PROSPECTIVE SURVEILLANCE FOR PRIMARY BLOODSTREAM INFECTIONS OCCURRING IN CANADIAN HEMODIALYSIS UNITS

Geoffrey Taylor, MD; Denise Gravel, BScN, MSc, CIC; Lynn Johnston, MD; John Embil, MD; Donna Holton, MD; Shirley Paton, RN, MN; Canadian Hospital Epidemiology Committee; Canadian Nosocomial Infection Surveillance Program*

ABSTRACT

OBJECTIVE: Bloodstream infections are a major cause of morbidity and mortality in patients receiving long-term hemodialysis. We wanted to determine the incidence of hemodialysis-related bloodstream infections in Canadian centers participating in the Canadian Nosocomial Infection Surveillance Program.

METHODS: Prospective surveillance for hemodialysis-related bloodstream infections was performed in 11 centers during a 6-month period. Bloodstream infections were defined by published criteria. Hemodialysis denominators included the number of dialysis procedures, the number of patient-days on dialysis, and the frequencies of different types of vascular access.

RESULTS: There were 184 bloodstream infections in 133,158 dialysis procedures (1.4 per 1,000) and 316,953 patient-days (0.6 per 1,000). Hemodialysis access through arteriovenous (AV) fistulae was associated with the lowest risk for bloodstream infection (0.2 per 1,000 dialysis procedures). The relative risk for infection was 2.5 with AV graft access, 15.5 with cuffed and tunneled central venous catheter (CVC) access, and 22.5 with uncuffed CVC access ($P < .001$). There was marked variation among the 11 centers in the means of vascular access used for hemodialysis. Significant variation in infection rates was observed among the centers when controlling for types of access.

CONCLUSIONS: There was a hierarchy of risk of hemodialysis-related bloodstream infection according to type of vascular access. There was significant variation in the type of vascular access being used among the Canadian hemodialysis centers, and also variation in access-specific infection rates between centers (*Infect Control Hosp Epidemiol* 2002;23:716-720).

Nosocomial infections account for up to half of all major complications of hospitalization.[1] Host risk factors for nosocomial infections have been described, but there is evidence of variation between facilities in risk-adjusted nosocomial infection rates. This variation may be attributable to differences in the use of invasive devices and in infection prevention and control practices.[2] Multi-institutional surveillance for nosocomial infections can contribute to their control, by allowing calculation of risk-adjusted infection rates. This allows facilities to compare their infection rates with those of similar institutions. Such comparisons may prompt hospitals with high infection rates to modify practices, thus allowing them to bring their rates into line with comparator facilities.[3-5]

Hemodialysis continues to be an important treatment option for individuals with end-stage renal disease. It is the primary method of treatment for long-term renal failure, as well as a short-term measure until renal transplantation or peritoneal dialysis can be performed. Infection, a common and serious complication of hemodialysis, is associated with significant mortality.[6-8] The major risk factor for the occurrence of hemodialysis-related bloodstream infec-

Dr. Taylor is from the Department of Medicine, University of Alberta, Edmonton, Alberta, Canada. Dr. Holton, Ms. Gravel, and Ms. Paton are from the Divisions of Nosocomial and Occupational Infections, Center for Infectious Diseases Prevention and Control, Health Canada, Ottawa, Ontario, Canada. Dr. Johnston is from the Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada. Dr. Embil is from the Department of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.

**The following members of the Canadian Nosocomial Infection Surveillance Program participated directly in this study: E. Bryce, Vancouver General Hospital, Vancouver, British Columbia; J. Embil, Health Sciences Center, Winnipeg, Manitoba; J. Conly, University Health Network, Toronto, Ontario; D. Gravel, Center for Diseases Prevention and Control, Health Canada; E. Henderson, Calgary Regional Health Authority, Calgary, Alberta; J. Hutchinson, Health Sciences Center, St. John's, Newfoundland; M. Ishak, Vernon General Hospital, Montreal, Quebec; L. Johnston, Queen Elizabeth II Health Sciences Center, Halifax, Nova Scotia; W. Thompson, The Moncton Hospital, New Brunswick; M. Miller, Jewish General Hospital, Montreal, Quebec; M. Mulvey, National Microbiology Laboratory, Winnipeg, Manitoba; S. Paton, Center for Diseases Prevention and Control, Health Canada; A. Simor, Sunnybrook and Women's College Health Sciences Center, Toronto, Ontario; G. Taylor, University of Alberta, Edmonton, Alberta; and D. Zoutman, Kingston General Hospital, Kingston, Ontario.*

The following members of the Canadian Nosocomial Infection Surveillance Program participated by assisting in design of the protocol: J. Embree, Health Sciences Center, Winnipeg, Manitoba; M. Gourdeau, Hôpital de L'Enfant-Jésus, Quebec, Quebec; D. Gregson, St. Joseph's Health Center, London, Ontario; J. Langley, IWK Hospital for Sick Children, Halifax, Nova Scotia; M. Loeb, Hamilton Health Sciences Corporation, Hamilton, Ontario; A. Matlow, Hospital for Sick Children, Toronto, Ontario; A. McGeer, Mount Sinai Hospital, Toronto, Ontario; D. Moore, Montreal Children's Hospital, Montreal, Quebec; and M. Ofner-Agostini, Center for Diseases Prevention and Control, Health Canada.

Address reprint requests to Dr. Geoffrey D. Taylor, 2E4.11 Walter McKenzie Center, University of Alberta Hospital, Edmonton, Alberta T6G 2B7, Canada.

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tion is vascular access.[9-12] Long-term percutaneous vascular access is required to facilitate hemodialysis. This can be accomplished by the use of autologous arteriovenous (AV) fistulae, prosthetic (AV) grafts, and central venous catheters (CVCs). CVCs may contain an external cuff and be tunneled subcutaneously for a distance or may be non-cuffed and inserted directly into a central vein without a subcutaneous tunnel.

No large, multicenter database has been published that would permit individual healthcare facilities to compare their use of vascular access, as well as their infection rates in hemodialysis populations, with that of other institutions. The Canadian Nosocomial Infection Surveillance Program (CNISP) was formed in 1994 as a collaboration between Health Canada and a network of hospitals, the Canadian Hospital Epidemiology Committee (CHEC). The objective of the CNISP is to collect, analyze, and disseminate data on the occurrence of nosocomial infections in Canadian hospitals. The CNISP set as a priority establishing Canadian benchmark data for the occurrence of hemodialysis-related bloodstream infection and determining the means of vascular access in Canadian hemodialysis centers.

METHODS

Eleven hospital-based hemodialysis units from nine provinces were recruited from the CHEC membership. All were adult units and ten were affiliated with academic medical centers. Participating centers are listed in the footnotes on the first page of this article.

Targeted surveillance for the occurrence of bloodstream infections in long-term hemodialysis units was prospectively performed for a 6-month period from December 1998 to May 1999 in participating units. Dialysis procedures and patient-days of dialysis in the units were collected. Patients with acute renal failure undergoing dialysis in intensive care unit settings were not included. Infections in patients in associated but geographically separate satellite units were included at some centers, but patients undergoing home hemodialysis were excluded. Numerator and denominator data from satellite units were collected in the same fashion as those from the hospital units.

Routine clinical practice in all of the units includes drawing blood for at least one set of cultures (two vials) in a febrile patient prior to prescribing antimicrobial therapy. The results of blood cultures were monitored in these patients. Any positive blood culture occurring in a patient receiving hemodialysis prompted a review of the patient's chart by trained and experienced practitioners from the hospital's infection control program.

Access-associated bloodstream infections were defined according to previously published criteria for definite or probable infection.[13] A positive blood culture was considered to represent a definite bloodstream infection if there was histologic evidence of septic thrombophlebitis in an excised vessel, or if a culture of the surface of the intravascular device or the skin was positive for the same organism as the blood culture.[14] A positive culture was considered to represent a probable bloodstream infection if there were positive blood cultures from two vials yielding the same organisms, if they were drawn from different sites, if *Staphylococcus aureus* or *Candida* species grew in one blood culture, or if coagulase-negative staphylococci, *Bacillus* species, *Corynebacterium* species, or *Enterococcus* species grew in a single vial from an immunocompromised patient. A positive blood culture of the same bacterial species in a patient in whom bloodstream infection had been previously documented was assessed on a case-by-case basis to determine whether it was likely to represent a continuation or relapse of the previous infection or a new infection. Following review, a bloodstream infection was considered to be related to vascular access if an alternative source could not be implicated. Blood culture isolates considered contaminants or to come from bacteremia secondary to an alternate source of infection were not included.

Rates of access-associated bloodstream infections in patients who received dialysis with uncuffed and cuffed CVCs, AV grafts, and AV fistulae were calculated using as denominators the number of times the access was used for dialysis (dialysis procedures) and the number of days the access was in situ and used by the patient (patient-days). Where there were two types of vascular access in use, patients were categorized by the higher-risk access. Relative risks (RRs) for access-associated bloodstream infections were used to establish a hierarchy of risk for each type of vascular access. Fisher's exact test was used to compare differences in proportions and calculate *P* values. Analysis of covariance (weighted by denominator for each center) was used to test for significant difference among vascular access incidence rates between the participating hospitals. An alpha level of 0.05 was considered statistically significant. Data were analyzed with Epi-Info 2000 (Centers for Disease Control and Prevention [CDC], Atlanta, GA) and SAS (version 8.1; SAS Institute, Inc., Cary, NC) software.

RESULTS

Surveillance was performed for 6 months (between December 1998 and May 1999) in the hemodialysis units. Overall, 133,158 hemodialysis procedures were conducted (range by site, 1,832 to 24,366). There were 316,953 patient-days of observation. An average of 1,778 patients underwent hemodialysis each month in the units. Of the 184 episodes of positive blood cultures meeting the case definition of access-related bloodstream infection, 57 were considered definite and 127 probable bloodstream infections. There were 64 instances of a blood culture growing a common skin contaminant in a single vial, which were excluded after review. Hemodialysis via AV fistulae access was most common, accounting for half of all dialysis procedures, and was associated with the lowest infection rate (0.2 per 1,000 dialysis procedures). Infection rates were higher when vascular access was achieved via AV graft (0.6 per 1,000 dialysis procedures; RR compared with AV fistulae, 2.5; 95% confidence interval [CI_{95}], 1.2 to 5.2), cuffed

TABLE 1
MICROBIAL ETIOLOGY OF BLOODSTREAM INFECTIONS

Organism (n = 206)*	All Access No. (%)	Uncuffed CVC (n = 84) No. (%)	Cuffed CVC (n = 94) No. (%)	AV Graft (n = 14) No. (%)	AV Fistulae (n = 14) No. (%)
Staphylococcus aureus	76 (36.8)	30 (35.7)	30 (31.9)	7 (50.0)	9 (64.4)
Coagulase-negative staphylococci	73 (35.8)	30 (35.7)	38 (40.4)	2 (14.3)	3 (21.4)
Enterococcus species	20 (9.8)	11 (13.1)	7 (7.5)	2 (14.3)	0 (0)
Streptococcus species	6 (2.9)	2 (2.4)	2 (2.1)	2 (14.3)	0 (0)
Enterobacter species	6 (2.9)	2 (2.4)	3 (3.2)	1 (7.1)	0 (0)
Pseudomonas species	5 (2.5)	2 (2.4)	2 (2.1)	0 (0)	1 (7.1)
Candida species	4 (1.9)	1 (1.2)	3 (3.2)	0 (0)	0 (0)
Klebsiella species	3 (1.4)	1 (1.2)	1 (1.1)	0 (0)	1 (7.1)
Corynebacterium species	3 (1.0)	1 (1.2)	2 (2.1)	0 (0)	0 (0)
Escherichia coli	2 (1.0)	1 (1.2)	1 (1.1)	0 (0)	0 (0)
Stenotrophomonas maltophilia	2 (1.0)	0 (0)	2 (2.1)	0 (0)	0 (0)
Other species†	6 (2.9)	3 (3.5)	3 (3.2)	0 (0)	0 (0)

CVC = central venous catheter; AV = arteriovenous; n= number of bloodstream infections.
*All reported organisms; 18 patients had two organisms and 4 patients had three organisms.
†Other species include *Clostridium perfringens* (1), *Proteus mirabilis* (1), *Serratia marcescens* (1), *Moraxella* species (1), *Acinetobacter lwoffi* (1), and unknown (2).

and tunneled CVC (3.1 per 1,000; RR, 15.5; CI_{95}, 8.2 to 21.5), and uncuffed and nontunneled CVC (5.2 per 1,000 dialysis procedures; RR, 22.5; CI_{95}, 12.5 to 39.4). When the two types of central venous access were compared, uncuffed and nontunneled catheters had a higher infection risk (RR, 1.6; CI_{95}, 1.17 to 2.21; P = .003). Rate calculations using patient-days as the denominator produced the same hierarchy of infection risk for different means of access and similar RRs (data not shown).

Dialysis treatments in nine satellite units accounted for 9.0% of all dialysis procedures. The infection rate was significantly higher in hospital units (1.4 per 1,000 dialysis procedures) than in satellite units (0.7 per 1,000 dialysis procedures) (RR, 1.92; CI_{95}, 1.0 to 3.8; P = .05). Differences in infection rates between hospital and satellite units remained significant when rates were stratified by means of vascular access.

There were 206 microorganisms isolated from blood culture specimens in these 184 cases (Table 1). Aerobic gram-positive cocci were the most frequent, accounting for 85.3% of all identified organisms. Methicillin-resistant strains accounted for 10% of *S. aureus* isolates; no vancomycin-resistant strains were detected among the 20 episodes of *Enterococcus* species bacteremia. There was a trend for infections associated with CVC access to be more frequently caused by coagulase-negative staphylococci (36% to 40%) compared with infections associated with graft or fistulae access (14% to 20%).

Among 11 units, type of vascular access used for hemodialysis varied significantly (P < .001). Although the median use of the lowest-risk method of access, AV fistulae, was 43% of hemodialysis procedures, the range by unit was from 17% to 67% (Table 2). Similarly, the use of higher-risk access, either cuffed or uncuffed CVC, varied significantly (cuffed, 0 to 58% of dialysis procedures; uncuffed, 0 to 38%). When the means of vascular access was controlled for, there was still significant variation in infection rates between centers (P = .004). Rates of infection associated with AV fistulae varied from a low of 0 per 1,000 dialysis procedures to a high of 6.3 per 1,000 in different centers. Rates of infection associated with cuffed CVCs ranged from 0 to 4.8 per 1,000 and rates of infection associated with uncuffed CVCs ranged from 0 to 12.0 per 1,000 (Table 3).

DISCUSSION

Currently, autologous AV fistulae, AV grafts, and CVCs are the preferred means of establishing vascular access in patients receiving hemodialysis. In this large, multicenter study, as in previous studies,[15-17] we were able to show a marked hierarchy in infection risk: lowest with AV fistulae and highest with uncuffed and nontunneled CVCs. It has been demonstrated recently that hemodialysis via CVC, compared with via fistulae or graft, increases not only infection rates, but also mortality.[18] In that study, the mortality rate related to all causes and infection was higher for both CVC access and AV graft access compared with AV fistulae access.

In the current study, uncuffed CVC access had a risk of infection more than 22 times higher than that of AV fistulae access. Cuffed and tunneled CVCs had significantly lower risk than uncuffed catheters, suggesting that if graft or fistulae access is not possible, cuffed catheters may be preferable. However, given the markedly higher risk with either type of CVC, there is a need for the development of percutaneous catheters with improved safety. Impregnation of central catheters with antibacterials[19,20] or antiseptics[21] has reduced the infection risk for general use catheters; however, in one clinical trial, a silver-impregnat-

TABLE 2
USE OF VASCULAR ACCESS DEVICES IN CANADIAN HEMODIALYSIS UNITS ACCORDING TO THE NUMBER OF DIALYSIS PROCEDURES*

Unit (No. of Dialysis Procedures)	Uncuffed CVC		Cuffed CVC		AV Graft		AV Fistulae	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
A (14,549)	816	(5.6)	8,479	(58.3)	2,780	(19.1)	2,474	(17.0)
B (24,366)	39	(0.2)	5,572	(22.9)	7,998	(32.8)	10,757	(44.1)
C (18,381)	2,027	(11.0)	2,516	(13.7)	2,078	(11.3)	11,760	(64.0)
D (15,331)	5,760	(37.6)	0	(0)	0	(0)	9,571	(62.4)
E (21,387)	2,161	(10.1)	4,688	(21.9)	4,654	(21.8)	9,884	(46.2)
F (7,132)	983	(13.8)	1,206	(16.8)	189	(2.7)	4,754	(66.7)
G (1,832)	416	(22.7)	0	(0)	781	(42.6)	635	(34.7)
H (5,443)	695	(12.8)	352	(6.5)	1,961	(36.0)	2,435	(44.7)
I (4,469)	217	(4.9)	738	(16.5)	1,922	(43.0)	1,592	(35.6)
J (11,102)	325	(2.9)	2,145	(19.3)	2,080	(18.7)	6,552	(59.1)
K (9,166)	0	(0)	2,478	(27.0)	1,220	(13.3)	5,468	(59.7)
Total (133,158)	13,439	(10.1)	28,174	(21.2)	25,663	(19.3)	65,882	(49.5)

CVC = central venous catheter; AV = arteriovenous.
*A difference exists between centers for the use of vascular access devices ($P < .001$).

TABLE 3
INCIDENCE RATES FOR PRIMARY BLOODSTREAM INFECTIONS IN CANADIAN HEMODIALYSIS UNITS ACCORDING TO THE HOSPITAL AND THE TYPE OF VASCULAR ACCESS*

Unit	Uncuffed CVC			Cuffed CVC			AV Graft			AV Fistulae		
	No.	Proc	IR	No.	Proc	IR	No.	Proc	IR	No.	Proc	IR
A	2	816	2.5	17	8,479	2.0	0	2,780	0.0	1	2,474	0.4
B	0	39	0.0	27	5,572	4.8	2	7,998	0.3	0	10,757	0.0
C	15	2,027	7.4	9	2,516	3.6	5	2,078	2.4	3	11,760	0.3
D	22	5,760	3.8	0	0	0.0	0	0	0.0	2	9,571	0.2
E	15	2,161	6.9	22	4,688	4.7	0	4,654	0.0	2	9,884	0.2
F	4	983	4.1	4	1,206	3.3	1	189	5.3	1	4,754	0.2
G	5	416	12.0	0	0	0.0	2	781	2.6	4	635	6.3
H	6	695	8.6	0	352	0.0	0	1,961	0.0	0	2,435	0.0
I	1	217	4.6	1	738	1.4	1	1,922	0.5	0	1,592	0.0
J	0	325	0.0	4	2,145	1.9	3	2,080	1.4	1	6,225	0.2
K	0	0	0.0	2	2,478	0.8	0	1,220	0.0	0	5,468	0.0
Total	70	13,439	5.2	86	28,174	3.1	14	25,663	0.6	14	65,882	0.2

No. = number of bloodstream infections; IR = incidence rate of bloodstream infections per 1,000 dialysis procedures; CVC = central venous catheter; AV = arteriovenous; Proc = procedures.
*Per 1,000 dialysis procedures. A difference was detected between centers for incidence rate ($P = .004$).

ed cuffed catheter did not reduce hemodialysis infections.[22] Currently, AV fistulae or graft is the safest form of vascular access for hemodialysis.

Comparison of rates between studies, or between sites in the same study, depends on appropriate numerators and denominators. In this study, we used Canadian definitions for definite or probable bloodstream infections to define cases.[23] These definitions differ slightly from CDC surveillance definitions of primary bloodstream infections in that common skin contaminants in a single blood culture vial are included for a patient with clinical signs of infection only if he or she is considered immunocompromised. In the CDC definition, such cases are included if the attending physician institutes appropriate therapy. As a result of the elimination of physician subjectivity from the definition of infection, we believe that the Canadian definition allows comparisons between centers to be more objective. Although the effect of this difference in definition on the number of cases excluded is unknown, we suspect it is slight.

A limitation to this study is the fact that 10 of the 11 participating institutions were academic medical centers, which may have populations of dialysis patients that are different from those in community hospitals. However, in Canada, almost all hemodialysis is regionally administered and geographically organized around hospitals and outlying satellite units. Hospital units conduct dialysis for both

ambulatory and hospitalized patients. The lower infection rate that we found in satellite units likely reflects the wholly ambulatory nature of this patient population.

Different denominators for calculation of hemodialysis-associated infection rates have been previously reported. On the basis of other intravascular device infections, either patient-days with vascular access in use or number of dialysis procedures performed is most appropriate.[24] Each captures the period of patient risk and, in this study, gave consistent results. Because percutaneously inserted CVCs are left in situ between dialysis procedures, whereas grafts and fistulae are accessed for each dialysis treatment, more appropriate denominators may be patient-days for CVCs and dialysis procedures for grafts and fistulae.

This study provides evidence of substantial variation in the process and infection outcomes of hemodialysis care in Canadian hemodialysis centers. Despite existing evidence of a difference in infection risk by type of access, it was noted that some centers relied heavily on higher-risk forms of access. Possible reasons for this variation are patient preference and local availability of resources (eg, ability to access surgical expertise to create grafts and fistulae). Where variation is not the result of patient factors such as anatomic availability of vessels to create an adequate AV fistula or graft, hemodialysis centers should strive to minimize the use of higher-risk forms of access.

Given the variation in the use of vascular access between centers, not unexpectedly, a marked variation in infection rates was observed between centers, ranging from 0.2 to 6.0 per 1,000 dialysis procedures. Even when means of access was controlled for, there were large and statistically significant variations in infection rates. Additional research is necessary to identify the source of this variation. Several possibilities can be considered. As in any surveillance study, it is possible that there was a diagnostic artifact. Because the definition of infection depends on a positive blood culture, if some centers were more inclined than others to manage febrile episodes without performing blood cultures, their calculated infection rates could have been falsely lower. However, standard clinical practice in these units was to perform blood cultures for febrile patients prior to initiating antimicrobial therapy. Although means of access was the most important risk factor for infection, it is also possible that the populations of the centers varied in other risk factors for infection, such as the prevalence of *S. aureus* carriage[25] or patient hygiene.[26] Finally, there may indeed be a true access-specific variation in rate, which may be attributable to nursing resources[27,28] or experience, or infection prevention and control practices.

Until there is further evaluation, centers experiencing higher rates need to review staffing levels, training, and infection prevention practices to determine whether infection rates can be reduced.

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