2010

A crossover intervention trial evaluating the efficacy of a chlorhexidine-impregnated sponge in reducing catheter-related bloodstream infections among patients undergoing hemodialysis

Bernard C. Camins
Washington University School of Medicine in St. Louis

Amy M. Richmond
Washington University School of Medicine in St. Louis

Kathrin L. Dyer
Washington University School of Medicine in St. Louis

Heather N. Zimmerman
Washington University School of Medicine in St. Louis

Daniel W. Coyne
Washington University School of Medicine in St. Louis

See next page for additional authors

A Crossover Intervention Trial Evaluating the Efficacy of a Chlorhexidine-Impregnated Sponge in Reducing Catheter-Related Bloodstream Infections among Patients Undergoing Hemodialysis •

Author(s): Bernard C. Camins , MD, MSCR, Amy M. Richmond , RN, MHS, CIC, Kathrin L. Dyer , MPH, Heather N. Zimmerman , MPH, Daniel W. Coyne , MD, Marcos Rothstein , MD, Victoria J. Fraser , MD

Reviewed work(s):
Source: *Infection Control and Hospital Epidemiology*, Vol. 31, No. 11 (November 2010), pp. 1118-1123
Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America
Stable URL: http://www.jstor.org/stable/10.1086/657075
Accessed: 07/03/2012 20:24

ORIGINAL ARTICLE

A Crossover Intervention Trial Evaluating the Efficacy of a Chlorhexidine-Impregnated Sponge in Reducing Catheter-Related Bloodstream Infections among Patients Undergoing Hemodialysis

Bernard C. Camins, MD, MSCR; Amy M. Richmond, RN, MHS, CIC; Kathrin L. Dyer, MPH; Heather N. Zimmerman, MPH; Daniel W. Coyne, MD; Marcos Rothstein, MD; Victoria J. Fraser, MD

BACKGROUND. Catheter-related bloodstream infections (CRBSIs) account for the majority of hemodialysis-related infections. There are no published data on the efficacy of the chlorhexidine-impregnated foam dressing at reducing the rate of CRBSI among patients undergoing hemodialysis.

DESIGN. A prospective, nonblinded, crossover intervention trial to determine the efficacy of a chlorhexidine-impregnated foam dressing to reduce the rate of CRBSI among patients undergoing hemodialysis.

SETTING. Two outpatient dialysis centers.

PATIENTS. A total of 121 patients who underwent dialysis through tunneled central venous catheters received the intervention during the trial.

METHODS. The primary outcome of interest was the incidence of CRBSI. A nested cohort study of all patients who received the chlorhexidine-impregnated foam dressing was also conducted. Backward stepwise logistic regression analysis was used to determine independent risk factors for development of CRBSI.

RESULTS. Thirty-seven CRBSIs occurred in the intervention group, for an incidence of 6.3 CRBSIs per 1,000 dialysis sessions, and 30 CRBSIs occurred in the control group, an incidence of 5.2 CRBSIs per 1,000 dialysis sessions (risk ratio, 1.22 [95% confidence interval {CI}, 0.75–1.97]; $P = .46$). The chlorhexidine-impregnated foam dressing was well tolerated, with only 2 patients (<2%) experiencing dermatitis that led to its discontinuation. The only independent risk factor for development of CRBSI was dialysis treatment at one dialysis center (adjusted odds ratio, 4.4 [95% CI, 1.77–13.65]; $P = .002$). Age of at least 60 years (adjusted odds ratio, 0.28 [95% CI, 0.09–0.82]; $P = .02$) was associated with lower risk of CRBSI.

CONCLUSIONS. The use of a chlorhexidine-impregnated foam dressing did not decrease the incidence of CRBSI among patients with tunneled central venous catheters who were undergoing hemodialysis.

Infect Control Hosp Epidemiol 2010; 31(11):1118-1123

Infections account for 16%–36% of all deaths among adults with end-stage renal disease.[1,2] The risk of bloodstream infection (BSI) among patients undergoing hemodialysis is significantly higher for those undergoing hemodialysis through a central venous catheter than for those undergoing hemodialysis through arteriovenous (AV) fistulae or grafts.[3-5] Maki et al[6] reported that a silver-impregnated cuff placed on the catheter hub decreased the rate of nontunneled catheter–related bacteremia almost 4-fold. Routine application of povidone-iodine ointment to temporary hemodialysis catheters was also shown to be effective in reducing catheter-related infections.[7]

The Biopatch Antimicrobial Dressing (Johnson & Johnson Wound Management, a division of Ethicon) is a novel catheter dressing impregnated with chlorhexidine gluconate. It is used in conjunction with the standard catheter dressing to prevent catheter-related BSI (CRBSI). The chlorhexidine-impregnated dressing was shown to be effective in reducing

From the Division of Infectious Diseases (B.C.C., K.L.D., H.N.Z., Y.J.F.) and Renal Division (D.W.C., M.R.), Department of Medicine, Washington University School of Medicine, and Department of Hospital Epidemiology and Infection Control, Barnes-Jewish Hospital (A.M.R.), St Louis, Missouri. (Present affiliations: Division of Infectious Diseases, Department of Medicine, Washington University School of Medicine [A.M.R.], St Louis, Missouri; Montana Department of Public Health and Human Services, Helena, Montana [H.Z.N.]; and Fulton County Health and Human Services, Atlanta, Georgia [K.L.D.].)

 0899-823X/2010/3111-0004$15.00. DOI: 10.1086/657075
Received October 6, 2009; accepted May 27, 2010; electronically published September 29, 2010.

microbial colonization of epidural catheters.[8] A randomized clinical trial performed with neonates who had central venous catheters in place demonstrated that the chlorhexidine-impregnated foam dressing, compared with the povidone-iodine rub, significantly decreased the rate of colonization of the central venous catheter but not the incidence of CRBSI.[9] Among neutropenic patients, a randomized, controlled trial showed that use of a chlorhexidine-impregnated dressing with tunneled central venous catheters resulted in fewer documented exit-site infections, but there was no difference in the catheter removal rate between the intervention and control groups.[10] Timsit et al[11] recently published a randomized, controlled trial demonstrating the efficacy of the chlorhexidine-impregnated foam dressing at reducing the rate of CRBSI among critically ill patients with nontunneled central venous catheters.

To our knowledge, there are currently no published studies of the efficacy of the chlorhexidine-impregnated foam dressing in patients undergoing hemodialysis. We recently conducted a crossover intervention trial to study the efficacy of the chlorhexidine-impregnated foam dressing to reduce the incidence of CRBSI among patients undergoing hemodialysis in an outpatient setting.

METHODS

We conducted a prospective, crossover intervention trial at 2 outpatient hemodialysis centers affiliated with Washington University School of Medicine and Barnes-Jewish Hospital in Saint Louis, Missouri, during the period from April 1, 2005, through March 31, 2006. Informed consent was obtained from patients before administration of the chlorhexidine-impregnated foam dressing. Any patient who underwent hemodialysis through a tunneled central venous catheter received the intervention if the dialysis center where he or she underwent dialysis were in the intervention arm of the study. The intervention was continued for every patient who underwent dialysis through a central venous catheter until the intervention period was over, the patient transferred his or her care to a different facility, until a central venous catheter was no longer necessary (ie, an AV graft or fistula was in place), or if the patient was intolerant of the intervention. The only exclusion criterion was a reported allergy to chlorhexidine-gluconate. This study was approved by the Washington University Human Research Protection Office.

Sample Size Estimate

In the 6-month period before the study, the combined incidence of CRBSI at both dialysis centers was 7.05 CRBSIs per 1,000 dialysis sessions, or 40 distinct CRBSIs after 5,766 dialysis sessions. On the basis of the study by Maki et al,[6] use of the chlorhexidine-impregnated foam dressing decreased the CRBSI rate by 62% (unpublished data). This suggested that if this intervention worked on dialysis catheters, the number of CRBSIs in the intervention group should decrease to 16 distinct CRBSIs in 5,766 dialysis sessions (2.28 CRBSIs per 1,000 dialysis sessions). On the basis of the number of dialysis sessions that occurred in the baseline period at both dialysis centers, we would have accumulated an adequate number of dialysis sessions within 1 year. This difference would have been statistically significant, with a P value of less than .001.

Protocols for routine catheter care before the study included the use of a sodium hypochlorite solution (0.114% by volume) for skin and/or catheter antisepsis prior to each dialysis session. The catheter exit site was dressed with a transparent dressing every 7 days unless there was visible blood or soiling or if the dressing came off. The same dressing change schedule was continued when the intervention began. A new dialysis catheter care protocol incorporating the use of the chlorhexidine-impregnated foam dressing was instituted and standardized at both hemodialysis centers at the start of the intervention. The only difference between the catheter care protocols of the hemodialysis centers during the study was the use of the chlorhexidine-impregnated foam dressing. Both dialysis centers had the same nurse-to-patient ratio and shared the same infection-prevention specialist, and although each had its own medical director, both were in the renal division of the affiliated medical school. The intervention was initiated in dialysis center A during the first 6-month period, whereas dialysis center B patients served as the control group. After 6 months, the chlorhexidine-impregnated foam dressing use was discontinued at dialysis center A and its use was instituted in dialysis center B. A nested cohort study including only patients for whom the chlorhexidine-impregnated foam dressing (intervention group) was applied was also performed to determine risk factors for development of CRBSI in this select population. CRBSIs were monitored by the infection control practitioner and the dialysis center staff. All blood cultures for all hemodialysis patients at the 2 dialysis centers were reviewed, as well were all of their hospital admissions, to identify CRBSI. Demographic information and all clinical data were collected from the Cyberren Database (Cybernius Medical), a clinical data management system for nephrology used by both dialysis centers.

Definitions

Definitions for infections were based on the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System guidelines,[12] with some modifications. A CRBSI was defined as a positive blood culture at the time the catheter was in place or within 48 hours after catheter removal, along with clinical signs and symptoms of sepsis (fever [temperature greater than 38.0°C] or hypotension [systolic blood pressure less than 90 mm Hg]) and no other documented primary site of infection. An infection was considered new only if the patient had not received any treatment for a catheter-related infection in the 21 days before the current infection. Assessment of the primary outcome was per-

TABLE 1. Characteristics of Patients who Received the Chlorhexidine-Impregnated Foam Dressing Intervention

Characteristic	All patients (n = 121)	Patients at dialysis center A (n = 55)	Patients at dialysis center B (n = 66)	P
Sex				
Male	52 (43)	25 (45)	27 (41)	.75
Female	69 (57)	31 (55)	39 (59)	
Age, years, median (range)	56 (19–88)	57 (26–87)	56 (19–88)	.93
Race				
African American	97 (80)	42 (76)	55 (83)	.46
White	23 (19)	13 (24)	10 (15)	
Other	1 (1)	0 (0)	1 (2)	
BMI, median (range)	27.1 (14.7–71.6)	25.9 (16.3–53.6)	27.8 (14.8–71.6)	.31

NOTE. Data are no. (%) of patients, unless otherwise indicated. BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

formed by the infection prevention specialist (A.M.R.), and adverse events were assessed by the principal investigator (B.C.C.). Both investigators were not blinded to the period in which the outcome occurred.

Outcomes

The primary outcome for this study was the incidence of CRBSI in the 2 groups measured in the number of CRBSIs per 1,000 dialysis sessions. A secondary outcome studied was the tolerability of prolonged used of the chlorhexidine-impregnated foam dressing. Infection rates between the control and intervention groups were compared using χ^2 analysis. For the nested cohort study, a patient who developed a CRBSI was only counted as a case patient once, even if he or she had multiple episodes of CRBSI, for the purposes of determining risk factors. Thirty-one patients accounted for 67 distinct episodes of CRBSI over the study period. Bivariate analysis of categorical variables in the cohort study was performed using the Mantel Hansel χ^2 test or the Fisher exact test. Continuous variables were compared using the Student t test or the Mann-Whitney U test. A 2-sided P value of less than or equal to .05 was considered to denote statistical significance. Multivariate analysis using backward stepwise logistic regression was performed to determine independent risk factors for development of a CRBSI. The final model was determined using the Hosmer-Lemeshow goodness-of-fit test. Interactions between variables were also tested, but no statistically significant interactions were demonstrated. Variables that were found to have a P value of less than or equal to .1 on bivariate analysis were included in the multivariate analysis logistic regression model. Data analysis was performed using SPSS, version 14 (SPSS).

RESULTS

One hundred twenty-one patients with tunneled central venous catheters were treated with the chlorhexidine-impregnated dressing at both dialysis centers over the 1-year period. Two patients withdrew consent after just 2 dialysis sessions, so use of the chlorhexidine-impregnated foam dressing was discontinued for these patients. Baseline patient characteristics are listed in Table 1. The intent-to-treat analysis included 5,847 dialysis sessions in the intervention period and 5,764 dialysis sessions in the control period. There were 37 CRBSIs during the intervention period (incidence, 6.3 CRBSIs per 1,000 dialysis sessions) and 30 CRBSIs during the control period (incidence, 5.2 CRBSIs per 1,000 dialysis sessions; relative risk [RR], 1.22 [95% confidence interval {CI}, 0.75–1.97]; P = .46) (Figure 1). In 2 patients (less than 2%), the use of the chlorhexidine-impregnated foam dressing was discontinued because of adverse events. Both patients were thought to have developed dermatitis, but 1 patient concomitantly received antimicrobial therapy for an exit-site infection, because it was difficult to ascertain whether the erythema was due to contact dermatitis or infection.

Variables studied for development of CRBSI on bivariate analysis are shown in Table 2. Receipt of hemodialysis at dialysis center A, a history of substance abuse, and frequent

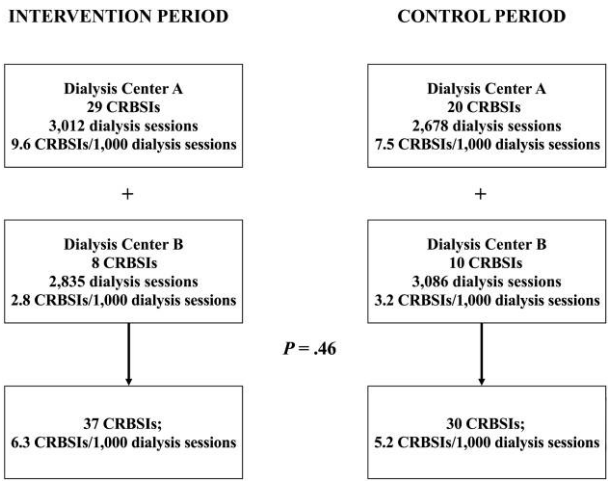

FIGURE 1. Results of the crossover intervention trial. CRBSI, catheter-related bloodstream infection.

TABLE 2. Bivariate Analysis Comparing Patients With and Without Catheter-Related Bloodstream Infection (CRBSI)

Characteristic	Patients with CRBSI (n = 31)	Control subjects (n = 90)	P
Sex			
Male	17 (55)	35 (39)	.12
Female	14 (45)	55 (61)	
Race			
African American	24 (77)	73 (81)	.72
White	7 (23)	16 (18)	
Age, ⩾60 years	7 (23)	41 (47)	.02
Age, median years	53	57	.01
Dialysis center			
A	22 (71)	33 (37)	.001
B	9 (9)	57 (63)	
Hypertension	31 (100)	83 (97)	.29
Congestive heart failure	2 (7)	20 (23)	.04[a]
Diabetes	18 (58)	41 (48)	.32
Obesity	11 (36)	17 (20)	.08
Peripheral vascular disease	9 (29)	19 (22)	.44
Receipt of immunosuppressants	1 (3)	5 (6)	.39
COPD and/or asthma	5 (16)	9 (11)	.41
Hepatitis B or C	3 (10)	5 (6)	.47
Cerebrovascular accident history	7 (23)	15 (17)	.53
HIV infection	1 (3)	1 (1)	.45
Tobacco use	3 (10)	17 (20)	.20
Substance abuse	5 (16)	1 (1)	.005[a]
History of surgery in past 30 days	3 (10)	14 (16)	.37
Admission in past 30 days	5 (16)	29 (34)	.06
Previous CRBSI in past 90 days	4 (13)	9 (11)	.71
Receipt of antibiotics in the past 30 days	3 (10)	18 (21)	.19
Dressing changes			
Once per week	11 (33)	53 (62)	.01
More than once per week	20 (67)	33 (38)	

NOTE. Data are no. (%) of patients, unless otherwise indicated. COPD, chronic obstructive pulmonary disease.

[a] Determined by the Fisher exact test.

dressing changes (more than once per week) were significant risk factors for development of CRBSI on bivariate analysis. A history of congestive heart failure and age of at least 60 years were associated with decreased risk of developing a CRBSI. Two variables on bivariate analysis had P values of less than .1: obesity (increased risk) and admission to the hospital in the previous 30 days (decreased risk). Demographic variables, such as age, sex, and race, as well as obesity, hospital admission in the past 30 days, frequency of dressing changes, and dialysis center, were included in the multivariate analysis model. The only independent predictor for development of CRBSI was dialysis treatment at dialysis center A. Age of at least 60 years was associated with decreased risk of developing a CRBSI (Table 3).

DISCUSSION

This is the first intervention trial using a chlorhexidine-impregnated foam dressing to reduce the risk of CRBSI in outpatient hemodialysis patients. Other investigators have studied other methods of reducing CRBSI among patients undergoing hemodialysis. Lok et al[13] randomized 169 patients receiving hemodialysis through a central venous catheter to receive either polysporin triple antibiotic ointment or placebo over a 6-month period. Fewer infections were observed in the treatment group (12% vs 34%; $P = .001$). The incidence of bacteremia was also lower in the treatment group. (0.63 vs 2.48 cases of bacteremia per 1,000 catheter-days; $P = .0004$).

TABLE 3. Independent Risk Factors for Development of Catheter-Related Bloodstream Infection

Variable	aOR (95% CI)	P
Care at dialysis center A	4.9 (1.77–13.7)	.002
Obesity	2.4 (0.89–6.63)	.08
Age, ⩾60 years	0.28 (0.09–0.82)	.02

NOTE. aOR, adjusted odds ratio; CI, confidence interval.

Johnson et al[14] also enrolled 50 patients in an open-label, randomized trial comparing the application of mupirocin ($n = 27$) thrice weekly around tunneled cuffed hemodialysis catheter exit sites versus the standard of care. Mupirocin-treated patients experienced significantly fewer catheter-related cases of bacteremia (7% vs 35%; $P < .01$). The mupirocin intervention also resulted in a delay in the occurrence of bacteremia (108 vs 55 days; $P < .01$). The same group of investigators conducted a similar study, but this time they randomly assigned patients to receive either thrice-weekly applications of honey or mupirocin at the catheter exit site, to reduce the risk of CRBSI. A total of 101 patients were enrolled in this open-label trial (51 honey-treated patients and 50 mupirocin-treated patients). The 2 interventions produced similar rates of CRBSI. Although the authors did not report an increase in mupirocin resistance, they did conclude that the use of honey is associated with a lower risk of development of resistance.[15]

Aside from the application of honey around the exit-site to prevent CRBSI, all of the interventions above have the potential for the development of antimicrobial resistance that may render the intervention ineffective. The use of a chlorhexidine-impregnated foam dressing to prevent CRBSI would have a decreased potential for the development of resistance, but in our study this intervention did not decrease the incidence of CRBSI among hemodialysis patients with tunneled central venous catheters. We speculate that the catheter exit site may have a reduced role in the pathogenesis of CRBSI in tunneled central venous catheters. The catheter hub may play a larger role in the pathogenesis of CRBSI in this patient population. The risk of CRBSI due to catheter hub bacterial colonization would not be affected by application of the chlorhexidine-impregnated foam dressing.

A unique aspect of this study is the cohort study that provides new information on potentially modifiable risk factors for the development of CRBSI among patients undergoing hemodialysis through central venous catheters. Previous studies have shown that the optimal vehicle for hemodialysis is an AV fistula or graft, because those pose less risk for CRBSI.[16,17] Central venous catheters in this cohort were used only as a temporizing vascular access until an AV fistula or graft was available or as last resorts. Most of the studies on risk factors for bacteremia among hemodialysis patients were based on large data sets containing only codes from *The International Classification of Diseases, Ninth Revision.* Risk factors for CRBSI reported in the literature include older age, female sex, and African American race.[18,19] Potentially modifiable risk factors include hemodialysis versus peritoneal dialysis, temporary catheter versus permanent catheter use, low serum albumin level, and dialyzer reuse. Although diabetes mellitus can be controlled through insulin therapy and diet, it is unknown whether strict control of blood glucose levels leads to a decreased risk of CRBSI among patients undergoing hemodialysis. Data on the contribution of diabetes to the development of CRBSI have been conflicting.[17-19] In this study, we discovered that one dialysis center had a higher risk for CRBSI. The potential differences between the 2 centers include more frequent dressing changes (54% vs 39%; $P = .1$) and more patients with a history of substance abuse (9% vs 2%; $P = .1$) received hemodialysis at dialysis center A. More frequent dressing changes were found to be associated with CRBSI on bivariate analysis, but this factor was eliminated from the logistic regression model because treatment at dialysis center A was a stronger predictor for CRBSI. Frequent dressing changes may lead to higher risk for contamination. On the other hand, they may also be a surrogate marker for frequent bleeding, more perspiration, or poor personal hygiene. A history of substance abuse was also a risk factor for CRBSI on bivariate analysis. Additional investigation is required to determine whether this association is due to relative immunosuppression related to substance abuse, catheter manipulation, personal hygiene differences, staphylococci colonization differences, and other factors.

Age of at least 60 years was associated with decreased risk of CRBSI, a finding inconsistent from those of previous studies.[18,19] The real reason for this finding is unknown; however, obesity and frequent dressing changes in this cohort (both had P values of less than .1 as risk factors on bivariate analysis) were associated with younger age (mean age, 51.2 vs 67.4 years; $P = .01$). The underlying reason that older age (ie, at least 60 years) was associated with decreased risk of CRBSI may have been that these patients were less likely to be obese and were more likely to adhere to the weekly dressing changes. The small sample size may have contributed to these individual risk factors (obesity and frequent dressing changes) not being independent risk factors for development of CRBSI in the logistic regression model.

This study has a few limitations. This study was not a randomized controlled trial. Randomization would have allowed for stratification on the type of catheter and dialysis center to remove potential biases. However this would have required a much bigger study population and inclusion of multiple dialysis centers, which would have been very costly. Despite careful standardization of the catheter care protocol and other processes of care, there were still differences in the dialysis center populations that may have affected the results of the study. These differences can be effectively accounted for by a randomized, controlled trial. The power analysis was based on previous efficacy data, which showed a 62% decrease in CRBSI rates among patients with nontunneled central venous catheters. Our study may not have had sufficient power to show a small difference in CRBSI rates between the intervention and control groups. Finally, there was no "washout" period before the crossover took place. It is unlikely that this would have had an impact on the results of the study, because the first CRBSI after crossover occurred more than 3 weeks after the date of the crossover.

Although not essential to evaluate the primary outcomes of this study, microbiological cultures of the catheter hubs or catheter exit sites were not done, so we were not able to

compare these with the bacterial isolates obtained from blood cultures collected from the patients in the trial. Information on organisms colonizing the skin and the catheter hubs could have helped elucidate the mechanisms behind the development of CRBSI in these hemodialysis patients. Nevertheless, this is the second largest intervention trial involving the exit site on patients who underwent dialysis through tunnelled central venous catheters to date. The crossover intervention trial design also has increased validity over a before-and-after intervention trial.

In a crossover intervention trial, the chlorhexidine-impregnated foam dressing did not significantly decrease CRBSI among patients undergoing hemodialysis with tunneled central venous catheters. In previous studies, application of antibiotics, such as mupirocin or polysporin, has been shown to be an effective intervention, so such interventions should be considered first to reduce the incidence of CRBSI among patients undergoing hemodialysis. The development of resistance to these antibiotics may still limit their use over long periods of time. Older age (at least 60 years) was associated with decreased risk of CRBSI in our patient population.

ACKNOWLEDGMENTS

Financial support. Johnson & Johnson Wound Management, a division of Ethicon. Salary support was also provided by the Barnes-Jewish Hospital Foundation, the National Institutes of Health (UL1RR024992, K12 HD052194, and 1K24AI06779401), and the Centers for Disease Control and Prevention (1U01CI000333–01).

Potential conflict of interests. B.C.C. served on the speaker's bureau for Ethicon. All other authors have no conflicts of interest relevant to this article.

Address reprint requests to Bernard C. Camins, MD, MSCR, Division of Infection Diseases, 660 South Euclid Avenue, Box 8051, Saint Louis, MO 63110-1093 (bcamins@dom.wustl.edu).

Presented in part: the 17th Annual Meeting of The Society for Healthcare Epidemiology of America; Baltimore, Maryland; April 14–17, 2007 (abstract 299).

REFERENCES

1. Causes of death. USRDS. United States renal data system. *Am J Kidney Dis* 1997;30(2 Suppl 1):S107-S17.
2. Mailloux LU, Bellucci AG, Wilkes BM, et al. Mortality in dialysis patients: analysis of the causes of death. *Am J Kidney Dis* 1991;18(3):326–335.
3. Taylor G, Gravel D, Johnston L, Embil J, Holton D, Paton S. Prospective surveillance for primary bloodstream infections occurring in Canadian hemodialysis units. *Infect Control Hosp Epidemiol* 2002;23(12):716–720.
4. Saeed Abdulrahman I, Al-Mueilo SH, Bokhary HA, Ladipo GOA, Al-Rubaish A. A prospective study of hemodialysis access-related bacterial infections. *J Infect Chemother* 2002;8(3):242–246.
5. Stevenson KB, Adcox MJ, Mallea MC, Narasimhan N, Wagnild JP. Standardized surveillance of hemodialysis vascular access infections: 18-month experience at an outpatient, multifacility hemodialysis center. *Infect Control Hosp Epidemiol* 2000;21(3):200–203.
6. Maki DG, Cobb L, Garman JK, Shapiro JM, Ringer M, Helgerson RB. An attachable silver-impregnated cuff for prevention of infection with central venous catheters: a prospective randomized multicenter trial. *Am J Med* 1988;85(3):307–314.
7. Levin A, Mason AJ, Jindal KK, Fong IW, Goldstein MB. Prevention of hemodialysis subclavian vein catheter infections by topical povidone-iodine. *Kidney Int* 1991;40(5):934–938.
8. Shapiro JM, Bond EL, Garman JK. Use of a chlorhexidine dressing to reduce microbial colonization of epidural catheters. *Anesthesiology* 1990;73(4):625–631.
9. Garland JS, Alex CP, Mueller CD, et al. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics* 2001;107(6):1431–1436.
10. Chambers ST, Sanders J, Patton WN, et al. Reduction of exit-site infections of tunnelled intravascular catheters among neutropenic patients by sustained-release chlorhexidine dressings: results from a prospective randomized controlled trial. *J Hosp Infect* 2005;61(1):53–61.
11. Timsit JF, Schwebel C, Bouadma L, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *JAMA* 2009;301(12):1231–1241.
12. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988;16(3):128–140.
13. Lok CE, Stanley KE, Hux JE, Richardson R, Tobe SW, Conly J. Hemodialysis infection prevention with polysporin ointment. *J Am Soc Nephrol* 2003; 14(1):169–179.
14. Johnson DW, MacGinley R, Kay TD, et al. A randomized controlled trial of topical exit site mupirocin application in patients with tunnelled, cuffed haemodialysis catheters. *Nephrol Dial Transplant* 2002;17(10):1802–1807.
15. Johnson DW, van EC, Mudge DW, et al. Randomized, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for the prevention of catheter-associated infections in hemodialysis patients. *J Am Soc Nephrol* 2005;16(5):1456–1462.
16. Oliver MJ, Rothwell DM, Fung K, Hux JE, Lok CE. Late creation of vascular access for hemodialysis and increased risk of sepsis. *J Am Soc Nephrol* 2004;15(7):1936–1942.
17. Abbott KC, Agodoa LY. Etiology of bacterial septicemia in chronic dialysis patients in the United States. *Clin Nephrol* 2001;56(2):124–131.
18. Powe NR, Jaar B, Furth SL, Hermann J, Briggs W. Septicemia in dialysis patients: incidence, risk factors, and prognosis. *Kidney Int* 1999;55(3): 1081–1090.
19. Jaar BG, Hermann JA, Furth SL, Briggs W, Powe NR. Septicemia in diabetic hemodialysis patients: comparison of incidence, risk factors, and mortality with nondiabetic hemodialysis patients. *Am J Kidney Dis* 2000; 35(2):282–292.