients (95.9 percent) were included in the intention-to-treat analysis, 1933 of whom received mupirocin and 1931 of whom received placebo. Of the patients included in the analysis, 3551 (91.9 percent) completed the study. Of the 479 patients who underwent randomization but did not complete the study, 249 received mupirocin (12.4 percent of the 2012 assigned to mupirocin), and 209 received placebo (10.4 percent of the 2018 assigned to placebo; P=0.05); the remaining 21 patients did not receive any study drug.

Patients in the two groups were similar with respect to demographic and surgical characteristics, preoperative functional status, the number and types of under-

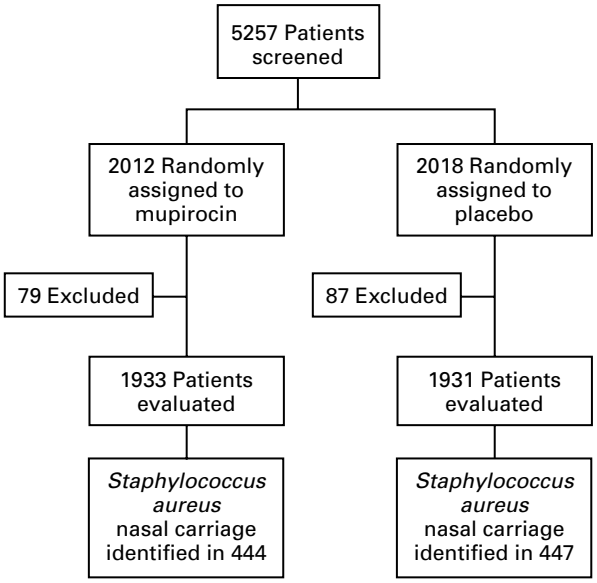

Figure 1. Patients Included in and Excluded from the Study.

lying diseases, and the types of surgical procedures (Tables 1 and 2). The only significant difference between the two groups was that patients who received placebo were more likely to have had renal disease than those who received mupirocin (17.4 percent vs. 14.9 percent; odds ratio, 1.20; 95 percent confidence interval, 1.01 to 1.44; P=0.04).

In both groups, 82.6 percent of patients received at least three doses of the treatment regimen. Overall, nasal carriage of *S. aureus* was eliminated in 83.4 percent of patients who received mupirocin, as compared with 27.4 percent of patients who received placebo (P<0.001) (Table 3). Carriage of *S. aureus* was eliminated from 81.3 percent of carriers (P<0.001) who received three to five doses of mupirocin and from 93.3 percent of patients who received six or more doses of mupirocin. Of those who had negative preoperative nasal cultures, 5.9 percent of placebo recipients had *S. aureus* in their nares postoperatively, as compared with 1.0 percent of mupirocin recipients (P<0.001). The preoperative and postoperative rates

TABLE 1. CHARACTERISTICS OF THE 3864 PATIENTS IN THE INTENTION-TO-TREAT POPULATION AND THE 891 PATIENTS WITH NASAL CARRIAGE OF *STAPHYLOCOCCUS AUREUS*, ACCORDING TO STUDY GROUP.*

CHARACTERISTIC	TOTAL POPULATION		*S. AUREUS* CARRIERS	
	MUPIROCIN	PLACEBO	MUPIROCIN	PLACEBO
Male sex — no./total no. (%)	979/1933 (50.6)	1016/1931 (52.6)	233/444 (52.5)	246/447 (55.0)
White race — no./total no. (%)	1873/1933 (96.9)	1859/1931 (96.3)	432/444 (97.3)	430/447 (96.2)
Age — yr	53.8±16.3	54.2±16.5	50.7±16.1	52.0±17.4
Body-mass index†	28.9±7.8	29.0±7.9	29.6±8.5	29.9±8.8
Karnofsky performance index	79.0±11.4	79.1±11.0	80.0±10.9	79.6±10.6
Death from underlying causes — no./total no. (%)	455/1933 (23.5)	454/1931 (23.5)	97/444 (21.8)	103/447 (23.0)
Median no. of coexisting illnesses	5	5	5	5
Diabetes — no./total no. (%)	307/1930 (15.9)	322/1928 (16.7)	65/442 (14.7)	71/447 (15.9)
Renal disease — no./total no. (%)	288/1933 (14.9)	336/1930 (17.4)	61/444 (13.7)	72/447 (16.1)
Cancer — no./total no. (%)	376/1931 (19.5)	378/1931 (19.6)	83/444 (18.7)	78/447 (17.4)
Pulmonary disease — no./total no. (%)	412/1930 (21.3)	433/1929 (22.4)	83/444 (18.7)	100/446 (22.4)
Obesity — no./total no. (%)	992/1930 (51.4)	1002/1928 (52.0)	241/443 (54.3)	264/447 (59.1)
Cigarette use — no./total no. (%)	583/1933 (30.2)	568/1930 (29.4)	117/444 (26.4)	121/446 (27.1)
Skin disease — no./total no. (%)	203/1930 (10.5)	199/1930 (10.3)	39/443 (8.8)	50/446 (11.2)
Previous surgery — no./total no. (%)	125/1930 (6.5)	108/1930 (5.6)	21/444 (4.7)	21/447 (4.7)
Preoperative infection — no./total no. (%)	487/1919 (25.4)	461/1920 (24.0)	85/444 (19.1)	82/446 (18.4)
Antibiotic use in prior month — no./total no. (%)	422/1921 (22.0)	400/1918 (20.9)	66/441 (15.0)	49/447 (11.0)
Immunosuppressive therapy — no./total no. (%)	198/1933 (10.2)	208/1931 (10.8)	43/444 (9.7)	42/447 (9.4)
S. aureus infection >1 mo previously — no./total no. (%)	162/1931 (8.4)	162/1931 (8.4)	39/444 (8.8)	44/447 (9.8)
Duration of preoperative stay — no./total no. (%)				
0 Days	1152/1927 (59.8)	1159/1929 (60.1)	263/444 (59.2)	264/446 (59.2)
1 Day	420/1927 (21.8)	412/1929 (21.4)	107/444 (24.1)	102/446 (22.9)
2–7 Days	246/1927 (12.8)	237/1929 (12.3)	56/444 (12.6)	64/446 (14.3)
≥8 Days	109/1927 (5.7)	121/1929 (6.3)	18/444 (4.1)	16/446 (3.6)

*Plus–minus values are means ±SD.

†Data on body-mass index (the weight in kilograms divided by the square of the height in meters) were missing for 1 of 1933 patients in the mupirocin group, 2 of 1931 patients in the placebo group, and 2 of 447 patients with nasal carriage in the placebo group.

TABLE 2. SURGICAL CHARACTERISTICS OF THE 3864 PATIENTS WHO COMPLETED THE STUDY AND THE 891 PATIENTS WITH NASAL CARRIAGE OF *STAPHYLOCOCCUS AUREUS*, ACCORDING TO STUDY GROUP.*

CHARACTERISTIC	TOTAL POPULATION		*S. AUREUS* CARRIERS	
	MUPIROCIN (N=1933)	PLACEBO (N=1931)	MUPIROCIN (N=444)	PLACEBO (N=447)
Surgery at UIHC — no. (%)	1782 (92.2)	1773 (91.8)	412 (92.8)	408 (91.3)
Service — no. (%)				
General surgery†	1206 (62.4)	1202 (62.2)	282 (63.5)	272 (60.8)
Neurosurgery	364 (18.8)	368 (19.1)	77 (17.3)	95 (21.3)
Cardiothoracic surgery	363 (18.8)	361 (18.7)	85 (19.1)	80 (17.9)
Inpatient — no. (%)	1626 (84.1)	1665 (86.2)	367 (82.7)	387 (86.6)
Wound classification — no. (%)‡				
Clean	1420 (73.7)	1458 (75.6)	330 (74.3)	356 (79.6)
Clean contaminated	420 (21.8)	396 (20.5)	99 (22.3)	78 (17.4)
Contaminated or dirty	87 (4.5)	75 (3.9)	15 (3.4)	13 (2.9)
Type of surgery — no. (%)§				
Routine or elective	1896 (98.4)	1901 (98.6)	435 (98.0)	440 (98.4)
Urgent or emergency	31 (1.6)	27 (1.4)	9 (2.0)	7 (1.6)
Lowest intraoperative body temperature — °C	34.2±4.0	34.2±3.8	34.1±4.1	34.3±3.6
Duration of surgery — min				
General surgery				
Median	168	168	165	182
25th–75th percentile	115–240	118–251	111–240	120–266
Neurosurgery				
Median	220	215	218	215
25th–75th percentile	180–291	169–303	192–283	175–325
Cardiothoracic surgery				
Median	302	305	296	295
25th–75th percentile	251–360	258–360	247–360	258–342
NNIS risk index¶	n=1877	n=1883	n=435	n=435
0	356 (19.0)	304 (16.1)	101 (23.2)	72 (16.6)
1	923 (49.2)	985 (52.3)	209 (48.0)	227 (52.2)
2	577 (30.7)	574 (30.5)	123 (28.3)	133 (30.6)
3	21 (1.1)	20 (1.1)	2 (0.5)	3 (0.7)

*Plus–minus values are means ±SD. UIHC denotes University of Iowa Hospitals and Clinics, and NNIS National Nosocomial Infections Surveillance System.

†Gynecologic surgery was included in the general-surgery category.

‡Data were available for 1927 of 1933 patients in the mupirocin group and 1929 of 1931 patients in the placebo group.

§Data were available for 1927 of 1933 patients in the mupirocin group and 1928 of 1931 patients in the placebo group.

¶Data on this scale from 0 to 3 were available for 1877 of 1933 patients in the mupirocin group, 1883 of 1931 patients in the placebo group, 435 of 444 patients with nasal carriage in the mupirocin group, and 435 of 447 patients with nasal carriage in the placebo group. Higher scores indicate a higher risk of infection.

of nasal carriage remained virtually unchanged among placebo recipients (Table 3).

Among patients included in the analysis, 438 (11.3 percent) had nosocomial infections: 218 (11.3 percent) in the mupirocin group and 220 (11.4 percent) in the placebo group. The rate of infection at the surgical site was 7.9 percent in the mupirocin group (152 patients) and 8.5 percent in the placebo group (164 patients). Swabs of infected wounds were cultured in the case of 111 of 152 mupirocin recipients (73.0 percent) and 127 of 164 placebo recipients (77.4 percent). After the exclusion of patients with surgical-site infections whose wounds were not cultured, the rate of *S. aureus* infection at surgical sites was 2.3 percent among mupirocin recipients and 2.4 percent among placebo recipients (Table 4).

Of the 129 patients with nosocomial infections who had nasal carriage of *S. aureus*, wound cultures were obtained from 107 (43 of 57 in the mupirocin group and 64 of 72 in the placebo group). The risk of nosocomial infection with *S. aureus* at any site among patients with nasal carriage of *S. aureus* was significantly lower among those who received mupirocin than among those who received placebo (odds ratio, 0.49; 95 percent confidence interval, 0.25 to 0.92; P=0.02) (Table 4). Seventeen carriers who received mupirocin

TABLE 3. PREOPERATIVE AND POSTOPERATIVE PREVALENCE OF NASAL CARRIAGE OF *STAPHYLOCOCCUS AUREUS.**

VARIABLE	MUPIROCIN GROUP		PLACEBO GROUP	
	ALL PATIENTS (N=1933)	*S. AUREUS* CARRIERS (N=444)	ALL PATIENTS (N=1931)	*S. AUREUS* CARRIERS (N=447)
	number/total number (percent)			
Preoperative nasal carriage	444/1933 (23.0)	444/444 (100)	447/1931 (23.1)	447/447 (100)
Postoperative nasal carriage	88†/1924 (4.6)	73/441 (16.6)	410‡/1924 (21.3)	323/445 (72.6)

*Postoperative nasal culture was not obtained for nine mupirocin recipients (three of whom were *S. aureus* carriers) and seven placebo recipients (two of whom were *S. aureus* carriers).

†Fifteen of these patients had negative preoperative cultures.

‡Eighty-seven of these patients had negative preoperative cultures.

TABLE 4. OVERALL AND *STAPHYLOCOCCUS AUREUS*–SPECIFIC RATES OF NOSOCOMIAL INFECTION AMONG PATIENTS WHO RECEIVED MUPIROCIN AND THOSE WHO RECEIVED PLACEBO.

TYPE OF INFECTION	MUPIROCIN RECIPIENTS			PLACEBO RECIPIENTS		
	TOTAL (N=1933)	*S. AUREUS* CARRIERS (N=444)	NONCARRIERS (N=1489)	TOTAL (N=1931)	*S. AUREUS* CARRIERS (N=447)	NONCARRIERS (N=1484)
	number/total number (percent)					
Nosocomial infection*	218/1933 (11.3)	57/444 (12.8)	161/1489 (10.8)	220/1931 (11.4)	72/447 (16.1)	148/1484 (10.0)
Nosocomial *S. aureus* infection*	45/1884 (2.4)	17/430 (4.0)	28/1454 (1.9)	55/1886 (2.9)	34/439 (7.7)†	21/1447 (1.5)
Surgical-site infection	152/1933 (7.9)	44/444 (9.9)	108/1489 (7.3)	164/1931 (8.5)	52/447 (11.6)	112/1484 (7.5)
S. aureus surgical-site infections‡	43/1892 (2.3)	16/432 (3.7)	27/1460 (1.8)	46/1894 (2.4)	26/439 (5.9)	20/1455 (1.4)

*This group includes *S. aureus* infections of the bloodstream, respiratory tract, catheter, and surgical site.

†P=0.02 for the comparison with the *S. aureus* carriers in the mupirocin group (odds ratio, 0.49; 95 percent confidence interval, 0.25 to 0.92).

‡Since not all wounds were cultured, the causative organisms were unknown for 49 nosocomial infections in the mupirocin group (14 were in *S. aureus* carriers, 12 of whom had surgical-site infections; and 35 were in noncarriers, 29 of whom had surgical-site infections), and 45 nosocomial infections in the placebo group (8 were in *S. aureus* carriers, 8 of whom had surgical-site infections; and 37 were in noncarriers, 29 of whom had surgical-site infections).

(4.0 percent) had nosocomial *S. aureus* infections: 16 were surgical-site infections and 1 was a bloodstream infection. Thirty-four carriers who received placebo (7.7 percent) had nosocomial *S. aureus* infections: 26 were surgical-site infections, 4 were bloodstream or catheter infections, and 4 were lower respiratory tract infections.

Among placebo recipients, the odds of a surgical-site infection with *S. aureus* was 4.5 times as high among patients with nasal carriage as among noncarriers (95 percent confidence interval, 2.47 to 8.21; P<0.001). Logistic-regression analysis showed that renal disease (P=0.32), preoperative use of antimicrobial agents (P=0.41), and perioperative use of antimicrobial agents (P=0.32) had no significant effect on the rate of surgical-site infections with *S. aureus*. The risk of such an infection was significantly higher among patients whose National Nosocomial Infections Surveillance System risk index was 2 (odds ratio, 3.37; 95 percent confidence interval, 1.56 to 7.29; P=0.002) or 3 (odds ratio, 8.24; 95 percent confidence interval, 2.03 to 33.52; P=0.003) than among those whose score was 0.

Of the 4030 patients who underwent randomization, 97 of the 2012 patients in the mupirocin group (4.8 percent) and 96 of the 2018 patients in the pla-

cebo group (4.8 percent) reported side effects such as rhinorrhea and itching at the application site. Five patients withdrew from the study because of adverse effects such as nasal burning, nasal bleeding, and headache; one of these patients received mupirocin, and four received placebo. Other adverse events that were not considered related to treatment were reported by 111 patients in the mupirocin group (5.5 percent) and 143 in the placebo group (7.1 percent). The death rate was similar in the two groups (2.2 percent in the mupirocin group [45 patients] and 2.7 percent in the placebo group [55 patients]). No deaths were attributed to mupirocin therapy.

Paired isolates were available from 39 of 89 patients who had surgical-site infections with *S. aureus.* The results of pulsed-field gel electrophoresis of samples from 33 patients (84.6 percent) demonstrated that the *S. aureus* strain isolated from the nares was identical to that isolated from the infected site. Furthermore, pulsed-field gel electrophoresis revealed 39 different strains among the 77 *S. aureus* isolates obtained from 77 patients with surgical-site infections and 8 strains that were shared by 1 or more patients. Four of the eight shared strains were isolated at approximately the same time.

A total of 150 *S. aureus* isolates (90 from wounds and 60 from the nares) from 77 patients with surgical-site infections and 871 isolates from the nares of patients were tested for in vitro susceptibility to mupirocin. Only 6 of 1021 *S. aureus* isolates (0.6 percent), obtained from six patients, were resistant to mupirocin during the four-year study period. The minimal inhibitory concentrations of mupirocin for the resistant strains ranged from 16 to 2048 μg per milliliter. Seven of the 871 isolates from patients were resistant to oxacillin (0.8 percent).

DISCUSSION

In this large, randomized, placebo-controlled, double-blind trial of *S. aureus* infections in surgical patients, there was no significant difference in the rate of surgical-site infections between the mupirocin and placebo groups. Several factors may explain why we did not detect a significant reduction in the rate of these infections. First, the rate of *S. aureus* infections at surgical sites was quite low. Second, only 47.2 percent of such infections occurred among patients with nasal carriage of *S. aureus,* which was substantially lower than our a priori estimate. Third, the results of pulsed-field gel electrophoresis suggested that some patients may have been infected with strains transmitted from health care workers or other patients. Perioperative prophylaxis with mupirocin would not prevent infections that originated in this manner.

In this study, however, mupirocin significantly decreased the rate of nosocomial infections due to *S. aureus,* specifically among patients with nasal carriage of *S. aureus,* the group expected to be at increased risk. Several studies have demonstrated that the risk of nosocomial infections of both the bloodstream and the lower respiratory tract is higher among patients who carry *S. aureus* in their nares.[30-33] Taken together our results and those of previous studies suggest that intranasal mupirocin prophylaxis may prevent nosocomial *S. aureus* infections at several sites. Nonetheless, an additional randomized clinical trial should be performed to identify surgical patients who would benefit the most from the prophylactic use of mupirocin and to determine whether such treatment is truly cost effective.

One concern is that prophylactic use of mupirocin might lead to widespread resistance. Using the short and defined course of mupirocin prescribed by the protocol, we identified only four isolates that were resistant to mupirocin, three of which were obtained from patients who were not treated with mupirocin. Thus, a single, short course of mupirocin for preoperative prophylaxis did not appear to select for mupirocin-resistant *S. aureus* isolates.

Although mupirocin prophylaxis did not reduce the overall rate of *S. aureus* infections at surgical sites, it significantly reduced the rate of nosocomial *S. aureus* infections. On the basis of other studies,[17,34,35] we believe that preoperative treatment with mupirocin will be cost effective in patients with nasal carriage of *S. aureus.*[17,34,35] We conclude that mupirocin therapy is safe, has a protective effect among nasal carriers of *S. aureus,* and is a reasonable adjuvant agent to prevent such infections in carriers after surgery.

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APPENDIX

The MARS Study Team comprised Suzanne Bentler, Kyce Brown, Will Bushnell, Stacy Coffman, Jane Finlay, Robert Forbes, Melinda Hintemeister, Christopher James, Bryce Helgerson, Alka Preston, and Judy Swift.

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