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Prospective study of the impact of open and closed infusion systems on rates of central venous catheter-associated bacteremia

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Objective: We sought to ascertain the effect of switching from an open infusion system to a closed system on rates and sequelae of central venous catheter (CVC)-associated bloodstream infection in the intensive care department (ICU) of 2 hospitals in Argentina.

Methods: A prospective, controlled, time-series, cohort trial was undertaken in adult patients admitted to 4 level-III adult ICUs in Buenos Aires, Argentina, who had a CVC in place for at least 24 hours. Rates of CVC-associated bloodstream infection during a period of active surveillance with an open system (baseline; externally vented, semirigid, noncollapsible, 1-port plastic bottles) were compared with rates after switching to a closed system (intervention; nonvented, collapsible, 2-port plastic bags).

Results: Between August 1999 and March 2002, 992 patients in the ICU with CVCs were enrolled. Patients during each study period (open system, 608; closed system, 384) were similar with respect to sex, severity-of-illness score, and prevalence of diabetes and cancer. Compliance with handwashing and CVC site care was also similar during the 2 study periods. The incidence of CVC-associated bacteremia during use of the closed system was significantly lower than during use of the open system (2.36 vs 6.52/1000 catheter-days, relative risk = 0.36, 95% confidence interval = 0.14-0.94, $P = .02$); bacteremias caused by gram-negative bacilli declined by 64%. In all, 17 patients with catheter-associated bacteremia died during the period when the open system was in use (2.8%), versus only 1 (0.2%) during use of the closed system (relative risk 0.09, $P = .003$). The calculated cost savings in the 20 hospital-month intervention period was \$53,768 and 130.9 ICU days.

Conclusion: Adoption of a closed infusion system resulted in major reductions in the incidence of catheter-associated bacteremia, related mortality, and cost. Because most Latin American hospitals still use externally vented fluid containers, switching to nonvented bags could substantially reduce rates of nosocomial bacteremia. (Am J Infect Control 2004;32:135-41.)

The Survey of Efficacy of National Infection Control study of the Centers for Disease Control and Prevention (CDC) in 1985 confirmed the efficacy of nosocomial infection control programs within hospitals^{1,2} and, with the influence of the Joint Commission on Accreditation of Hospitals, active infection control programs were established within hospitals throughout North America. Unfortunately, similar programs are not yet statutorily mandatory in most Latin American countries, and the majority of Latin

American hospitals, including those in Argentina, do not have formal nosocomial infection control programs. As a consequence, few Latin American health care workers are familiar with published infection control guidelines,³ especially for infusion therapy.⁴

Patients who are hospitalized are at substantial risk of nosocomial bacteremia developing, especially within the intensive care department (ICU). Most nosocomial bacteremias originate from an intravascular device (IVD), particularly the central venous catheter (CVC).⁵⁻⁷ Catheter-associated bacteremias prolong hospitalization and greatly increase the cost of health care but, most importantly, are associated with attributable mortality in the range of 10% to 25%.⁷⁻¹⁰

Published CDC guidelines to prevent IVD-associated bloodstream infection (BSI) have been available since the 1980s.¹¹ The 1996,¹² and 2002¹³ intravenous (IV) guidelines of the CDC's Healthcare Infection Control Practice Advisory Committee (HICPAC) are widely used throughout North America and worldwide. Moreover, new technologies, which implicitly reduce risk, have been shown to further reduce rates of IVD-associated BSI.¹⁴⁻²⁴

There are 2 types of IV fluid containers in use worldwide: a glass or semirigid plastic bottle, which

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Fig 1. Open and closed infusion systems studied.

must be externally vented to ambient air to allow fluid egress (open system); and a collapsible plastic bag, which does not require external venting to empty (closed system). Open systems have been supplanted by closed systems throughout North America and Western Europe. During the 1970s, outbreaks of infusion-related bacteremia in North American hospitals were traced to contamination of infusate in open infusion systems.^{25–28} More recently, hospitals in Mexico,^{29,30} Brazil,³¹ and Greece³² have experienced outbreaks with open systems. Other studies showed that the extrinsic or in-use contamination plays the most important part in bacterial contamination of the infusion system.³³

The risk of contamination of IV fluids during setup, admixture preparation, and administration is high,^{29,30} especially in Latin American hospitals.^{30,34–36} Moreover, if the system needs to be vented, as is mandatory with glass bottles or semirigid plastic containers in developing countries, there are additional risks of extrinsic contamination.

We report the results of a prospective, controlled, time-series study undertaken to determine the impact of switching from an open, semirigid, noncollapsible, 1-port infusion system to a closed, collapsible, 2-port system on endemic rates of CVC-associated bacteremia and associated mortality in 4 ICUs in 2 medical centers in Argentina.

METHODS

The study was conducted in 2 hospitals in Buenos Aires, Argentina: Bernal Medical Center and Colegiales Medical Center. Each has an active infection control program, with a physician trained in internal medicine, infectious diseases, and hospital epidemiology, and an infection control nurse.³⁷ Bernal Medical Center is a private 150-bed hospital situated in the province of

Buenos Aires with 1 medical-surgical ICU (17 beds) and 1 coronary care department (15 beds); Colegiales Medical Center is a private 180-bed hospital in the city of Buenos Aires with 1 medical-surgical ICU (10 beds) and 1 coronary care department (10 beds). All ICUs in the study centers operate at the highest Argentinean level of complexity (IV), providing care for patients who have undergone open heart operation, neurosurgery, gastrointestinal operation, or orthopedic operation, and patients with trauma or serious medical illnesses. The institutional review board at each center approved the study protocol.

Data collection

All patients hospitalized in one of the study ICUs with a CVC in place for 24 hours or longer were enrolled in the study. An infection control nurse at each study center prospectively extracted data from patient charts. The principal investigator (V. D. R.) trained data collectors at each center before initiation of the trial. Each study patient's sex, average severity-of-illness score on entry to the ICU,³⁸ duration of CVC use, exposure to antibiotics and other invasive devices, and all active infections identified while in the ICU were recorded. All data collection sheets were screened for errors and missing data by a study coordinator. Every patient with suspected IVD-associated BSI was personally examined and evaluated by the principal investigator (V. D. R.).

Definitions

Definitions for CVC-associated BSI were adopted from those of the CDC National Nosocomial Infections Surveillance program.^{39,40} "Laboratory confirmed BSI" was defined as: (1) patient had a recognized pathogen cultured from 1 or more percutaneous blood cultures, and the positive blood culture did not appear to be related to an infection at another body site; with common skin commensals (eg, diphtheroids, *Bacillus*, *Propionibacterium*, coagulase-negative staphylococci or micrococci), the organism was cultured from 2 or more blood cultures drawn on separate occasions; and (2) the patient had at least one of the following signs or symptoms: fever > 100.4°F, chills, or hypotension.

Culture technique

Decisions to obtain blood cultures were made independently by patients' attending physicians. Standard laboratory methods were used to identify microorganisms recovered from positive blood cultures.⁴¹

Infusion systems studied

The open infusion system studied consisted of a semirigid plastic container that required insertion of a needle through the bung to permit air to enter; the

Table 1. Number of months of each study phase in the 2 centers

Hospital	No. of months (CVC-days)		Total
	Open system	Closed system	
Bernal	19 (August 1, 1999 – March 30, 2001)	12 (April 1, 2001 – March 30, 2002)	31
Colegiales	7 (January 1, 2001 – July 30, 2001)	8 (August 1, 2001 – March 30, 2002)	15
Total	26	20	46

CVC, Central venous catheter.

Table 2. Baseline characteristics of study patients on admission to an intensive care department during the 2 study phases

	Open system (n = 608)	Closed system (n = 384)	P value
Males, No. (%)	332 (54.60)	216 (56.25)	.73
Age (y) mean $\pm$ SD	71.7 $\pm$ 12.0	70.2 $\pm$ 14.0	.08
Severity-of-illness score, mean $\pm$ SD	3.3 $\pm$ 0.8	3.2 $\pm$ 0.9	.07
Surgical patients, n (%)	218 (35.8)	138 (35.9)	.98
Diabetes, No. (%)	92 (15.2)	60 (15.6)	.88
Cancer, No. (%)	28 (4.6)	16 (4.2)	.75
Mechanical ventilation, No. (%)	329 (54.1)	191 (49.7)	.35
Urinary catheter, No. (%)	549 (90.3)	339 (88.2)	.74
CVC, No. (%)	608 (100.0)	384 (100.0)	1.00
Duration of CVC placement, days, mean $\pm$ SD	3.57 $\pm$ 0.22	3.90 $\pm$ 0.26	.35

CVC, Central venous catheter.

closed system consisted of a collapsible polyvinyl bag that did not require an external vent to empty (Fig 1).

Study design

Active surveillance for CVC-associated infections and compliance with infection control practices was started during the preintervention period and continued throughout the intervention period in each study center, using CDC methodologies and criteria.^{38,42} The preintervention period lasted 19 months (August 1999–March 2001) at Bernal Medical Center and 7 months (January–July 2001) at Colegiales Medical Center; the intervention period lasted 12 months (April 2001–March 2002) at Bernal Medical Medical Center and 8 months (August 2001–March 2002) at Colegiales Medical Center (Table 1).

Handwashing compliance,⁴³ placement of gauze on IVD insertion sites,⁴ marking of the date on the IV administration set, and condition of the gauze dressing were assessed and entered into a standard form by a research nurse who observed health care worker behavior in the study units twice a week. Compliance with insertion site and administration set care required placement of a gauze dressing over the CVC insertion site and a label on the IV administration set documenting the date it was replaced. The criteria for condition of the gauze were as follows: absence of blood; absence

of moisture; absence of gross soilage; and coverage of insertion site.

Data analysis

Outcomes assessed during the preintervention and intervention period included the incidence density rate of CVC-associated BSI (number of cases/1000 CVC-days), total ICU days, total cost of ICU care, and crude mortality of patients with CVC-associated BSI.

Software (EpiInfo, Version 6.04b, Centers for Disease Control and Prevention, Atlanta, Ga) was used for statistical analyses. Baseline differences between treatment groups were analyzed using chi-square test for dichotomous variables and Student *t* test for continuous variables; where appropriate, Fisher exact test was used. Relative risk (RR) ratio, 95% confidence interval (CI), and *P* value were determined for all primary and secondary outcomes. *P* values < .05 in single-tailed tests were considered significant.

RESULTS

During the study, 992 patients were enrolled: 608 during use of the open system and 384 while the closed system was in exclusive use. Patients from the 2 study periods were similar demographically and with respect to the prevalence of diabetes and cancer, mean severity-of-illness score, proportion of surgical patients,

Table 3. Compliance with handwashing and central venous catheter site dressing during the 2 study phases

	Open system	Closed system	P value
Handwashing compliance, n (%)	3096 (65.9)	1922 (69.5)	.07
Sterile dressing on site, n (%)	2386 (98.4)	1353 (98.4)	.99

Table 4. Incidence of central venous catheter-associated bacteremia during the 2 study phases

	Open system	Closed system	RR (95% CI)	P value
Catheter-days, No.	4140	2117		
Catheter-associated bacteremias, No.	27	5		
Incidence, per 1000 CVC-days	6.52	2.36	0.36 (0.14-0.94)	.02

CI, Confidence interval; CVC, central venous catheter; RR, relative risk.

mechanical ventilation and exposure to urinary catheters (Table 2), mean durations of CVC use (3.6 ± 0.2 and 3.9 ± 0.3 days, $P = .35$), and compliance with handwashing and catheter site care (Table 3).

There were 27 episodes of catheter-associated bacteremia during the period of use of the open system, and 5 during the use of the closed system (6.52 vs 2.36/1000 catheter-days, $RR = 0.36$, 95% $CI = 0.14-0.94$, $P = .02$) (Table 4). Deaths of patients with catheter-associated bacteremia occurred in 2.8% and 0.2% of the study patients during the baseline (open) and intervention (closed) periods, respectively ($RR 0.09$, 95% $CI 0.01-0.70$, $P = .003$).

Gram-negative bacilli were recovered from CVC-associated BSIs during the baseline open-system period in 37% of cases, staphylococci or enterococci from 59%; during the closed-system period, 80% of BSIs were caused by staphylococci or enterococci, only 20% by gram-negative bacilli (Table 5). There were major reductions in the incidence of both gram-positive and gram-negative CVC-associated BSIs with the switch to an open infusion system, although CVC-associated BSIs caused by gram-negative bacilli declined most strikingly ($RR 0.16$, 95% $CI 0.02-1.24$, $P = .04$).

In a previous study we quantified the attributable extra costs of CVC-associated BSI in Argentina.⁷ CVC-associated BSIs extended ICU length of stay by 11.90 days, and resulted in added ICU costs of \$4888. Assuming a baseline CVC-associated BSI rate of 6.52 per 1000 CVC-days, 14 infections would have been expected to occur in the 2117 line-days in the 20 months during the intervention period. The calculated cost savings in the 20 hospital-month intervention period was \$53,768, and 130.9 ICU days.

Table 5. Microbial profile of central venous catheter associated blood stream infection during the 2 study periods

Microorganism	Open system	Closed system	P value
Gram-positive bacteria, n (%)	16 (59%)	4 (80%)	.08
<i>Staphylococcus aureus</i>	10	2	
Coagulase-negative staphylococci	5	1	
Enterococci	1	1	
Gram-negative bacteria, n (%)	10 (37%)	1 (20%)	.04
<i>Escherichia coli</i>	3	0	
<i>Enterobacter</i>	2	0	
<i>Klebsiella</i>	3	0	
<i>Proteus</i>	2	0	
<i>Acinetobacter</i>	0	1	
Yeasts (<i>Candida</i>), n (%)	1 (11%)	0 (0%)	.40
Culture-documented BSIs, n (%)	27 (100%)	5 (100%)	

BSI, Bloodstream infection.

DISCUSSION

Patients who are critically ill commonly require central venous access for administration of large volumes of IV fluid, medications, or blood products, or for hemodynamic monitoring. Unfortunately, use of CVCs is associated with substantial risk of BSI, in the range of 2% to 10% (2-25/100 CVC-days).^{18,44} When CVC-associated BSI occurs, studies have shown increased length of stay, excess costs, and increased attributable mortality.^{7,8,45-53} Digiovine et al⁸ found that CVC-associated BSIs resulted in a 10-day excess length of hospitalization and increased direct medical costs nearly \$35,000 per patient. Rello et al⁵⁴ found that CVC-associated BSIs prolonged hospitalization by 20 days and increased the costs of health care 3124 euros (\$3583.28). Most importantly, CVC-associated BSIs appear to be associated with increased attributable mortality: Collignon⁵⁵ reported that CVC-associated BSIs resulted in excess mortality of 12% whereas Pittet et al^{54,56} found an attributable mortality of 25%.

CVC-associated BSIs are largely preventable,^{11,12,57} and randomized trials have documented the efficacy of simple interventions, such as mandating use of maximal barrier precautions during CVC insertion,⁵⁸ limiting CVC use to the minimum number of days necessary,^{59,60} use of chlorhexidine rather than iodophors or alcohol for cutaneous antisepsis,²⁰ and use of anti-infective-coated catheters,^{24,61} to reduce rates of CVC-associated BSI. Unfortunately, most hospitals in Latin America, including those in Argentina, lack resources to implement most recommended preventative technologies. More importantly, most hospitals lack even basic infection control programs, and

caregivers are unaware of simple, yet efficacious and inexpensive, methods for preventing IVD-associated BSI, such as handwashing compliance, sterile occlusive dressing,⁴ maximal barrier precautions at the time of insertion,⁵⁸ site care, and changing IV administration sets not more frequently than every 72 hours.⁶²

Contamination of infusate or catheter hubs has been the cause of most epidemics of infusion-related bacteremia.⁵ Intrinsic contamination of parenteral fluids (micro-organisms introduced during manufacture) is now considered very rare in North America,⁵ and widespread use of closed infusion systems would seem, in theory, likely to reduce the risk of extrinsic contamination of infusate during administration in the hospital.

Most hospitals in developing countries, including those in Argentina, use open, externally vented, glass or semirigid infusion systems, with or without air filters, which increase the risk of extrinsic contamination, especially by gram-negative bacilli that can multiply rapidly in commercial IV admixtures.^{25-27,36}

In this study, an open infusion system was associated with a high rate of catheter-associated bacteremia, whereas switching to a closed system reduced risk markedly. Most notably, the greatest reduction was seen with bacteremias caused by gram-negative bacilli, consistent with the hypothesis that closed systems most importantly reduce contamination of in-use infusate by more virulent gram-negative bacilli (which have the capacity to multiply rapidly in glucose-containing parenteral admixtures⁵). Switching to a closed infusion system in our study was also associated with a commensurate reduction in deaths of patients with catheter-associated bacteremia.

Whereas risk factors for nosocomial bacteremia and compliance with basic infection control practices were comparable during the 2 phases, our study has limitations. The study design did not permit determination of the epidemiologic mechanisms responsible for the striking differences in outcome (eg, reduced contamination of infusate). In addition, because the participants were not concurrently randomized to the 2 infusion systems, it is possible that the differences in catheter-associated bacteremia could have derived from undetected differences in how caregivers handled or manipulated patient infusions.

In a second-level general teaching hospital in Mexico, Munoz et al²⁹ cultured running IV infusions and found a 29.6% contamination rate during a baseline period. In a multicenter cross-sectional study in Mexico, Macias et al³⁰ found a 2% contamination rate; lapses in aseptic technique and breaks in the infusion system while injecting IV medications were risk factors for in-use contamination. The CDC HICPAC guideline for prevention of IVD-related infections recommends limiting manipulations of and entry into running

infusions and that persons handling or entering an infusion first wash their hands or put on clean gloves.

Our findings raise questions about the safety of open infusion systems, especially in developing countries with limited resources for training of health care workers in basic infection control practices. Because many hospitals in developing countries still use open rigid or semirigid fluid containers, switching to closed, nonvented, collapsible bags could substantially reduce rates of nosocomial bacteremia.

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