Hemodialysis Infection Prevention with Polysporin Ointment

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Abstract. Hemodialysis patients in whom permanent vascular access cannot be achieved are dependent on a central venous catheter. In such patients, catheter-related infections are a common and serious complication. This study was a randomized clinical trial to determine if topical Polysporin Triple antibiotic ointment applied to the central venous catheter insertion site could reduce the incidence of catheter-related infections. A total of 169 patients receiving hemodialysis through a central venous catheter were randomized to receive Polysporin Triple or placebo using a double-blind study design. In the 6-mo study period, infections were observed in more patients in the placebo group than in the Polysporin Triple group (34 *versus* 12%; relative risk, 0.35; 95% CI, 0.18 to 0.68; $P = 0.0013$). The number of infections per 1000 catheter days (4.10 *versus* 1.02; $P < 0.0001$) and the number of bacteremias per 1000 catheter days (2.48 *versus* 0.63; $P = 0.0004$) were also greater in the placebo group. Within the 6-mo study period, there were 13 deaths in the placebo group as compared with 3 deaths in the Polysporin Triple group ($P = 0.0041$). When all available follow-up information was included, the difference in survival remained significant (19 *versus* 9 deaths; $P = 0.0027$). Within the first 6 mo, infections were observed in 7 of the 13 placebo subjects who died (54%) as compared with no infections in the three Polysporin Triple subjects who died. The prophylactic application of topical Polysporin Triple antibiotic ointment to the central venous catheter insertion site reduced the rate of infections and was associated with improved survival in hemodialysis patients. *charmaine.lok@uhn.on.ca*

Infection is the most common cause of morbidity and the second most common cause of death in hemodialysis (HD) patients (1–5). Bacteremia accounts for more than 75% of these infectious deaths (4). Hemodialysis vascular access is implicated as the source of bacteremias in 48 to 73% (3,6–7) of cases with patients dependent on central venous catheters (CVC) being at highest risk (2,7–9). Currently, approximately 20% of patients are dialyzed using permanent catheters; both their placement rate and length of use has increased (1,4). *Staphylococcus aureus* has previously been the primary etiologic agent implicated in causing approximately half of the bacteremic episodes (7,10) and 70% of the vascular access site infections (11–12). However, recent studies have reported a greater percentage and variety of Gram-negative bacteria isolated in catheter-related infections (13–16). Polysporin Triple (PT) is an antibiotic ointment composed of 500 U/g bacitracin, 0.25 mg/g gramicidin, and 10,000 U/g polymyxin B and is active topically against most skin flora (*e.g.*, *S. aureus*, coagulase negative staphylococcus, and most Gram-negative bacteria). Previous studies have demonstrated success in preventing catheter-related infections using topical povidone-iodine (17) or mupirocin (12,18,19), antibiotic or silver-coated catheters (20–22), and other novel methods (23–25). However, the optimal strategy for long-term infection prophylaxis for tunneled permanent catheters has not been established in the current environment of changing microbes and clinical practice. The objective of this study was to determine if topical PT ointment applied at the catheter exit site could reduce the incidence of hemodialysis catheter-related infections over a 6-mo period.

Materials and Methods

Study Design

This multicenter study was a double-blind, placebo-controlled, randomized clinical trial. The patients, clinicians, microbiologists, pharmacist, and data managers were unaware of the treatment allocation. Patients were stratified into two groups before randomization on the basis of the time interval between CVC insertion and study enrollment (≤7 d was called "incident catheter," and others were called "prevalent catheter"). Patient randomization was performed at an independent central randomization facility via a computer-generated random number list, using blocked randomization with a block size of 4. Written informed consent was obtained from all patients or their legal representative. The study protocol was approved by the Research Ethics Boards of the participating Canadian institutions and the funding agency. The use of a placebo ointment on a chlorhexidine-cleansed site was justified at the time, as the study was designed and approved before the Canadian Society of Nephrology guidelines for vascular access (26) were published.

Study Population

The study population consisted of consecutive individuals with end-stage renal disease (ESRD) who required hemodialysis and used

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a permanent tunneled cuffed catheter in the internal jugular vein as their vascular access for dialysis. All such patients who met the inclusion criteria were approached to enter the study. The inclusion criteria were age greater than 18 yr and a need for a cuffed catheter as the primary source of vascular access for one of the following reasons: ESRD without permanent vascular access, recent conversion from peritoneal dialysis to HD, or recent loss of an arteriovenous fistula or graft. Exclusion criteria were as follow: acute renal failure, antibiotic use by any route in the week before enrolling in the study, known allergy to any component of PT, use of a temporary HD catheter (non-cuffed), use of the CVC for purposes other than access for HD, *e.g.*, chemotherapy or TPN, active malignancy, or involvement in another drug trial.

Study Treatment and Outcomes

A placebo ointment was prepared that matched the PT ointment with respect to appearance and consistency. The study ointment (treatment or matched placebo) was contained in brown opaque 50-g glass jars marked only with the patient's name and study number to ensure masking of the study from trained hemodialysis nurses who applied the ointment. After enrollment, the study ointment was applied at the end of each dialysis session for 2 consecutive weeks (6 sessions) and then with the patient's weekly dressing change and when dressing changes were clinically indicated. A high compliance with ointment application was assured by obtaining input from the HD nurses during the study design phase and random checks comparing the amount of ointment used for patients enrolled at similar times.

The study dressing protocol was standardized to reflect the current practice of the two institutions and included cleansing around the exit site with a Chlorhexidine gluconate (0.5% in 70% alcohol) applicator, a 1-cm cotton swab application of study ointment to the CVC exit site, and then application of a 2×2 in. dry gauze dressing secured with a porous, nontransparent adhesive (hypafix). To avoid erosion and to ensure compatibility with the chlorhexidine and PT, the catheters used were not glycol based. All catheters (Uldall Cook, Cook Canada Inc.) and Cardiomed (Cardiomed Supplies Inc.) were placed by interventional radiologists using aseptic techniques (sterile gowns, gloves, mask, cap, drape). Suspected cases of infection were identified by trained HD nurses who would then notify the attending physician to examine the patient. The findings were documented by the nurse on a questionnaire and submitted to the primary investigator for review, confirmation, and classification. The primary endpoint was the proportion of patients with a catheter-related infection within 6 mo after entry into the study. These infections included: (*1*) exit site infection (ESI); (*2*) tunnel infections; and (*3*) bacteremia. This endpoint was evaluated in a blinded fashion by the primary investigator (CL) according to the Canadian definitions for catheter-related infections (27). Cases with "definite" and "probable" infections (Table 1) were classified as infections, as was agreed before the commencement of the study.

All catheter-related infections were treated by the patient's attending staff nephrologist according to their usual practice. If a new catheter was clinically indicated, the patient continued to receive the same ointment to which they had been assigned. Swabs for cultures and sensitivities at the catheter exit site were taken if an exit or tunnel infection was suspected and blood cultures if a bacteremia was suspected. Surveillance nasal and catheter exit site swabs were obtained at the time of patient enrollment and every 3 mo for the duration of the study. Site-specific laboratories were used for microbiologic identification of organisms using standard methods (28). The study ended when the last enrolled subject completed the minimum 6-mo study period.

Statistical Analyses

A minimum of 36 patients in each treatment group was required to detect a 50% difference between the treatment and placebo groups with respect to infections per patient with 80% power using a two-sided test with an α of 0.05 (based on the previous year's average of 0.7 infections/patient per yr between the two institutions). The follow-up period for the primary endpoint was defined from the beginning of the study to be 6 mo. A follow-up period of 12 mo was considered too long for reliable results, because beyond 6 mo the rate of infection appears to decline, the need for secondary catheters rises, and there is substantially greater risk that confounding factors could cloud the study results. We assessed differences in proportions using Fisher's exact test and the number of infections per 1000 catheter-days using the exact binomial test (29). Time-to-event distributions were estimated using the Kaplan-Meier method and compared using the log-rank test (30). The relative risk reduction and number of patients needed to treat (NNT) to prevent one infection, bacteremia, and death were determined (31). Analyses were based on an intention-to-treat approach, except for the exclusion of seven blinded subjects who never started treatment. Analyses were performed using SAS, version 8.e (SAS Institute, Cary, NC).

Results

Of 172 patients approached to participate in this clinical trial, 169 (98%) consented and entered the study between November 1999 and November 2000 (154 patients from the University Health Network-Toronto General Hospital and 15 from Sunnybrook and Women's College Health Sciences Center). Of the 169 patients randomized, study treatment (blinded PT or placebo ointment) was not initiated for seven patients. The reasons for patients not beginning assigned treatment were recovery of kidney function not requiring dialysis (two cases, one in each group), changed mind shortly after randomization (one case assigned to placebo), renal transplant (one case assigned to PT), and requiring long-term antibiotics for non–dialysis-related medical reasons (three cases, one assigned to PT). Of these cases, two from each group did not yet have their catheter inserted at the time of withdrawal. These seven blinded patients who did not initiate protocol treatment were excluded from the analyses; however, in sensitivity analyses including these 7 patients, the results remain unchanged. Analysis and results of the remaining 162 patients are reported here. Overall, 94 (58%) of the patients remained in the study for at least 6 mo: 44% of the placebo group, and 71% of the PT group. The most common reasons for less than 6 mo of follow-up were a mature, usable permanent access (15% of the 162 cases), death (10%), and transfer to a nonstudy dialysis unit (7%). Any infectious complications that resulted in less than 6 mo follow-up were related to deaths as noted in a later section of this paper. No patients were lost to follow-up (Figure 1).

Table 2 gives the baseline patient characteristics by treatment group. Rates of infection were not statistically different by baseline characteristics (Table 3).

Infections

A higher proportion of patients experienced an infection in the placebo group as compared with the PT group (34% *versus*

Table 1. Definitions of catheter-related infections

Definition	Definite	Probable
Exit site infection	Purulent discharge at exit site	Erythema, tenderness, induration (2 of 3) at exit site without a positive culture of serous discharge
	or	or
	Erythema, tenderness, induration (2 of 3) at exit site with a positive culture of serous discharge	Above without discharge but lack of alternative explanation
Tunnel infection	Purulent discharge or aspirate from a tunnel or pocket site not contiguous with exit site	Erythema, tenderness, induration (2 of 3) at a tunnel or pocket site not contiguous with exit site and serous discharge or aspirate from that site without a positive culture
	or	or
	Erythema, tenderness, induration (2 of 3) at a tunnel or pocket site not contiguous with exit site with a positive culture of serous discharge or aspirate from that site	Above without discharge but lack of alternative explanation
Catheter-related bacteremia	Confirmation of septic thrombophlebitis with a single positive blood culture	Two or more positive blood cultures with no evidence for source other than the device
	or	or
	Single positive blood culture and positive culture of catheter segment with identical organism	Single positive blood culture for *S. aureus* or *Candida* with no evidence for source other than device
	or	or
	>-10-fold colony count difference in blood cultures drawn from device and peripheral blood	Single positive blood culture for coagulase negative *staphylococci, Bacillus, Corynebacterium jeikeium, Enterococcus, Trichophyton,* or *Malassezia* in immunocompromised or neutropenic host or in patient receiving total parenteral nutrition with no evidence for source other than a centrally placed device
	or	
	Single positive blood culture and positive culture from discharge or aspirate from exit site, tunnel, or pocket, with identical organism	

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12%; $P = 0.0013$; Table 4). This represented a 65% relative risk reduction (relative risk, 0.35; 95% CI, 0.18 to 0.68); the NNT with PT to prevent one infection was 5 (95% CI, 3 to 11). Sixteen of the 27 patients with an infection in the placebo group and 8 of the 10 patients with infections in the PT group experienced only a single infection. In the placebo group, the number of infections per 1000 catheter-days was greater (4.10 *versus* 1.02; $P < 0.0001$) and the time to first infection was shorter ($P = 0.0002$, log-rank test; Figure 2). The above-mentioned treatment comparisons were also consistently significant when all available follow-up was used for the analysis.

Of the 43 infections in the placebo group, 26 were bacteremia and 17 were exit site infections. Fourteen (54%) of bacteremias and 14 (82%) of the ESI were defined as "definite" in this group. Of the 13 infections in the PT group, eight were bacteremia and five were ESI. Three (38%) of bacteremias and four (80%) of ESI were defined as "definite" in the PT group. The majority of infections (54%) were caused by coagulase-negative staphylococci, and *S. aureus* accounted for 18% of infections (Table 5).

Bacteremias

The proportion of patients who experienced a bacteremia was significantly higher in the placebo group than in the PT group (24% *versus* 10%; $P = 0.020$; Table 3). This represented a 60% relative risk reduction (relative risk, 0.40; 95% CI, 0.19

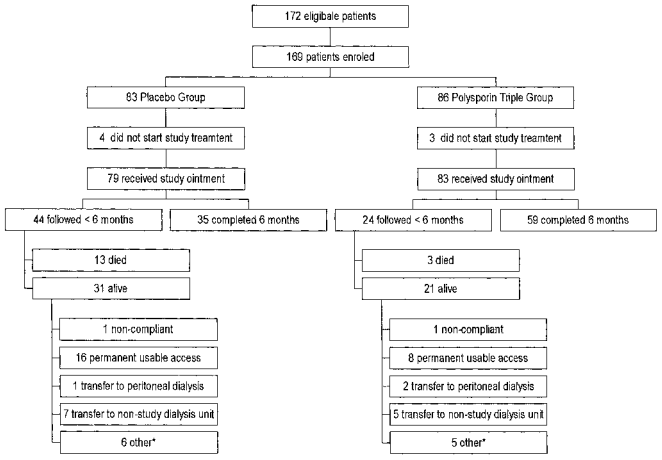

Figure 1. Flow and status of patients. *Other: recovery of renal function (two in each group), skin sensitivity to ointment (one in each group), developed active malignancy and use of long-term antibiotics (one in placebo), kidney transplant (one in placebo), required long-term antibiotics for active skin disorder (one in PT group) and for leg amputation (one in PT group), and began using novel access (one in placebo).

to 0.86) and a NNT of 7 (95% CI, 4 to 33). The rate of bacteremias was 2.48 per 1000 catheter-days in the placebo group as compared with 0.63 in the PT group ($P = 0.0004$). The time to first bacteremia was significantly shorter in the placebo group ($P = 0.0056$, log-rank test; Figure 3).

Mortality

There were 13 deaths in the placebo group as compared with 3 deaths in the PT group within the 6-mo study period ($P = 0.0041$, log-rank test; Figure 4). This represented a 78% relative risk reduction and a NNT of 8 (95% CI, 5 to 27). No infections were observed in the three patients who died in the PT group (Table 6). In contrast, 7 (54%) of the 13 patients in the placebo group who died within the first 6 mo had infections before death. Of those with a preceding infection, all were hospitalized and 100% had bacteremias in the placebo group *versus* no hospitalizations and no bacteremias in the treatment group. When all available follow-up information was used, the survival advantage demonstrated by the PT group persisted (19 deaths in the placebo group and 9 in the PT group; $P = 0.0027$, log-rank test).

Morbidity Related to Infections

More patients in the placebo group than in the PT group required hospitalization (24% *versus* 7%; $P = 0.0041$) and required catheter removal due to infections (27% *versus* 10%; $P = 0.0071$; Table 4).

Prevalence of S. aureus Nasal and Exit Site Carriage

Fifteen percent of patients in the placebo group and 13% of patients in the PT group had *S. aureus* nasal carriage at baseline. The prevalence remained stable over time and similar between the two treatment groups (data not shown). Five percent of patients in the placebo group and 4% of patients in the PT had *S. aureus* colonized at the catheter exit site at baseline. The catheter prevalence dropped markedly in the first few months for both groups. Within the first 6 mo, there was a consistent 22 to 25% colonization of non–*S. aureus* organisms at the exit site in the placebo-treated group compared with 10 to 11% in the PT group.

Discussion

Worldwide, increasing numbers of people are reaching ESRD and requiring renal replacement therapy. In the United States, there are more than 215,000 people who require hemodialysis (4). Once dialysis is required, a safe and reliable means of vascular access is essential; central venous catheterization provides rapid access and is an accepted procedure while patients await more definitive access (1,4,32). However, this approach is associated with infection risks (9,33,34). For example, catheter exit site infections are commonly associated with bacteremias (8 to 21% of cases) and are important causes of catheter loss (8,13). Bacteremias and tunnel infections are not only the leading cause of catheter loss, but they are associated with recurrence of infection, serious metastatic complications, and death (2,6–9,32).

Previous studies have evaluated prophylactic therapies to reduce catheter-related infections. Many have demonstrated important reductions in *S. aureus* skin colonization, exit site infections, and bacteremias using various agents. Current guidelines (26,35) for the use of povidone-iodine in the prevention of HD catheter-related infections are based primarily on the study by Levin *et al.* (17). They evaluated 10% povidone-iodine ointment applied to gauze adjacent to the skin entry site compared with gauze alone in a randomized trial of 129 patients. All patients had single lumen nontunelled subclavian catheters and had their skin and catheter hub prepped with povidone-iodine solution at each dressing change (3 times per wk). They found a septicemia rate of 1/63 in the treated group *versus* 11/66 in the control group and significant reductions in exit site infections and catheter tip colonization. The mean catheter duration was 38.6 d in the treatment group and 36.2 d in the control group. Other studies have demonstrated a reduction in infection rates when topical mupirocin has been applied to the catheter exit site (19) and nares (11,12,18). For example, Sesso *et al.* found a marked increase in *S. aureus* bacteremia when mupirocin was not used (hazard ratio of 7.2) in their trial of mupirocin *versus* povidone-iodine applied to the exit site of temporary catheters. However, the results of these studies are difficult to generalize because they examined primarily non-cuffed, temporary catheters at subclavian sites, which carry a different risk of infection (8,36–38) and are not recommended in current guidelines (26,35). Thus, current guidelines are imperfect in that they advocate tunneled cuffed venous catheters inserted at the internal jugular vein as the method of choice for permanent catheter use (>3 wk duration) (35) but recommend an agent (povidone-iodine) for infection prophylaxis that is unproven in that situation. For this and other reasons, this study was ethically justified. In addition, the value of previously studied single-drug antibiotic prophylaxis is lim-

Table 2. Baseline patient characteristics

Baseline Characteristic	Placebo	PT	Overall
Number of patients	79	83	162
Median age in yr (min, max)	64 (25,87)	68 (24,89)	66 (24,89)
Ethnicity			
White	50	47	97 (60%)
Asian	5	12	17 (10%)
South East Asian	14	17	31 (19%)
Black	10	7	17 (10%)
Male gender	53	52	105 (65%)
S. aureus nasal colonization	12	11	23 (14%)
S. aureus exit site colonization	4	3	7 (4%)
Catheter status at randomization			
prevalent	52	57	109 (67%)
incident	27	26	53 (33%)
Duration on HD[a] in yr (mean)	1.8	1.9	1.9
Etiology of renal disease			
diabetes	27	24	51 (31%)
glomerulonephritis	11	16	27 (17%)
interstitial nephritis	2	1	3 (2%)
hypertension	17	18	35 (22%)
other	22	24	46 (28%)
Comorbidities			
coronary artery disease	47	48	95 (59%)
congestive heart failure	8	5	13 (8%)
diabetes	46	55	101 (62%)
hypertension	64	65	129 (80%)
active skin lesion, *e.g.*, psoriasis	0	2	2 (1%)
Laboratory measures (means)			
creatinine[b] (mg/dl)	7.6	7.0	7.3
urea[c] (mg/dl)	44.8	39.2	4.2
hemoglobin[d] (g/dl)	10.9	10.7	10.8
albumin[d] (g/dl)	4.1	3.9	4.0
IV iron use	30	37	67 (41%)
Erythropoiten use	72	74	146 (90%)

[a] HD, hemodialysis.
[b] SI, μmol/L = mg/dl $\times$ 88.4.
[c] SI, mmol/L = mg/dl $\times$ 0.357.
[d] SI, g/L = g/dl $\times$ 10.

ited by the increasing prevalence of resistance to agents such as mupirocin (39–41). Other studies that have demonstrated a reduced rate of skin colonization and bacteremias include those involving catheters coated with chorhexidine-silver sulfadiazine (21,22,42,43) or minocycline and rifampin (20). These studies are limited by their short-term catheterization and efficacy (42), reduced antimicrobial activity over time (43,44), potential for microbial resistance (45), and generalizability to the chronic hemodialysis population.

The key strengths of our study are the long duration of follow-up, use of guideline-recommended cuffed, tunneled catheters at the internal jugular site, and evaluation of a simple, low cost, prophylactic agent less susceptible to microbial resistance in a placebo-controlled design. Our study patients appear representative of the general dialysis population (Table 2). Furthermore, in the placebo group, the rate of bacteremia was similar to our baseline rate (2.7/1000 catheter-days in the year before the study) and the overall rate of infection (4.1/1000 catheter-days) was consistent with our two institutions' pretrial infection rate and with that reported in the literature (8,13–15).

This is the first study of prophylactic topical therapy in the prevention of permanent HD catheter-related infections that appears to have demonstrated an improvement in mortality. Although cardiac causes accounted for the majority of deaths (46%), many of these patients had a preceding catheter-related infection, particularly serious bacteremias requiring hospitalization. Septicemias have been found to double the risk of death from any cause and increase the future risk of death from septicemia by 5 to 9 times (2). Mortality due to septicemia in

Table 3. Rate of infection by patient baseline characteristics

Baseline Characteristic	Infection Rate	P[a]
Age (yr)		
< 65 years	25% (19/75)	0.57
> 65 years	21% (18/87)	
Ethnicity		
White	20% (19/97)	0.50
Asian	24% (4/17)	
South East Asian	26% (8/31)	
Black	35% (6/17)	
Gender		
male	21% (22/105)	0.44
female	26% (15/57)	
Prevalent catheter at randomization	23% (25/109)	1.00
Incident catheter at randomization	23% (12/53)	
Duration on HD		
< 1 yr	19% (18/96)	0.18
> 1 yr	29% (19/66)	
Etiology		
diabetes	22% (11/51)	.084
glomerulonephritis	7% (2/27)	
hypertension	34% (12/35)	
other	24% (12/49)	
Comorbidities		
coronary artery disease		
no	24% (23/95)	0.71
yes	21% (14/67)	
congestive heart failure		
yes	31% (4/13)	0.50
no	22% (33/149)	
diabetes		
no	21% (21/101)	0.44
yes	26% (16/61)	
hypertension		
yes	26% (33/129)	0.11
no	12% (4/33)	
Labs		
creatinine		
< 620 umol/L	16% (13/81)	0.060
≥ 620 umol/L	30% (24/81)	
urea		
< 15 mmol/L	22% (18/81)	1.00
≥ 15 mmol/L	23% (19/81)	
hemoglobin		
< 108 g/L	27% (21/79)	0.35
> 108 g/L	19% (16/83)	
albumin		
≤ 40 g/L	21% (15/72)	0.71
> 40 g/L	24% (22/90)	
IV iron use		
yes	21% (14/67)	0.85
no	23% (22/94)	
EPO use[b]		
yes	23% (34/146)	1.00
no	19% (3/16)	

[a] Fisher's exact test.
[b] Erythropoiten, subcutaneous route.

Table 4. Results at 6 mo

	Placebo	PT	Relative Risk (95% CI)[a]	*P*
Number of patients	79	83		
At least one infection	27 (34%)	10 (12%)	0.35 (0.18 to 0.68)	0.0013[b]
At least one bacteremia	19 (24%)	8 (10%)	0.40 (0.19 to 0.86)	0.020[b]
Number of infections per 1000 catheter-days	4.10	1.02	0.25 (0.20 to 0.31)	<0.0001[c]
Number of bacteremias per 1000 catheter-days	2.48	0.63	0.25 (0.19 to 0.34)	0.0004[c]
Number of infections	43	13		
Organism type-all infections				
S. aureus	7 (16%)	3 (23%)		
CNS[e]	24 (56%)	6 (46%)		
Other[f]	12 (28%)	4 (31%)		
At least one hospitalization	19 (24%)	6 (7%)	0.30 (0.13 to 0.71)	0.0041[b]
At least one catheter removal[g]	21 (27%)	8 (10%)	0.36 (0.17 to 0.77)	0.0071[b]
Number of deaths	13 (16%)	3 (4%)	0.22 (0.07 to 0.74)	0.0041[d]

[a] Relative risk and 95% confidence interval.
[b] Fisher's exact test.
[c] Exact binomial test.
[d] Log-rank test.
[e] Coagulase-negative staphylococci.
[f] Other organisms include enterococcus, corynebacterium, Gram-negatives (*e.g.*, enterobacter), and yeast.
[g] Catheter removed due to infection.

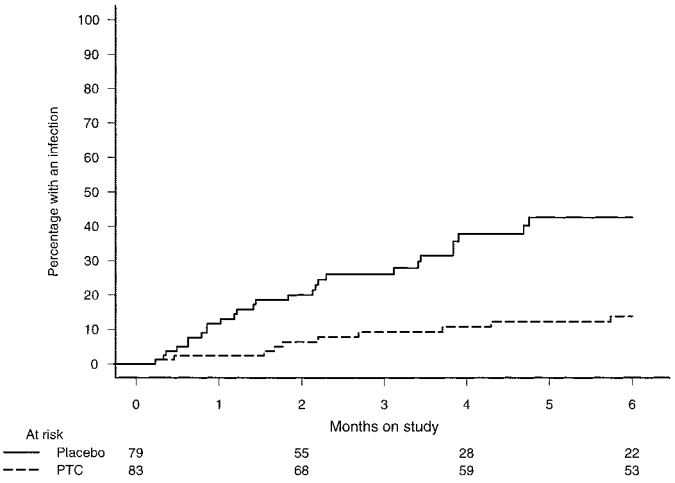

Figure 2. Percentage of patients with an infection.

a dialysis patient is 30-fold to 50-fold higher than in the general population (46). Patients on hemodialysis are often considered frail and "immunocompromised" (47). Thus, serious infection may further compromise a poor baseline health state, rendering them less able to cope with intercurrent illnesses. We postulated that because the PT-allocated group was protected from serious infections (bacteremias) they may have maintained a better general health state than patients in the placebo group, who suffered from catheter-related infections. This trial was designed to determine whether topical PT antibiotic ointment applied to the central venous catheter insertion site could reduce the incidence of catheter-related infections and was found to do so. We also found an association between the use of PT and improved survival. Because survival was identified *a priori* to be a secondary endpoint rather than the primary endpoint further evaluation is necessary in this area due to the relatively low event rate and because other factors may have played a role in the observed difference in survival between the two study groups.

Correlations between organisms cultured from the skin at the catheter exit site and those subsequently isolated from the tip (17,19,48) suggest a pathogenic role between exit site colonization and bacteremia. Organisms may enter the bloodstream by migrating from the skin insertion site along the external surface of the catheter, colonize the lumen and distal intravascular tip, and ultimately lead to a serious bacteremia. Our study demonstrated a lower rate of *S. aureus* nasal and catheter colonization; this may therefore explain, in part, the lower rate of *S. aureus* infections in our study compared with some of the literature (9,12,13,17). However, our study is consistent with others with staphylococcal species being the predominant (60 to 100%) bacterial isolates responsible for the infectious events (8,9,13,32,46). The reasons for such a low rate of *S. aureus* colonization compared with the earlier literature is unclear; however, we speculate that shifts in organism types colonizing these sites may be related to the rigorous cleansing around the

Table 5. Microorganisms causing infections[a]

Organism	Exit Site		Bacteremia		Total
	Placebo	PT	Placebo	PT	
Gram-positive bacteria					
CNS[b]	13	3	11	3	30 (54%)
Corynebacterium species			1		1 (2%)
S. aureus	1	2	6	1	10 (18%)
Enteroccocus	1		2		3 (5%)
Gram-negative bacteria					
Alcaligenes species			2		2 (4%)
Enterobacter species	2		1		3 (5%)
Proteus mirabilis			1		1 (2%)
Stenotrophemonous species				2	2 (4%)
Micrococcus species			1		1 (2%)
Yeast					
Candida			1	2	3 (5%)
Overall	17	5	26	8	56 (100%)

[a] Within the first 6 mo.
[b] Coagulase-negative staphylococci.

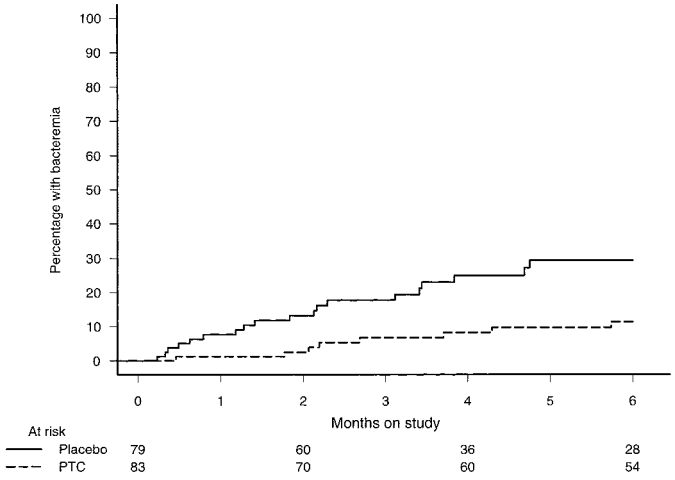

Figure 3. Percentage of patients with bacteremia.

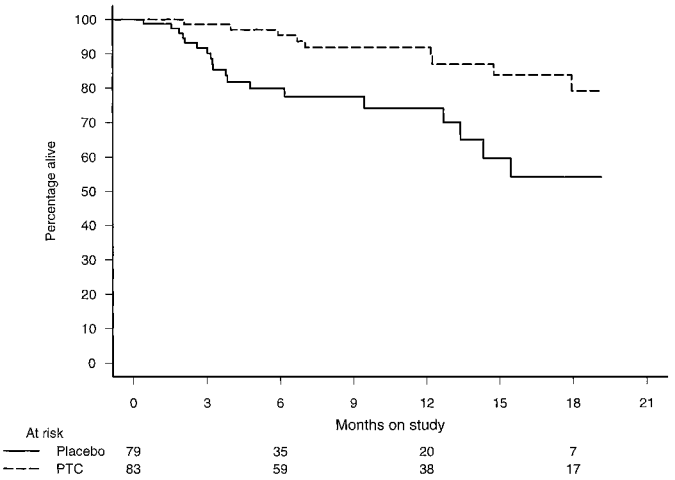

Figure 4. Percentage alive.

exit sites with agents such as chlorhexidine (49). The organisms obtained during the baseline and surveillance swabs (nares and exit site) are being identified by molecular subtyping techniques (pulsed field gel electrophoresis) for ongoing work to gain a better understanding of this change in flora. PT was effective in a dialysis population where the catheter exit sites were colonized with a variety of organisms (Table 5). The benefits of the triple antibiotic formulation include providing the broad-spectrum coverage to make this possible and the reduced likelihood of organisms developing resistance (28). Topical agents with narrower microbial coverage may have been less effective. However, the primary concern with the use of broad-spectrum antibiotics is the potential for increasing yeast infection. As noted in Table 5, there was no difference in the number of yeast infections in the placebo *versus* PT group; most individuals who did develop a yeast infection were immunocompromised or had a predisposing risk factor. One patient in the placebo group and two in the PT group experienced a yeast-related infection. The patient in the placebo group with a yeast-related infection had an embedded piece of catheter and was previously infected with yeast species. In the PT group, one was HIV-positive and one was on long-term tapering steroids for four previous failed transplants. In patients predisposed to yeast infection, multiple and/or broad-spectrum antibiotics, even topical, should be avoided if possible.

The applications of our study must be considered in the context of hemodialysis patients using a permanent tunneled internal jugular dialysis catheter (none of our patients had temporary or subclavian lines). This study population received

Table 6. Causes of death, infections, and organisms for patients who died within 6 mo

ID	Cause of Death	Study Day of Death	Incident or Prevalent Catheter	Study Day of Infection(s)	Type of Infection(s)	Organism Causing Infection(s)
1	Cardiac arrhythmia	13	Incident			
2	Cardiac hemorrhage disseminated HSV	47	Prevalent			
3	Withdrew care, pneumonia	57	Incident			
4	Cancer	62	Incident			
5	Cardiac arrhythmia	64	Prevalent	15	Bacteremia	CNS[a]
6	Catheter-related sepsis	79	Prevalent	66	Bacteremia	Proteus mirabilis Enterobacter sp.,
7	Withdrew care, multiple infections	92	Prevalent	26,37,39	ESI, ESI, Bacteremia	CNS, Enterobacter sp.
8	Withdrew care, multiple infections	96	Prevalent	43, 88	Bacteremia, Bacteremia	CNS, CNS
9	Cardiac arrhythmia	98	Incident			
10	Withdrew care	99	Incident	95	Bacteremia	*Enterobacter sp.*
11	Cardiac arrhythmia	115	Prevalent			
12	Catheter-related sepsis	117	Incident	56	Bacteremia	*Candida sp.*
13	Catheter-related sepsis	145	Prevalent	145	Bacteremia	*Corynebacterium sp.*
14[b]	GI related	63	Incident			
15[b]	Withdrew care	121	Prevalent			
16[b]	Cardiac arrhythmia	180	Incident			

[a] Coagulase-negative staphylococci.
[b] Patients 14 to 16 were in the PT-treated group; patients 1 to 13 were in the placebo group.

skin preparation with chlorhexidine only, thus we cannot answer questions of superiority of PT *versus* another agent for infection prophylaxis. Lastly, we did not formally evaluate the relationships between recurrent catheter problems, recurrent infection, dialysis adequacy, and its effect on the probability of infection; however, we are encouraged by our analysis of time to first infection and bacteremia when comparing the effect of PT with placebo in preventing catheter-related infections.

In summary, we have demonstrated a significant decrease in catheter-related infections, bacteremic episodes, catheter loss, and hospitalizations while possibly influencing mortality by the use of PT to the catheter exit site in catheter-dependent chronic hemodialysis patients. Application of this ointment for prophylactic treatment of permanent hemodialysis catheters should be considered, given its simplicity, low expense, and potential to dramatically reduce infectious complications and their related costs.

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