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A COMPARISON OF TWO ANTIMICROBIAL-IMPREGNATED CENTRAL VENOUS CATHETERS

Rabih O. Darouiche, M.D., Issam I. Raad, M.D., Stephen O. Heard, M.D., John I. Thornby, Ph.D., Olivier C. Wenker, M.D., Andrea Gabrielli, M.D., Johannes Berg, M.D., Nancy Khardori, M.D., Hend Hanna, M.D., Ray Hachem, M.D., Richard L. Harris, M.D., and Glen Mayhall, M.D., for the Catheter Study Group*

ABSTRACT

Background The use of central venous catheters impregnated with either minocycline and rifampin or chlorhexidine and silver sulfadiazine reduces the rates of catheter colonization and catheter-related bloodstream infection as compared with the use of unimpregnated catheters. We compared the rates of catheter colonization and catheter-related bloodstream infection associated with these two kinds of antiinfective catheters.

Methods We conducted a prospective, randomized clinical trial in 12 university-affiliated hospitals. High-risk adult patients in whom central venous catheters were expected to remain in place for three or more days were randomly assigned to undergo insertion of polyurethane, triple-lumen catheters impregnated with either minocycline and rifampin (on both the luminal and external surfaces) or chlorhexidine and silver sulfadiazine (on only the external surface). After their removal, the tips and subcutaneous segments of the catheters were cultured by both the roll-plate and the sonication methods. Peripheral-blood cultures were obtained if clinically indicated.

Results Of 865 catheters inserted, 738 (85 percent) produced culture results that could be evaluated. The clinical characteristics of the patients and the risk factors for infection were similar in the two groups. Catheters impregnated with minocycline and rifampin were 1/3 as likely to be colonized as catheters impregnated with chlorhexidine and silver sulfadiazine (28 of 356 catheters [7.9 percent] vs. 87 of 382 [22.8 percent], $P<0.001$), and catheter-related bloodstream infection was 1/12 as likely in catheters impregnated with minocycline and rifampin (1 of 356 [0.3 percent], vs. 13 of 382 [3.4 percent] for those impregnated with chlorhexidine and silver sulfadiazine; $P<0.002$).

Conclusions The use of central venous catheters impregnated with minocycline and rifampin is associated with a lower rate of infection than the use of catheters impregnated with chlorhexidine and silver sulfadiazine. (N Engl J Med 1999;340:1-8.)

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INFECTION associated with the use of central venous catheters can result in serious medical complications and expensive care.[1] In prospective, randomized clinical trials, the use of central venous catheters impregnated with either minocycline and rifampin[2] or chlorhexidine and silver sulfadiazine[3] was associated with reduced rates of catheter colonization and catheter-related bloodstream infection, as compared with unimpregnated catheters. In vitro studies[4] and studies in animals[5] have suggested that catheters impregnated with minocycline and rifampin can resist infection more effectively than catheters impregnated with chlorhexidine and silver sulfadiazine, but the clinical efficacy of these two types of antiinfective catheters has not been compared directly. We compared catheters impregnated with minocycline and rifampin with those impregnated with chlorhexidine and silver sulfadiazine in terms of the rates of colonization of catheters and bloodstream infection.

METHODS

Patients

The trial was conducted between December 1995 and July 1997 in 12 university-affiliated hospitals. The study was approved by the appropriate institutional review boards. Hospitalized adults

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who were at high risk for catheter-related infection (such as patients in intensive care units or those who were immunocompromised) and were likely to require a central venous catheter for three or more days were eligible for the study. Pregnant women and patients with a history of allergy to any of the antimicrobial agents used for impregnating the catheters were excluded. All enrolled patients or their legal guardians gave informed consent.

Catheters

Patients were randomly assigned to undergo implantation of 7-French, 20-cm-long, noncuffed, triple-lumen polyurethane central venous catheters impregnated with either minocycline and rifampin (Cook Spectrum, Cook Critical Care, Bloomington, Ind.) or chlorhexidine and silver sulfadiazine (Arrowguard Blue, Arrow International, Reading, Pa.). Both types of catheter are available for clinical use; the retail prices of a catheter tray are $70 and $61, respectively. The catheters impregnated with minocycline and rifampin provided antimicrobial activity on both the external and the internal surfaces. Examination by high-performance liquid chromatography showed that these catheters contained higher amounts of minocycline and rifampin (11.08 and 10.50 mg per catheter, respectively) than those previously studied (2.79 and 0.28 mg per catheter, respectively).[2,5] In contrast, only the external surface of catheters impregnated with chlorhexidine and silver sulfadiazine (0.75 and 0.70 mg per catheter, respectively) provided antimicrobial activity.[3] All study catheters were sterilized with ethylene oxide before use.

Randomization

A special randomization scheme was used to help match the two study groups closely. Catheter trays wrapped in identical folders were randomly assigned in blinded fashion according to computer-generated identification numbers, in blocks of six (three from each group), so that the catheter trays would be removed from the box one at a time in the prescribed, random order from the top to the bottom. Blocks of six catheters were then shipped to the participating hospitals for assignment to specified patient-care units. In each case, the patients, nurses, physicians, and principal investigators who assessed the outcomes in each hospital were unaware of the type of catheter inserted.

Insertion and Maintenance of Catheters

Attending physicians, house staff, or supervised medical students inserted the catheters into the subclavian, jugular, or femoral vein using maximal sterile-barrier precautions. To avoid the potential confounding effect of the controversial practice of catheter exchange over a guide wire, we determined at the outset of the trial to study only catheters inserted through a new venipuncture. Randomly selected study catheters could be inserted subsequently at new sites in the same patient, so long as that patient had only one study catheter at a time. At the time of catheter insertion and at each dressing change, the insertion site was disinfected with 10 percent povidone–iodine. The dressing was changed and the insertion site was inspected three times a week. Coordinators at each study location evaluated patients daily until the catheter was removed. The decision to remove the catheter was made solely by the patient's physician, who kept the catheter in place until it was no longer needed or until an adverse event, such as catheter-related infection or catheter occlusion, necessitated its removal.

Cultures

Four-centimeter segments from the tips and subcutaneous sections of the aseptically removed catheters were cultured by the roll-plate method,[6] then cultured by the sonication method.[7] To help identify the sources of organisms that colonize catheters, swab cultures of surrounding skin were obtained at the times of catheter insertion and catheter removal in four participating hospitals. In patients in whom catheter-related infection was suspect-ed on clinical grounds, one or more peripheral-blood samples for culture were collected before or immediately after catheter removal. Recovered organisms were identified by standard microbiologic methods.

Molecular Typing

Bacterial isolates from cultures of blood, catheters, and, when available, skin of patients in whom catheter-related bloodstream infection was diagnosed were typed by genomic fingerprinting with the use of the repetitive-element polymerase chain reaction.[8] If the same bacterial species was isolated from different sites in a single patient, DNA-fingerprint patterns were compared for similarity by visual inspection of band patterns and by computer-assisted analysis (RFLPscan Plus, Scanalytics, Billerica, Mass.). Bacterial isolates were considered similar if fingerprint patterns differed by no more than one amplification band.

Antimicrobial Susceptibility

To help determine whether these antimicrobial-impregnated catheters increase the likelihood of the emergence of antibiotic resistance, we compared the minimal inhibitory concentrations and minimal bactericidal concentrations for bacteria isolated from the two kinds of catheters by a standard broth-microdilution assay.[9]

Definitions

We adopted the definitions of catheter colonization and infection proposed by the Centers for Disease Control and Prevention[10,11] and used in previous clinical trials.[2] Catheter colonization was defined as the growth of 15 or more colony-forming units in culture of catheter segments prepared by the roll-plate method or 1000 or more colony-forming units in cultures prepared by the sonication method from either the tip or a subcutaneous segment of the catheter. Catheter-related bloodstream infection was defined as the isolation of the same organism (i.e., the same species with identical antimicrobial susceptibility) from the colonized catheter and from peripheral blood in a patient with clinical manifestations of sepsis and no other apparent source of bloodstream infection.

Statistical Analysis

Before undertaking this study, we estimated the number of catheters that would be required for an adequate examination of the hypothesis that catheters impregnated with minocycline and rifampin are significantly less likely to be colonized than catheters impregnated with chlorhexidine and silver sulfadiazine. On the basis of previous reports, we estimated that 7 percent of catheters impregnated with minocycline and rifampin[2] and 13.6 percent of catheters impregnated with chlorhexidine and silver sulfadiazine[3] would be colonized. Randomly assigning approximately 362 catheters that could be evaluated to each group would have allowed us to detect with 80 percent power a significant difference in the rates of colonization between the two types of catheters at a two-tailed significance level of 5 percent.

The significance of the differences between the two study groups was determined with use of Student's t-test or the Wilcoxon rank-sum test for continuous variables and Fisher's exact test or the chi-square test for categorical variables. All P values were based on two-tailed tests of significance. The proportions of catheters that were free of colonization and not associated with bloodstream infection as a function of the length of time they had been in place were compared between the groups with use of a log-rank test on Kaplan–Meier estimates. A multivariate logistic-regression model was used to estimate the simultaneous effects of multiple variables on the incidence of catheter colonization and catheter-related bloodstream infection. To avoid rejecting variables that might have influenced the risk of catheter colonization or catheter-related bloodstream infection, variables that were significant at a P value of 0.25 or less in the univariate analysis were entered in stepwise fashion into logistic-regression analyses and

tested for an independent effect. The limit for entering or removing variables in the logistic-regression models was a P value of 0.05 or less. All computations were performed with SAS/STAT software.[12] An independent monitoring board composed of experts on infectious diseases reviewed and helped interpret the findings of the study. An interim analysis of the data was not performed.

RESULTS

Characteristics of Patients and Catheters

A total of 865 study catheters (414 impregnated with minocycline and rifampin and 451 impregnated with chlorhexidine and silver sulfadiazine) were inserted into 817 patients. Complete data could be evaluated for 738 catheters (85 percent): 356 impregnated with minocycline and rifampin and 382 impregnated with chlorhexidine and silver sulfadiazine, inserted in 698 patients. The remaining 127 catheters (58 impregnated with minocycline and rifampin and 69 impregnated with chlorhexidine and silver sulfadiazine, with similar patient and catheter characteristics) were not cultured (84 were removed without notification of study coordinators, 19 were grossly contaminated during removal, and 24 were not available for other reasons) and therefore were excluded from further analysis. The two groups of catheters that could be evaluated were similar with respect to characteristics of patients and catheters (Table 1).

Colonization of Catheters

Eighty-seven of 382 catheters impregnated with chlorhexidine and silver sulfadiazine (22.8 percent) and 28 of 356 catheters impregnated with minocycline and rifampin (7.9 percent) were colonized according to at least one method of assessment (relative risk, 2.90; 95 percent confidence interval, 1.94 to 4.33; P<0.001). Catheters impregnated with minocycline and rifampin were less likely to be colonized than those impregnated with chlorhexidine and silver sulfadiazine, whether the catheter remained in place for seven days or less (13 of 217 catheters [6.0 percent] vs. 45 of 210 [21.4 percent], P<0.001) or for more than seven days (15 of 139 [10.8 percent] vs. 42 of 172 [24.4 percent], P<0.002). Analysis of the Kaplan–Meier estimates of the risk of catheter colonization according to the length of time the catheters were in place in each group showed that catheters impregnated with minocycline and rifampin were significantly less likely to be colonized (P<0.001 by the log-rank test). The overall beneficial effect of the use of catheters impregnated with minocycline and rifampin was seen in all hospitals that contributed more than 32 catheters that could be evaluated. Catheters impregnated with minocycline and rifampin were also significantly less likely to be colonized than catheters impregnated with chlorhexidine and silver sulfadiazine (P<0.001) according to each of the four combinations of cath-

TABLE 1. CHARACTERISTICS OF THE PATIENTS AND ANTIMICROBIAL-IMPREGNATED CATHETERS.*

CHARACTERISTIC	MINOCYCLINE–RIFAMPIN CATHETERS (N=356)	CHLORHEXIDINE–SILVER SULFADIAZINE CATHETERS (N=382)
No. of patients	350	370
Male sex (%)	59	63
Median age (yr)	56	56
Underlying disease (%)		
Cancer	28	26
Cardiopulmonary disease	32	34
Neurologic disorder	16	19
Other	24	21
Patients in intensive care unit (%)	66	67
Risk factors for infection (%)		
Hyperalimentation	16	16
Immunosuppressive therapy	22	20
Bone marrow transplantation	6	4
Neutropenia	5	3
Mechanical ventilation	60	65
Other intravascular catheter	53	54
Urinary catheter	85	86
Receiving systemic antibiotics (%)	89	90
Insertion site (%)		
Subclavian vein	54	53
Jugular vein	38	36
Femoral vein	8	11
Duration of placement (days)		
Mean	8.4	8.2
Median	6	7
Range	1–55	1–36
Reason for removal (%)		
Catheter no longer needed	67	69
Suspected catheter infection	14	13
Occluded catheter	3	1
Other	16	17

*A total of 738 catheters that could be evaluated were inserted into 698 patients; some patients received 1 or more catheters of each type. The catheters and patients were included in both groups in such cases.

eter segment and culture method (tip–roll plate, tip–sonication, subcutaneous segment–roll plate, and subcutaneous segment–sonication) or any combination of these assessment methods.

Catheters impregnated with chlorhexidine and silver sulfadiazine were significantly more likely than those impregnated with minocycline and rifampin to be colonized with coagulase-negative staphylococci (18 percent vs. 4 percent; relative risk, 4.16; 95 percent confidence interval, 2.42 to 7.14; P<0.001), gram-positive bacilli (2 percent vs. 0.3 percent; relative risk, 7.46; 95 percent confidence interval, 0.94 to 58.8; P=0.04), or gram-negative bacilli (4 percent vs. 1 percent; relative risk, 3.96; 95 percent confidence interval, 1.35 to 11.63; P=0.007). However, the rates of colonization of catheters with *Staphylococcus aureus* (1 percent vs. 0), enterococci (2 percent vs. 2 percent), and yeast (2 percent vs. 3 percent) did not differ significantly between the two groups.
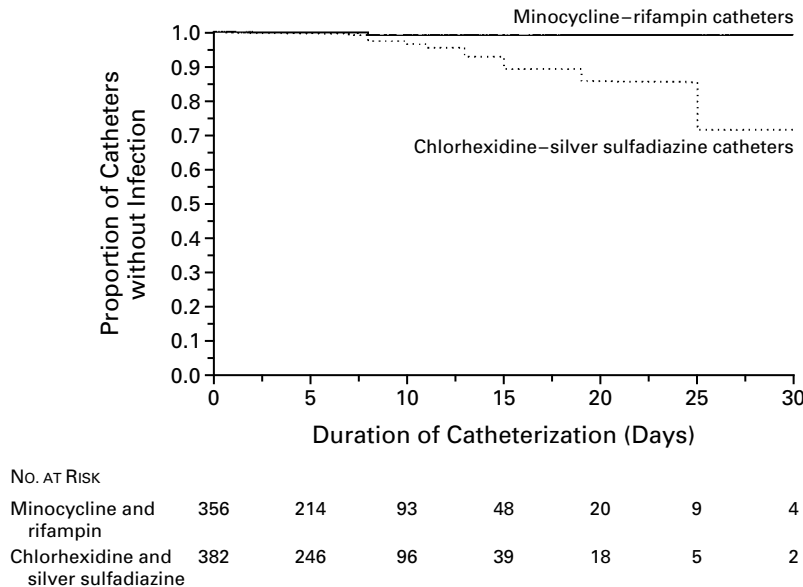
Figure 1. Kaplan–Meier Curves for Freedom from Bloodstream Infection with Catheters Impregnated with Either Minocycline and Rifampin or Chlorhexidine and Silver Sulfadiazine.

The numbers of catheters in each group that were at risk for causing infection at various times are shown below the figure. The risk of bloodstream infection was significantly lower for catheters impregnated with minocycline and rifampin than for those impregnated with chlorhexidine and silver sulfadiazine (P=0.001 by the log-rank test).

Factors that may have increased the likelihood of catheter colonization (detected by any of the assessment methods) in the univariate analysis (P≤0.25) were entered into a multivariate logistic-regression model, which identified the following predisposing factors as significant (P≤0.05): insertion of the catheter into the femoral or jugular vein (odds ratio as compared with other locations, 3.05; 95 percent confidence interval, 1.86 to 5.01; P<0.001), use of a catheter impregnated with chlorhexidine and silver sulfadiazine (odds ratio as compared with minocycline and rifampin, 2.80; 95 percent confidence interval, 1.68 to 4.66; P<0.001), hospitalization in the intensive care unit (odds ratio as compared with other wards, 2.60; 95 percent confidence interval, 1.47 to 4.62; P=0.001), male sex (odds ratio, 2.45; 95 percent confidence interval, 1.43 to 4.20; P=0.001), and mechanical ventilation (odds ratio, 1.97; 95 percent confidence interval, 1.14 to 3.41; P=0.01).

Catheter-Related Bloodstream Infection

In 14 cases, bloodstream infection was attributed to an indwelling study catheter. These catheters had been in place for a median of 11 days. Thirteen cases of catheter-related bloodstream infection occurred among the catheters impregnated with chlorhexidine and silver sulfadiazine (3.4 percent), as compared with one case among the catheters im-

pregnated with minocycline and rifampin (0.3 percent; relative risk, 12.05; 95 percent confidence interval, 1.59 to 90.9; P<0.002). Two patients died as a result of bloodstream infections associated with catheters impregnated with chlorhexidine and silver sulfadiazine. Among the catheters that remained in place for more than seven days, the rate of associated bloodstream infection was significantly higher for catheters impregnated with chlorhexidine and silver sulfadiazine than for catheters impregnated with minocycline and rifampin (11 of 172 catheters [6.4 percent] vs. 1 of 139 [0.7 percent], P=0.01). The rates of catheter-related bloodstream infection per 1000 catheter-days were 0.3 (95 percent confidence interval, 0.01 to 1.85) for catheters impregnated with minocycline and rifampin and 4.1 (95 percent confidence interval, 2.22 to 6.99) for catheters impregnated with chlorhexidine and silver sulfadiazine (P<0.001). Figure 1 shows the Kaplan–Meier estimates of the risk of catheter-related bloodstream infection according to duration of catheterization in each group and shows that catheters impregnated with minocycline and rifampin were superior (P=0.001 by log-rank test). The same conclusion was reached when we considered only the results from culture of the catheter tip (1 infection among 356 catheters [0.3 percent] vs. 11 among 382 [2.9 percent], P=0.006) or the subcutaneous

segment (1 of 356 [0.3 percent] vs. 12 of 382 [3.1 percent], P=0.003).

Enterococcus faecalis caused the single case of bloodstream infection related to a catheter impregnated with minocycline and rifampin. Organisms implicated in the 13 cases of bloodstream infection associated with catheters impregnated with chlorhexidine and silver sulfadiazine included coagulase-negative staphylococci (8 cases; in 1 a diphtheroid was also present), methicillin-resistant *S. aureus,* vancomycin-resistant *E. faecalis, Enterobacter cloacae, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* (1 case each). Fourteen of 115 colonized catheters (12 percent) resulted in bloodstream infection; there was no difference in the likelihood of infection between catheters colonized with coagulase-negative staphylococci and catheters colonized with other organisms. Catheters impregnated with minocycline and rifampin had a significant protective effect against catheter-related bloodstream infection by coagulase-negative staphylococci as compared with catheters impregnated with chlorhexidine and silver sulfadiazine (rate of infection, 0 of 356 vs. 8 of 382; P=0.008).

The clonal relation of isolates from blood and catheter cultures was confirmed by DNA typing in 13 of 14 cases (Fig. 2). Skin swabs were cultured at the time of the removal of the catheter from seven patients with catheter-related bloodstream infection. In five of these cases (71 percent), the culture yielded bacteria of the same species with a DNA-fingerprint pattern similar to that of the isolates from the catheter and the blood; a different organism grew from skin cultures in the other two patients (29 percent), suggesting that catheter infection may have originated from contamination of the catheter hub.

Factors that may have increased the risk of catheter-related bloodstream infection in the univariate analysis (with P≤0.25 as the criterion) were entered into a multivariate logistic-regression model, which identified the following predisposing factors as significant (P≤0.05): catheterization for more than seven days, use of a catheter impregnated with chlorhexidine and silver sulfadiazine, and male sex (Table 2).

Analysis of data for only the first catheter insertion (698 catheters) also demonstrated that the use of catheters impregnated with minocycline and rifampin was associated with lower rates of colonization of the catheter than the use of catheters impregnated with chlorhexidine and silver sulfadiazine (79 of 359 catheters impregnated with chlorhexidine and silver sulfadiazine were colonized [22.0 percent], vs. 28 of 339 [8.3 percent] for minocycline and rifampin; relative risk, 2.66; 95 percent confidence interval, 1.78 to 4.0; P<0.001) and bloodstream infection (12 of 359 [3.3 percent] vs. 1 of 339 [0.3 percent]; relative risk, 11.33; 95 percent confidence interval, 1.48 to 83.3; P=0.003). Although there was a trend toward a lower risk of nos-

ocomial bacteremia with catheters impregnated with minocycline and rifampin than with catheters impregnated with chlorhexidine and silver sulfadiazine (6.7 percent vs. 10.2 percent), the difference was not significant (P=0.12). There were no significant differences between the two groups in the proportions receiving therapy with vancomycin (23 percent vs. 25 percent) or antibiotics in general (89 percent vs. 90 percent) and the mean duration of stay in the intensive care unit (8.7 vs. 8.6 days).

Antimicrobial Susceptibility

The ranges of the minimal inhibitory concentrations and minimal bactericidal concentrations of minocycline and rifampin for *S. epidermidis* and enterococci were similar for isolates cultured from the two types of catheters (Table 3). Moreover, in the two cases in which the same organism was isolated from paired cultures of skin obtained before insertion and at the time of removal of a catheter impregnated with minocycline and rifampin (*S. epidermidis* in one case and enterococcus in the other), the minimal inhibitory concentrations and minimal bactericidal concentrations of minocycline and rifampin for the corresponding paired isolates were similar.

Adverse Effects of the Catheters

There were no local or systemic hypersensitivity reactions associated with the use of either catheter.

DISCUSSION

Recent comparative studies have shown that the use of central venous catheters impregnated either with minocycline and rifampin[2] or with chlorhexidine and silver sulfadiazine[3] is associated with lower rates of catheter colonization and bloodstream infection than the use of unimpregnated catheters. Although three smaller clinical trials (which studied 72, 282, and 308 catheters that could be evaluated)[13-15] showed a nonsignificant trend toward lower rates of bloodstream infection with catheters impregnated with chlorhexidine and silver sulfadiazine than with unimpregnated catheters, none had sufficient power to determine that there were no differences. We compared two very differently prepared antiinfective catheters. As we hypothesized, our findings indicated that the antiinfective efficacy of catheters impregnated with minocycline and rifampin was superior to that of catheters impregnated with chlorhexidine and silver sulfadiazine.

The majority of cases of catheter-related bloodstream infection are associated with the short-term use of noncuffed central venous catheters.[16] On average, 5 percent[2,3,14,15] of the 3 million short-term, unimpregnated central venous catheters that are inserted annually in the United States lead to bloodstream infection,[16] resulting in about 150,000 cases of catheter-related bloodstream infection a year. Our
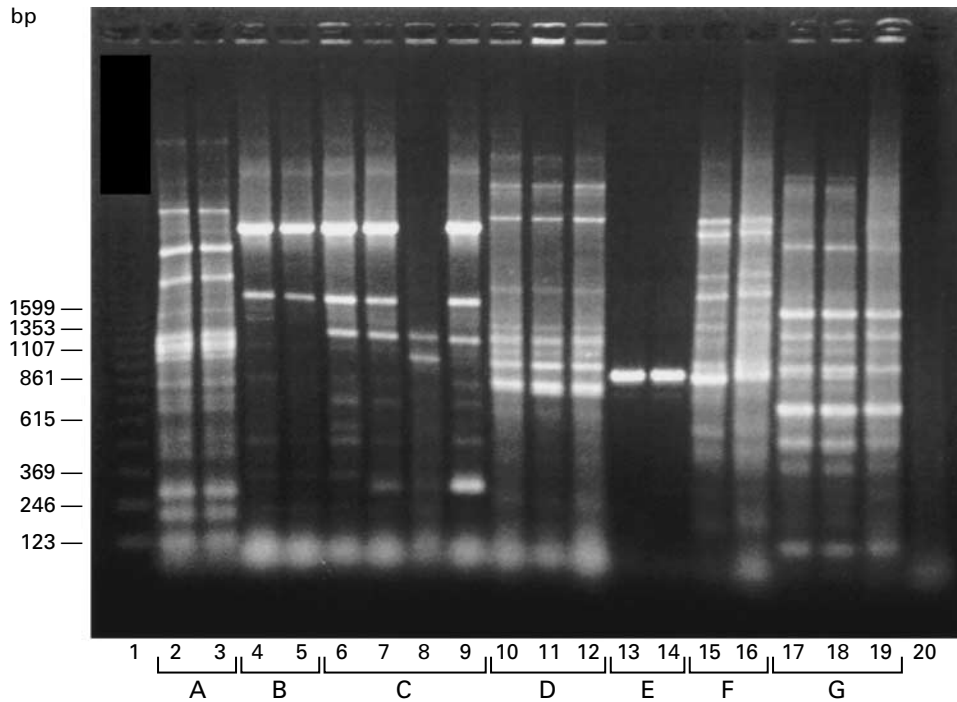
Figure 2. Representative DNA-Fingerprint Patterns in Repetitive-Element Polymerase-Chain-Reaction Analysis of Isolates from Cultures of Catheter Segments, Peripheral Blood, and Skin from Seven Patients with Catheter-Related Bloodstream Infection.

The DNA fragments were separated by electrophoresis on an agarose gel and stained with ethidium bromide. Isolates from each of the seven patients (A through G) are indicated by brackets. Lane 1 shows molecular-weight markers; lane 2, diphtheroid isolated from the catheter of Patient A; lane 3, diphtheroid isolated from the blood of Patient A; lane 4, *Staphylococcus epidermidis* isolated from the catheter of Patient B; lane 5, *S. epidermidis* isolated from the blood of Patient B; lane 6, coagulase-negative staphylococcus isolated from the catheter of Patient C; lane 7, coagulase-negative staphylococcus isolated from the blood of Patient C; lane 8, coagulase-negative staphylococcus isolated from the skin of Patient C before insertion of the catheter; lane 9, coagulase-negative staphylococcus isolated from the skin of Patient C at the time of catheter removal; lane 10, vancomycin-resistant enterococcus isolated from the catheter of Patient D; lane 11, vancomycin-resistant enterococcus isolated from the blood of Patient D; lane 12, vancomycin-resistant enterococcus isolated from the skin of Patient D at the time of catheter removal; lane 13, *Enterococcus faecalis* isolated from the catheter of Patient E; lane 14, *E. faecalis* isolated from the blood of Patient E; lane 15, *Pseudomonas aeruginosa* isolated from the catheter of Patient F; lane 16, *P. aeruginosa* isolated from the blood of Patient F; lane 17, *Klebsiella pneumoniae* isolated from the catheter of Patient G; lane 18, *K. pneumoniae* isolated from the blood of Patient G; lane 19, *K. pneumoniae* isolated from the skin of Patient G at the time of catheter removal; and lane 20, the negative control. In each of the seven patients, the DNA-fingerprint patterns of isolates from catheter segments and blood were similar. Although the coagulase-negative staphylococcus isolated from the skin of Patient C before the insertion of the catheter (lane 8) had a DNA-fingerprint pattern that was different from that of the isolates from the catheter (lane 6) and blood (lane 7), the staphylococcus isolated from the skin at the time of catheter removal shared a similar pattern with catheter and blood isolates in all three patients (Patient C, Patient D, and Patient G) for whom the patterns for isolates from skin are shown, suggesting that the skin is the most important source of infection associated with catheters.

findings of remarkably low rates of catheter-related bloodstream infection (0.3 percent) and catheter colonization (7.9 percent) associated with the use of catheters impregnated with minocycline and rifampin are similar to previously reported rates.[2] However, we found rates of catheter colonization (22.8 percent) and bloodstream infection (3.4 percent) associated with the use of catheters impregnated with chlorhexidine and silver sulfadiazine that were higher than those reported by Maki and colleagues (13.5 percent and 1 percent, respectively).[3] The differences in rates of colonization of catheters could be attributed, at least in part, to our use of roll-plate and sonication cultures of both the tips and subcutaneous segments, as compared with the use by Maki et al. of only roll-plate culture of the catheter tips alone.[3] As in other reports,[7,17] the roll-plate culture had a limited sensitivity for the diagnosis of catheter colonization (78 of 115 catheters [68 percent]) and catheter-related bloodstream infection (12 of 14 [86 percent]) in our study.

Unlike catheters impregnated with minocycline and

TABLE 2. RESULTS OF UNIVARIATE AND MULTIVARIATE ANALYSES OF FACTORS
ASSOCIATED WITH CATHETER-RELATED BLOODSTREAM INFECTION.

FACTOR	UNIVARIATE ANALYSIS	MULTIVARIATE ANALYSIS*	
	P VALUE	P VALUE	OR (95% CI)
Duration of catheterization >7 days	0.001	0.005	8.66 (1.90–39.40)
Chlorhexidine–silver sulfadiazine catheter	0.002	0.02	11.04 (1.42–85.60)
Mechanical ventilation	0.002	—	—
Male sex	0.01	0.03	9.15 (1.18–71.2)
Hyperalimentation	0.01	—	—
Insertion by house staff or students	0.07	—	—
Patient in intensive care unit	0.10	—	—
Indwelling urinary catheter	0.12	—	—
Other intravascular catheter	0.14	—	—

*OR denotes odds ratio, and CI confidence interval.

TABLE 3. ANTIMICROBIAL SUSCEPTIBILITY OF BACTERIAL ISOLATES CULTURED
FROM CATHETERS.*

ISOLATE AND ANTIBIOTIC	MINOCYCLINE–RIFAMPIN CATHETERS†		CHLORHEXIDINE–SILVER SULFADIAZINE CATHETERS‡	
	MIC RANGE	MBC RANGE	MIC RANGE	MBC RANGE
	micrograms per milliliter			
Coagulase-negative staphylococci				
Minocycline	0.06–1	1–16	0.12–128	0.12–128
Rifampin	0.06–128	0.06–128	0.12–128	0.12–128
Enterococci				
Minocycline	1–8	4–128	0.5–16	2–128
Rifampin	1–128	64–128	1–128	16–128

*MIC denotes minimal inhibitory concentration, and MBC minimal bactericidal concentration.

†Eleven isolates of coagulase-negative staphylococci and four of enterococci were tested.

‡Forty-five isolates of coagulase-negative staphylococci and five of enterococci were tested.

rifampin, in which antimicrobial activity is present on both the external and the internal surfaces of the catheter, the antimicrobial activity of catheters impregnated with chlorhexidine and silver sulfadiazine is limited to the external surface. The difference might be an important determinant of the difference in efficacy between these two antimicrobial-impregnated catheters. For instance, catheters impregnated with chlorhexidine and silver sulfadiazine reduced colonization of the external surface as compared with uncoated catheters in studies in which the roll-plate method alone was used to culture only the catheter tips[2] or both the catheter tips and the subcutaneous segments.[14,15] Our use of sonication cultures that retrieve organisms from both the external and internal surfaces is justified by the role of luminal colonization in causing catheter-related blood-

stream infection.[18] Other factors that may have contributed to the superior efficacy of the catheters impregnated with minocycline and rifampin include the particular method used to incorporate the antimicrobial agents into the catheter material and the resulting concentration and availability of those agents on the catheter surface.

Although antimicrobial resistance is an issue of potential concern, we and others[2] have, so far, found a very low likelihood that antibiotic resistance will result from the use of antimicrobial-impregnated catheters. However, continued surveillance for resistance is required as part of the further clinical use of such catheters. Although it is possible that the use of any antiinfective catheter that reduces ultrastructural colonization may decrease the likelihood of the development of resistance to systemically administered anti-

biotics such as vancomycin,[19] the actual effects of the use of antimicrobial-impregnated catheters on infection-control measures require further evaluation.

In conclusion, our results demonstrate that the capacity of catheters impregnated with minocycline and rifampin to resist infection is superior to that of catheters impregnated with chlorhexidine and silver sulfadiazine, particularly in patients who require vascular access for seven or more days. Despite their proven efficacy, antimicrobial-impregnated catheters should complement rather than replace adequate aseptic practices.[10,11]

APPENDIX

In addition to the authors, the following members of the Catheter Study Group participated in the clinical trial: C. Robertson, M. Wall, J. Jones, M. Mansouri, C. Stewart, and S. Dunbar (Baylor College of Medicine, Houston); J. Dupuis, A. Buzaid, K. Price, A. El-Rahwan, J. Abbas, and S. Sidarous (University of Texas M.D. Anderson Cancer Center, Houston); I. Toth, K. Longtine, and A. Breuggemann (University of Massachusetts Medical Center, Worcester); K. Rand (University of Florida College of Medicine, Gainesville); S. Bjornson (University of Cincinnati Medical Center, Cincinnati); and P. Falk (University of Texas Medical Branch, Galveston).

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