Staphylococcus Aureus Prophylaxis in Hemodialysis Patients Using Central Venous Catheter: Effect of Mupirocin Ointment

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Abstract. Central venous catheterization is a common technique to establish rapid and temporary access for hemodialysis. However, it is a known risk factor for *Staphylococcus aureus* infection and bacteremia. Mupirocin is a topical antibiotic with high *in vitro* anti-staphylococcal activity. A randomized prospective trial was conducted to assess the effectiveness of mupirocin ointment in the prevention of *Staphylococcus aureus* skin and catheter colonization, and episodes of bacteremia in 136 end-stage renal disease patients. Of these, 67 received skin disinfection at the venous catheter insertion site with povidone iodine (control group), and 69 received the same treatment followed by application of 2% mupirocin ointment at the cannula site after catheter placement and at the end of each dialysis session. Patients were followed until catheter removal and were monitored for the development of *Staphylococcus aureus* skin/catheter colonization and episodes of bacteremia. Median duration of catheter use was greater in the mupirocin than in the control group (37 *versus* 20 d, $P < 0.01$). Patients in the mupirocin group had a significantly lower rate of *Staphylococcus aureus* isolation from the pericatheter skin (1.76 per 1000 *versus* 14.27 per 1000 patient-days, $P < 0.001$) and from the catheter surface (3.17 per 1000 *versus* 14.27 per 1000 patient-days, $P < 0.001$). The proportion of patients with *Staphylococcus aureus* skin infection at the insertion site was lower in the mupirocin group (4.3% *versus* 23.9%, $P = 0.001$). *Staphylococcus aureus*-associated bacteremia was observed in 17 patients (two in the mupirocin group [0.71 episodes per 1000 patient-days] and 15 in the control group [8.92 per 1000 patient-days], $P < 0.001$). The hazard ratio of developing *Staphylococcus aureus* bacteremia was 7.2 (95% confidence interval, 1.6 to 31.6) times greater in patients not receiving mupirocin. Mupirocin applied to the insertion site significantly reduces the risk of *Staphylococcus aureus* skin and catheter colonization, exit-site infection, and *Staphylococcus aureus* bacteremia in hemodialysis patients. (J Am Soc Nephrol 9: 1085–1092, 1998)

Central venous cannulation has become an accepted technique for establishing rapid access for hemodialysis patients while they await more definitive access (1–7). In tertiary referral centers, due to the frequent admission of patients with recently diagnosed end-stage renal disease (ESRD), without predialysis care and in emergency conditions, the use of these catheters for initial hemodialysis access has become commonplace and prolonged (8).

Infection is a major cause of morbidity among patients with renal failure and is second only to cardiovascular events as a cause of death in patients on maintenance dialysis (9). The frequency of *Staphylococcus aureus* bacteremia associated with vascular catheterization has been increasing in recent years (1–7,10–12). It often begins as a local colonization or infection of the skin at the insertion site of the catheter (10,13,14). This type of complication has been responsible for considerable morbidity, because it requires early removal of the catheter, use of systemic antibiotics, an alternative access site, and longer hospitalization.

Mupirocin is a nonsystemic antibiotic with high *in vitro* anti-staphylococcal activity (15) and is effective in eradicating *Staphylococcus aureus* carriage and treating skin infections (16–18). In a previous study, Hill *et al.* (14) reported that, in patients undergoing cardiothoracic surgery, mupirocin applied to the insertion site of internal jugular cannula reduced the rate of colonization of cannula tips by coagulase-negative *Staphylococci*. In the present study, we conducted a randomized trial to assess the effectiveness of prophylaxis with mupirocin ointment applied to the insertion site of central venous hemodialysis catheters in the prevention of *Staphylococcus aureus* skin and catheter colonization, and episodes of bacteremia compared with the use of povidone iodine alone.

Materials and Methods

A randomized prospective trial was conducted at the Escola Paulista de Medicina, a tertiary referral center in São Paulo, Brazil, with a dialysis unit that serves 35 to 40 patients weekly. Approximately 110 patients are treated in the unit per year. The study was approved by the institutional review board, and informed consent was obtained from all participants.

Patients eligible for central venous cannulation who were enrolled

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in the study included new ESRD patients without permanent venous access, those with peritoneal dialysis problems requiring urgent transfer to hemodialysis, and patients with sudden loss of arteriovenous fistula. Patients were excluded if they had acute renal failure, had used a central venous catheter within 1 mo of the beginning of the study, or presented with septicemia or a life-threatening infection.

Venous catheters (Mahurkar® dual lumen catheters, Quinton Instrument Co., Bothell, WA) were inserted by nephrology staff physicians, either in the internal jugular or subclavian positions, according to the aseptic Seldinger technique. All catheters were sutured in place without a subcutaneous tunnel or adhesive transparent dressing. After initial insertion of the catheters, only trained dialysis nurses changed the dressings or manipulated the cannulas, using rigorous aseptic technique. The catheters were initially injected with 2500 to 3000 U of heparin sodium and then flushed with the same dose after each dialysis. From June 1994 to December 1996, 136 patients were selected for the study. They were randomly assigned to receive skin disinfection at the catheter insertion site with 10% povidone iodine solution or after the same skin preparation, the application of sterile 2% calcium mupirocin ointment. Approximately 10 mm of ointment was squeezed from a 15-g tube with an outlet diameter of 5 mm (SmithKline Beecham Laboratories, Rio de Janeiro, Brazil) directly onto the cannulation site, immediately after catheter placement and at the end of each dialysis session (three times weekly) when the catheter was redressed. The cannulation site, cannula hub, and site connections were covered with sterile occlusive gauze dressing.

The randomization was performed using sealed, sequentially numbered envelopes. The sequence of alternative interventions was obtained from a computerized random number list, using blocked randomization (blocking size varying from 4 to 6).

At the time of inclusion in the study, demographic and clinical data were recorded. In addition, patients had the anterior nares cultured for *Staphylococcus aureus*.

Follow-Up

Catheter dressings were removed before each dialysis. One of us (Dr. Barbosa) assessed the cannula site for inflammation or the presence of pus at redressing and when the catheter was removed. Participants were followed up until the catheter was removed, which occurred for the following reasons: catheter malfunction, viability of an arteriovenous fistula, the presence of local erythema and a purulent discharge, or bacteremia without another identifiable source of infection. If local erythema alone was present, the cannula was left *in situ*, provided there was no evidence of bacteremia or systemic infection. No patient was lost to follow-up, and no catheter was exchanged over guidewire. No patient used more than one catheter during the study period. Catheters were only used for dialysis.

Immediately before cannula removal, the skin around the site was sampled for culture with a saline-moistened cotton swab and then prepared with povidone iodine. When there were signs of local infection, the pericatheter skin area was sampled for culture. When a patient presented with a fever (>37.8°C), with or without other signs of infection, blood cultures were collected from peripheral veins, using standard aseptic technique.

Definitions

Staphylococcus aureus catheter-associated bacteremia was considered confirmed (definite) if the following criteria were met: (*1*) one or more blood cultures yielded *Staphylococcus aureus* while the catheter was in place; (*2*) fever >37.8°C was accompanied by rigors; (*3*) clinical examination, chest radiography, laboratory investigation, and microbiologic data that did not suggest another source of *Staphylococcus aureus* bacteremia; and (*4*) recovery of *Staphylococcus aureus* on catheter tip culture. The diagnosis of *Staphylococcus aureus* catheter-associated bacteremia was considered probable if criteria *2*, *3*, and *4* were met but the blood culture revealed no growth and, in addition, no other source of infection that could have explained the fever had been detected. Catheter exit-site *Staphylococcus aureus* infection was defined if there were: (*1*) objective signs of pericatheter skin infection on physical examination (erythema, drainage or purulent exudate at the catheter site); and (*2*) recovery of *Staphylococcus aureus* from the material expressed from the catheter exit-site.

Microbiology

Nares and pericatheter skin samples were obtained using sterile, premoistened calcium alginate swabs (Cefar-Farmaco Diagnostic, São Paulo, Brazil) and were transported to the microbiology laboratory, where they were immediately streaked onto plates containing tryptic soy agar with 5% sheep blood and mannitol-salt agar (DIFCO Laboratories, Detroit, MI). All cultures were incubated at 35°C for 48 h and examined daily for evidence of growth. Gram-positive cocci that produced catalase and coagulase were identified as *Staphylococcus aureus*. Oxacillin-resistant *Staphylococcus aureus* strains were defined as a zone of inhibition less than 11 mm (disk content of oxacillin was 1 μg). Blood samples (20 ml) were collected in Bactec bottles, and cultures were processed by an automated method of isolation of microorganisms (Bactec 9240, Becton Dickinson).

After the catheter was removed, approximately 50 mm of the catheter tip was rolled across Rodac® plates containing tryptic soy agar with 5% sheep blood (AS, Oxoid, Basingstoke, Hampshire, United Kingdom), and mannitol-salt agar (ASM, Oxoid), prepared previously in the laboratory, according to the semiquantitative method of Maki *et al.* (19). Catheters yielding >15 colony-forming units were considered significantly colonized. The microbiologists processing the specimens were unaware of the patients' allocation group.

Statistical Analyses

Sample Size. We estimated that 140 patients would be needed (70 per group) to detect a 50% difference (*i.e.*, a reduction from 46 to 23%) in the overall rate of *Staphylococcus aureus* isolation (from the skin, catheter, or blood) between the two groups, assuming $\alpha = 0.05$ (two-tailed) and $\beta = 0.20$.

The *t* test or the Mann–Whitney test was used to compare continuous variables. Fisher's exact test or χ^2 tests were used to compare proportions. Incidence rates were compared by incidence density χ^2 statistics (20). Cumulative probabilities of developing *Staphylococcus aureus* colonization/infection or bacteremia were estimated by the Kaplan–Meier method; statistical significance between probability curves was assessed by the log-rank test. The Cox proportional hazards regression analysis was used to compare the risk of *Staphylococcus aureus* isolation between groups. Hazard ratios (risk ratios [RR]) and 95% confidence intervals (CI) were calculated. The BMDP Statistical Software (Los Angeles, CA, 1992) was used to analyze the data. A *P* value <0.05 (two-tailed) was used to indicate statistical significance.

Results

One hundred and thirty-six patients were entered into the study; 69 were assigned to prophylaxis with mupirocin and 67 to the control group. The cumulative follow-up time was 4518 patient-days. Median (range) duration of follow-up was 22.5 d

(3 to 142 d). All patients were followed up until catheter removal.

Baseline characteristics of the patients in the study groups are shown in Table 1. There was a greater proportion of female patients in the mupirocin group compared with the control group. The former group had a greater but nonsignificant proportion of non-white individuals and of patients of lower educational level.

Patient features during the catheterization period are shown in Table 2. In the mupirocin group, the frequency of hospitalization was lower, the median duration of catheter use was longer (37 *versus* 20 d, $P < 0.01$), and the median number of dialysis sessions using the catheter was greater (16 *versus* 9, $P < 0.01$). Among the causes of catheter removal, those associated with clinical infection of the insertion site and/or fever were less common in patients receiving mupirocin (Table 2).

The main study outcomes related to *Staphylococcus aureus* isolation are shown in Table 3. Patients in the mupirocin group had a significantly lower rate of *Staphylococcus aureus* isolation from the pericatheter skin area, catheter surface, or blood samples. After 30 d of catheter placement, the cumulative probability of not having *Staphylococcus aureus* recovered from samples of the skin around the catheter was 96.4% (95% CI, 91.5 to 100) in the mupirocin group and 62% (95% CI, 47.9 to 76.1) in the control group ($P < 0.001$) (Figure 1). The proportion of patients with clinical infection due to *Staphylococcus aureus* in the skin around the catheter was much lower in the mupirocin group (4.3% [3 of 69] *versus* 23.9% [16 of 67], $P = 0.001$). The risk of *Staphylococcus aureus* isolation in

Table 1. Baseline patient characteristics

Characteristic	Mupirocin ($n = 69$)	Control ($n = 67$)
Age, yr		
mean (SEM)	48.4 (2.0)	44.6 (1.9)
range	16 to 80	16 to 74
Male/female, *n* (%)	34/35 (49.3/50.7)	46/21 (68.7/31.3)[a]
Race, *n* (%)		
white	41 (59.4)	50 (74.6)
non-white	28 (40.6)	17 (25.4)
Education, *n* (%)		
illiterate/primary school	55 (79.7)	44 (65.7)
secondary/high-school/college	14 (20.3)	23 (34.3)
Income (U.S.$/mo)		
median (range)	500 (65 to 3000)	500 (115 to 6000)
Primary diagnosis, *n* (%)		
glomerulonephritis	12 (17.4)	9 (13.4)
hypertension	28 (40.6)	27 (40.3)
diabetes mellitus	11 (15.9)	14 (20.9)
interstitial nephritis	2 (2.9)	4 (6.0)
other/unknown	16 (23.1)	13 (19.4)
Comorbid factors at study entry, *n* (%)		
bacterial infection[b]	16 (23.2)	14 (20.9)
pulmonary edema		1 (1.5)
malignancy		1 (1.5)
chronic obstructive lung disease	1 (1.4)	
gastric bleeding	1 (1.4)	
Patients starting dialysis, *n* (%)	49 (71.0)	56 (84.8)
Previous catheter use, *n* (%)	8 (11.6)	7 (10.4)
Nasal *Staphylococcus aureus* carriage, *n* (%)	28 (40.6)	27 (40.3)
Laboratory parameters[c]		
serum creatinine, mg/dl	10.8 (0.7)	9.9 (0.5)
serum urea nitrogen, mg/dl	101.3 (5.6)	95.3 (6.1)
serum albumin, g/dl	3.3 (0.1)	3.3 (0.1)
hematocrit, %	25.8 (0.8)	24.4 (0.7)

[a] $P < 0.05$ for comparison with the mupirocin group.

[b] In the mupirocin group: urinary tract infection, $n = 8$; peritonitis, $n = 3$; arteriovenous fistula infection, $n = 2$; pneumonia, $n = 1$; subcutaneous abscess, $n = 1$; and otitis, $n = 1$. In the control group: urinary tract infection, $n = 7$; peritonitis, $n = 2$; pneumonia, $n = 2$; arteriovenous fistula infection, $n = 1$; sinusitis, $n = 1$; and ocular infection, $n = 1$.

[c] Obtained immediately before a dialysis session.

Table 2. Characteristics of the patients and causes of catheter removal, by treatment group[a]

Characteristic	Mupirocin (n = 69)	Control (n = 67)
Hospitalization, n (%)[b]	51 (73.9)	58 (86.6)[c]
median (range) duration, days	6 (1 to 46)	5 (2 to 56)
Use of antibiotics, n (%)	17 (24.6)	17 (25.4)
median (range) duration, days	8 (4 to 14)	10 (5 to 14)
Catheter location, n (%)		
internal jugular vein	19 (27.5)	20 (29.9)
subclavian vein	50 (72.5)	47 (70.1)
Duration of catheter placement		
median (range), days	37 (4 to 142)	20 (3 to 136)[d]
No. of cumulative days catheter in place	2836	1682
Median (range) no. of dialysis sessions	16 (2 to 65)	9 (2 to 44)[d]
No. of cumulative dialysis sessions	1270	735
Causes of catheter removal, n (%)[e]		
local skin infection	6 (8.7)	25 (37.3)
local skin infection + fever	3 (4.3)	15 (22.4)
fever without known source of infection	9 (13.0)	6 (9.0)
inadequate blood flow	17 (24.6)	5 (7.5)
inadvertent withdrawal	1 (1.4)	1 (1.5)
no longer needed	33 (47.8)	15 (22.4)

[a] For causes of catheter removal, P value represents an overall test of significance.
[b] Number of hospitalizations due to infectious episodes: 5 (7.2%) in the mupirocin group and 14 (20.9%) in the control group ($P < 0.05$).
[c] $P < 0.05$, for the comparison between mupirocin and control group.
[d] $P < 0.01$, for the comparison between mupirocin and control group.
[e] $P < 0.001$, for the comparison between mupirocin and control group.

the skin and in catheter samples was 7.7 and 4.5 times greater, respectively, in patients not receiving mupirocin prophylaxis. *Staphylococcus aureus* was recovered from the catheter of nine patients in the mupirocin group and from 24 patients in the control group. Of these, *Staphylococcus aureus* bacteremia was diagnosed in two patients of the mupirocin group and in 15 patients of the control group.

Eleven cases of confirmed *Staphylococcus aureus* bacteremia were detected (two oxacillin-resistant *Staphylococcus aureus* and nine oxacillin-sensitive *Staphylococcus aureus*). Blood cultures were positive for *Staphylococcus aureus* in 12 patients. All but one of these cases had simultaneous catheter colonization. The incidence rate of *Staphylococcus aureus* bacteremia was 0.35 per 1000 patient-days in the mupirocin group and 5.95 per 1000 patient-days in the control group ($P < 0.001$). Six additional cases had probable *Staphylococcus aureus* bacteremia (one in the mupirocin group). The overall risk of developing *Staphylococcus aureus* bacteremia was 7.2 times greater in the control than in the mupirocin group. The overall incidence rate of *Staphylococcus aureus* bacteremia was 1.58 per 1000 dialysis sessions and 20.41 per 1000 dialysis sessions in the mupirocin and control groups, respectively ($P < 0.001$). After 15 d of catheter placement, the cumulative probability of remaining free of developing *Staphylococcus aureus* bacteremia (confirmed or probable) was 96.6% (95% CI, 92.1 to 100) and 82.0% (95% CI, 72.4 to 91.6) for the mupirocin and control groups, respectively. The corresponding figures after 30 d were 96.6% (95% CI, 92.1 to 100) and 75.7% (95% CI, 64.5 to 86.9) ($P < 0.001$ for the comparison of overall curves) (Figure 2).

Table 4 shows more detailed results of all microorganisms isolated from samples collected at various sites in the study groups. In addition to the reduction in *Staphylococcus aureus* isolation, patients receiving mupirocin also had a significantly lower incidence of coagulase-negative *Staphylococci* isolation from both the skin and the catheter. The overall proportion of Gram-negative organisms identified was not significantly different between the groups. There were no adverse reactions associated with mupirocin use, and there were no catheter-related deaths.

Discussion

Our results show that the application of mupirocin to the skin around the catheter insertion site reduces the risk of *Staphylococcus aureus* skin and cannula colonization. In addition, it is effective in preventing episodes of *Staphylococcus aureus* pyodermatitis and bacteremia. The number of patients we needed to treat to prevent one episode of *Staphylococcus aureus* exit-site infection or bacteremia was five. The isolation of coagulase-negative *Staphylococci* from the skin or the catheter was also lower in the mupirocin group. Mupirocin appli-

Table 3. Number of *Staphylococcus aureus* isolates according to the site of culture, incidence rates, and relative risks of *Staphylococcus aureus* isolation and episodes of bacteremia[a]

Variable	Mupirocin (n = 69)	Control (n = 67)
Site		
pericatheter skin		
no. of positive isolates (%)	5 (7.2)	24 (35.8)[b]
incidence rate/1000 patient-days	1.76	14.27[b]
RR (95% CI)	1	7.7 (2.9 to 20.9)[b]
clinical signs of skin infection, n (%)	3 (4.3)	16 (23.9)[c]
associated with bacteremia,[d] n (%)	1 (1.5)	11 (16.4)[c]
catheter		
no. of positive isolates (%)	9 (13.0)	24 (35.8)[c]
incidence rate/1000 patient-days	3.17	14.27[b]
RR (95% CI)	1	4.5 (2.0 to 10.0)[b]
associated with bacteremia,[d] n (%)	2 (2.9)	15 (22.4)[b]
pericatheter skin or catheter or blood		
no. of positive isolates (%)	13 (18.8)	30 (44.8)[c]
incidence rate/1000 patient-days	4.58	17.84[b]
RR (95% CI)	1	4.3 (2.2 to 8.5)[b]
Bacteremia		
confirmed		
no. of episodes (%)	1 (1.4)	10 (14.9)[c]
incidence rate/1000 patient-days	0.35	5.95[b]
RR (95% CI)	1	11.0 (1.4 to 85.8)[c]
confirmed or probable		
no. of episodes (%)	2 (2.9)	15 (22.4)[b]
incidence rate/1000 patient-days	0.71	8.92[b]
RR (95% CI)	1	7.2 (1.6 to 31.6)[b]

[a] For the relative risk estimates, the reference category is the mupirocin group. Estimates are adjusted for gender. RR, relative risk; CI, confidence interval.
[b] $P < 0.001$, for the comparison between mupirocin and control group.
[c] $P < 0.01$, for the comparison between mupirocin and control group.
[d] Confirmed or probable bacteremia.

cation was well tolerated, and we did not observe adverse reactions with its use.

Despite the improvement of dialysis techniques, bacterial infection remains a leading cause of death in patients on chronic dialysis. In more than half of these patients, vascular access is the portal of entry of sepsis (21,22). Venous cannulation has gained popularity as a convenient method for rapidly establishing temporary venous access for hemodialysis. However, it is a known risk factor for bacteremia (10,21,22). The incidence of catheter-related *Staphylococcus aureus* bacteremia has increased significantly in the past 15 years (1–7,10–12). This complication often begins with *Staphylococcus aureus* colonization and local skin infection at the insertion site, and its source is usually the patient's own cutaneous flora (13,14,22,23). In our hemodialysis patients, the frequent isolation of *Staphylococcus aureus* at the skin insertion site, taken with the efficacy of topical mupirocin, supports the view that it is the skin at the insertion site, rather than the lumen, that serves as the major source of colonizing organisms. Several studies have confirmed a correlation between organisms cultured from the skin at the insertion site and those subsequently isolated from the cannula tip (10,13,14).

The importance of nasal/skin colonization with *Staphylococcus aureus* and subsequent infection is well documented in hemodialysis patients (23–27). In fact, nasal carrier status is reported to be high among these patients (up to 57% in some studies) (23–27). In the present study, 40% of patients were *Staphylococcus aureus* nasal carriers. Elimination of nasal *Staphylococcus aureus* carriage has been effected with topical mupirocin applied to the anterior nares of healthy individuals (16), health care workers (18), continuous ambulatory peritoneal dialysis patients (28), and hemodialysis patients (27). Nasal mupirocin led to a fourfold reduction in the incidence of *Staphylococcus aureus* bacteremia per patient-year (from 0.097 to 0.024) in hemodialysis patients who were carriers (27).

In the present study, patients in the mupirocin group had greatly reduced rates of skin infection and skin/catheter colonization despite the greater duration of catheterization. Mupirocin use would appear to allow a longer duration of catheter

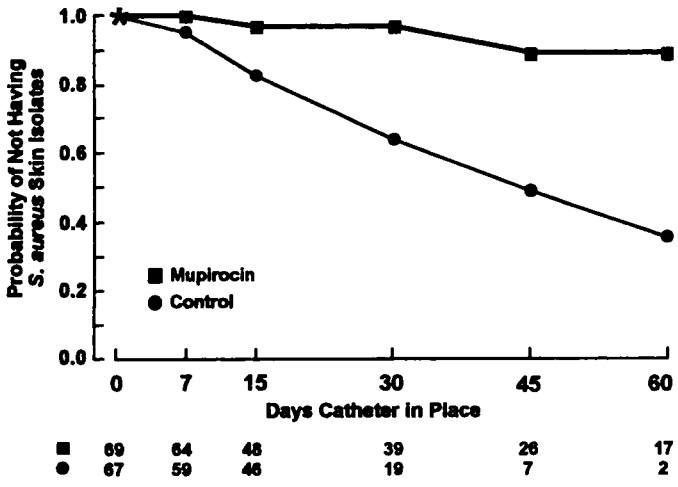

Figure 1. Probability of not having *Staphylococcus aureus* pericatheter skin isolates. $P < 0.001$ for comparison between curves. The number of patients at risk at each time interval is shown at the bottom of the graph.

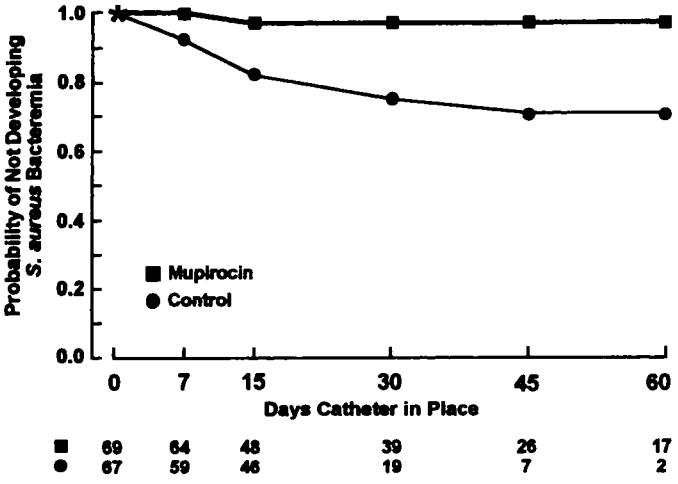

Figure 2. Probability of not developing *Staphylococcus aureus* bacteremia (confirmed or probable). $P = 0.001$ for comparison between curves. The number of patients at risk at each time interval is shown at the bottom of the graph.

placement while the patient awaits a definitive access site. In the mupirocin group, the incidence rates of *Staphylococcus aureus* catheter colonization and bacteremia were significantly reduced to 3.17 per 1000 patient-days and 0.35 per 1000 patient-days, respectively. In this group, 13 and 1.4% of the patients had *Staphylococcus aureus* catheter colonization and bacteremic episodes, respectively. Previous studies of subclavian catheter-related infections showed a wide variation of patients with catheter colonization (2.2 to 31%) and incidence rates of bacteremia ranging from 1.6 to 8.6 per 1000 patient-days (2–7,29–33). In our control group, if we consider only the confirmed cases of catheter-related bacteremia due to *Staphylococcus aureus* ($n = 10$) or other identified microorganisms (*Staphylococcus epidermidis* [$n = 1$] and Gram-negative bacteria [$n = 1$]), then the overall incidence rate of bacteremia was 7.13 per 1000 patient-days, which is similar to that reported in other prospective studies of subclavian cannulation (2,6,29,30,33). In the mupirocin group, this rate was more than 15 times lower (only one episode due to *Staphylococcus aureus*).

Given the frequency, morbidity, and cost of catheter-associated infections, it is surprising how few careful studies of skin antiseptics or antimicrobial ointments have been performed. Hill *et al.* (14), studying patients undergoing cardiothoracic surgery, observed that the application of mupirocin after skin disinfection with tincture of iodine reduced skin flora and staphylococcal colonization of central venous cannulas from 25 to 5%. Previous studies of topical antimicrobial ointments (containing polymyxin, bacitracin, and neomycin) (34–37) have usually investigated heterogeneous groups of patients, cannulated for a few days, and indicate that local application of antibiotic ointment confers little benefit in the prevention of cannula colonization. Most of these studies were performed more than 25 years ago and are virtually irrelevant in light of subsequent changes in intravenous infusion technology and improvements in catheter design and materials. More recently, Levin *et al.* (30) reported that 10% topical povidone iodine ointment at the catheter exit-site was effective in reducing hemodialysis subclavian catheter tip colonization (from 37 to 17%) and episodes of septicemia (from 17 to 2%) when compared with gauze dressing alone. New technological approaches have been evaluated for the control of catheter-related infections. Two recent studies have shown that catheters coated with chlorhexidine-silver sulfadiazine (38) or minocycline and rifampin (39) are associated with reduced risk for catheter-related colonization and bloodstream infections. These studies were limited to critically ill patients (without chronic renal failure) with triple-lumen central venous catheters *in situ* for an average of only 6 d. Emergence of resistant bloodstream pathogens and adverse reactions are still important concerns. Other studies with antiseptic or antimicrobial impregnation of catheters have shown no such benefit (31,32).

Poor personal hygiene has been associated with the development of vascular access infections in hemodialysis patients (21). The key role of nurse training in the management of the dialysis catheter dressing and its manipulation has been stressed (5). In fact, health care providers should adhere to existing recommendations, including use of maximal barrier precautions during catheter insertion and use of skilled personnel to insert and maintain these catheters (40).

Our study has some limitations. A placebo ointment was not used in the control group due to practical and economic reasons. However, because our outcome measures were very objective and clearly defined, and because the laboratory personnel processing the culture samples were blind to the patients' group assignment, it is unlikely that this factor has affected our results. Although treatment of *Staphylococcus aureus* nasal carriers did not form part of this study, it did not appear to influence the results, because the percentage of nasal carrier patients was similar in both groups. *In vitro* testing of *Staphylococcus aureus* susceptibility to mupirocin was not available; therefore, we were unable to investigate the question

Table 4. Microorganisms isolated from the skin around the catheter, catheter surface, and blood culture samples[a]

Microorganism	Pericatheter Skin		Catheter		Blood	
	Mupirocin	Control	Mupirocin	Control	Mupirocin	Control
OSSA	4	21	6	19	1	8
ORSA	1	3	3	5	1	2
Coagulase-negative *Staphylococci*	9	16	8	18		1
Streptococcus sp.					1	
Bacillus sp.				1		
Corynebacterium sp.				2		
Gram-negative rods	4	4	5	5	2	3
No growth	43	17	47	17	7	7
Mixed culture[b]	8	6				

[a] ORSA, oxacillin-resistant *Staphylococcus aureus*; OSSA, oxacillin-sensitive *Staphylococcus aureus*.
[b] Does not include *Staphylococcus aureus*.

of antimicrobial resistance to this agent. Other studies have reported that this rarely occurs (41).

We conclude that 2% mupirocin applied to the insertion site, in addition to standard skin disinfection with povidone iodine, significantly reduces the risk of *Staphylococcus aureus* skin and catheter colonization, infection at the insertion site, and bacteremia in hemodialysis patients. Additional studies are warranted to confirm these findings and to examine the effectiveness of this intervention in other types of intravenous catheters.

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