

ORIGINAL ARTICLE

Attributable Cost and Length of Stay for Patients With Central Venous Catheter–Associated Bloodstream Infection in Mexico City Intensive Care Units: A Prospective, Matched Analysis

Francisco Higuera, MD; Manuel Sigfrido Rangel-Frausto, MD; Victor Daniel Rosenthal, MD, CIC, MSc; Jose Martinez Soto, MD; Jorge Castañon, MD; Guillermo Franco, MD; Natividad Tabal-Galan, RN, ICP; Javier Ruiz, MD; Pablo Duarte, MD; Nicholas Graves, PhD

BACKGROUND. No information is available about the financial impact of central venous catheter (CVC)–associated bloodstream infection (BSI) in Mexico.

OBJECTIVE. To calculate the costs associated with BSI in intensive care units (ICUs) in Mexico City.

DESIGN. An 18-month (June 2002 through November 2003), prospective, nested case-control study of patients with and patients without BSI.

SETTING. Adult ICUs in 3 hospitals in Mexico City.

PATIENTS AND METHODS. A total of 55 patients with BSI (case patients) and 55 patients without BSI (control patients) were compared with respect to hospital, type of ICU, year of hospital admission, length of ICU stay, sex, age, and mean severity of illness score. Information about the length of ICU stay was obtained prospectively during daily rounds. The daily cost of ICU stay was provided by the finance department of each hospital. The cost of antibiotics prescribed for BSI was provided by the hospitals' pharmacy departments.

RESULTS. For case patients, the mean extra length of stay was 6.1 days, the mean extra cost of antibiotics was \$598, the mean extra hospital cost was \$11,591, and the attributable extra mortality was 20%.

CONCLUSIONS. In this study, the duration of ICU stay for patients with central venous catheter–associated BSI was significantly longer than that for control patients, resulting in increased healthcare costs and a higher attributable mortality. These conclusions support the need to implement preventive measures for hospitalized patients with central venous catheters in Mexico.

Infect Control Hosp Epidemiol 2007; 28:31-35

Bloodstream infection (BSI) is a major cause of mortality among critically ill patients.¹⁻¹⁰ The presence of a central venous catheter (CVC) is a major risk factor for the development of BSI.^{4,11-13} Several studies have demonstrated that CVC-associated BSIs are associated with an extended hospitalization duration and increased patient morbidity.^{5,14} One important means of reducing CVC-associated BSI in Latin America and elsewhere has been implementation of infection control programs that emphasize improved hand hygiene adherence,^{15,16} improved care of the catheter-insertion site,¹⁷⁻²³ and use of antimicrobial agent–impregnated catheters.²⁴ We report the findings of a prospective, multicenter, nested, matched case-control study that assessed attributable extra length of stay (LOS), antibiotic use, costs, and mortality

among patients with CVC-associated BSI who were hospitalized in intensive care units (ICUs) in Mexico City.

METHODS

Setting

The study was conducted in 3 hospitals in Mexico City. Each center had an infection control team comprising an internal medicine physician with formal education in infectious diseases and an infection control nurse.²⁵

General Hospital (hospital A) is a public 1,100-bed hospital; Specialties Instituto Mexicano del Seguro Social (IMSS) Hospital (hospital B) and Gabriel Mancera IMSS Hospital (hospital C) are social-security hospitals of 600 beds and 400

From the General Hospital (F.H., G.F., J.R., P.D.), the Specialties Instituto Mexicano del Seguro Social Hospital (M.S.R.-E., J.C., N.T.), and the Gabriel Mancera IMSS Hospital (J.M.S.), Mexico City, Mexico; the Medical College of Buenos Aires, Buenos Aires, Argentina (V.D.R.); and the School of Public Health, Queensland University of Technology, Queensland, Australia (N.G.).

Received January 16, 2006; accepted March 30, 2006; electronically published January 3, 2007.

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TABLE 1. Baseline Characteristics of Intensive Care Unit (ICU) Patients in Mexico City With Central Venous Catheter–Associated Bloodstream Infection

Characteristic	Case patients (n = 55)	Control patients (n = 55)	P
Mean length of stay \geq 5 d	55 (100)	55 (100)	>.99
Mean age, y	46.22	43.69	.43
Male sex	25 (45)	25 (45)	>.99
Admitted to medical or surgical ICU	55 (100)	55 (100)	>.99
Mean severity of illness score	3.98	3.49	.32
ICU type, hospital			
Medical-surgical, General Hospital	26	26	>.99
Neurosurgical, General Hospital	16	16	>.99
Medical-surgical, Specialties IMSS Hospital	10	10	>.99
Medical-surgical, Gabriel Mancera IMSS Hospital	3	3	>.99

NOTE. Data are no. (%) of patients, unless otherwise indicated. IMSS, Instituto Mexicano del Seguro Social.

beds, respectively. The ICUs of the hospitals treat patients who have had open heart surgery, neurosurgery, or orthopedic surgery performed and patients who have a complicated medical illness. The institutional review board at each center approved the study protocol.

Study Population and CVC Practices

We included all patients admitted to the study ICUs during the 18-month period from June 2002 through November 2003 who had had a CVC in place for at least 24 hours. Patients at hospital A were admitted from June 2002 through November 2003, patients at hospital B were admitted from November 2002 through November 2003, and patients at hospital C were admitted from April through November 2003. Nontunneled, non-antimicrobial-impregnated CVCs were inserted from the bedside by treating physicians after the skin was prepared with povidone-iodine.

At the beginning of the surveillance period, measures to improve healthcare worker compliance with hand washing, care of CVC sites, and care of intravenous administration sites were implemented. Measures comprised education, training, outcome surveillance, process surveillance, and performance feedback.²⁶

Nosocomial Infection Surveillance and Data Collection

All patients admitted to the hospital with a CVC-associated BSI detected by prospective nosocomial surveillance were enrolled and included as case patients. An infection control nurse at each study center collected data prospectively from patient medical records. The study coordinator (V.D.R.) trained the data collectors at each center before commencement of the study. For each study patient, age and sex, hospital, ICU type, mean severity of illness score, and LOS were recorded. In addition, antibiotic consumption was recorded. We followed the recommendations of a 1969 World Health

Organization European symposium on the consumption of drugs. We also used the Anatomical Therapeutic Chemical Classification system, which is a common classification system for drug use, and the defined daily dose (DDD) was used as the comparative unit of drug consumption.²⁷ Active surveillance for CVC-associated BSI was performed at each study center, starting in June 2002 and finishing in November 2003.

Definitions

Centers for Disease Control and Prevention definitions were used to define CVC-associated BSI as laboratory-confirmed BSI or clinical primary nosocomial sepsis.²⁸

Laboratory-confirmed BSI. To meet the criteria for laboratory-confirmed BSI, the first criterion was recovery of a recognized pathogen unrelated to infection at another body site from one or more cultures of percutaneous blood. Common skin commensals (eg, diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, and micrococci) must have been recovered from 2 or more cultures of blood specimens drawn on separate occasions. The second criterion was the presence of at least 1 of the following signs or symptoms unrelated to infection at another body site: fever (temperature of greater than 38°C [greater than 100.4°F]), chills, and/or hypotension.

Clinical primary nosocomial sepsis. To meet the criteria for clinical primary nosocomial sepsis, the presence of at least 1 of the following clinical signs unrelated to another recognizable cause of infection was required: fever (temperature, $>38^{\circ}\text{C}$ [$>100.4^{\circ}\text{F}$]), hypotension (systolic blood pressure, <90 mm Hg), and/or oliguria (urine output, <20 mL/h). However, for these patients, blood cultures were either not performed or did not yield pathogens, and no infection was apparent at another body site. The physician recommended treatment for sepsis.

TABLE 2. Studies in Which Central Venous Catheter–Associated Bloodstream Infection Was Associated With Extra Costs

Study	Country	Extra cost, US\$
Liu et al. ³⁵	Taiwan	66,302
Orsi et al. ¹⁴	Italy	21,612
Pittet et al. ⁵	United States	29,000
Elward et al. ³⁶	United States	39,219
Payne et al. ³⁷	United States	5,875
Rosenthal et al. ¹⁰	Argentina	4,888

Culture Techniques

The patients' attending physicians independently decided whether to perform cultures of catheters and blood cultures. We used the semiquantitative culture method for identifying organisms from catheter culture,²⁹ and results were compared with organisms isolated from blood culture, when available. Specimens not immediately cultured were refrigerated at 4°C. All cultures were inoculated with specimens within 8 hours of catheter removal. Standard laboratory methods were used to identify microorganisms in blood and catheter cultures.²⁹⁻³¹

Selection and Matching of Case and Control Patients

To conduct the study, we analyzed patients with CVC-associated BSI (case patients) and patients without CVC-associated BSI (control patients) who were hospitalized for at least 5 days in the facility to which they were admitted. ICU type, year of admission to the ICU, LOS, sex, age, and mean severity of illness score were recorded.³² Each case patient was matched to one control patient.³³

Cost Estimation

The duration of ICU stay was obtained prospectively for each patient, and the number of ICU bed–days were used as a proxy for fixed costs of ICU stay. Current expenditures on fixed costs were used to convert the number of ICU bed–days into US dollars. DDDs³⁴ and their associated market prices were provided by the hospitals' pharmacy departments. The consumption of all other resources that reflect variable costs (ie, cash expenditures) were obtained from each study center's finance department, and the relevant market price was assumed to reflect opportunity costs. The extra cost attributable to BSI was defined as the median difference in variable costs (ie, cash expenditures) and LOS between case patients and their matched control patients. A monetary valuation of the opportunity costs of the ICU bed–days lost to BSI was also made.

Outcomes

The primary outcome effects evaluated in this study included additional days of hospitalization, extra costs, and attributable mortality of CVC-associated BSI.

Statistical Analysis

Epi Info statistical software, version 6.04b (Centers for Disease Control and Prevention), was used to perform the data analysis. The χ^2 analysis (for dichotomous variables) and the Student *t* test (for continuous variables) were used to analyze baseline differences between treatment groups. When appropriate, the Fisher exact test was used. Relative risk ratios, 95% confidence intervals, and *P* values were assessed for all primary and secondary outcomes.

RESULTS

During the study period (June 2002 through November 2003), 1,615 adult patients were admitted to the study ICUs; 172 (10.6%) of these patients developed a CVC-associated BSI (22 [40%] had laboratory-confirmed BSI, and 33 [60%] had clinical sepsis). Fifty-five (31.9%) of the 172 patients had a LOS of 5 days or more and were included in the study. Fifty-five control patients were matched with case patients on the basis of a LOS longer than 5 days, hospital, ICU type, sex, age, and mean severity of illness score. Baseline characteristics were not different between case and control patients (Table 1).

The cumulative number of ICU bed–days was 739 for case patients and 406 for control patients. The mean number of ICU–days was 13.4 for case patients and 7.34 days for control patients. The cumulative number of extra ICU bed–days for case patients was 333, with a mean excess LOS of 6.05 days per case patient (Table 2). Each ICU bed–day lost to BSI was assumed to be worth \$1,200, on the basis of data provided by the finance department of each hospital. This finding implies that the value of the 333 lost bed–days in terms of alternative use was \$579,133, or \$7,260 per BSI case (Table 2). The additional costs of antibiotics were \$32,912, or \$598 per case patient; the additional value of the remaining variable costs was \$146,622, or \$2,666 per BSI case. The total costs were \$1,593,149 for case patients and \$955,648 for control patients, for a difference of \$637,501, or \$11,591 per BSI case (Table 2). Case patients were much more likely to have received antimicrobial therapy, with a mean of 10.3 extra antibiotic DDDs (Table 2). Twenty-three case patients (41.8%) and 12 control patients (21.8%) died, for an attributable mortality due to CVC-associated BSI of 20.0% (relative risk, 1.92 [95% confidence interval, 0.95-3.85]; *P* = .06).

DISCUSSION

The presence of a CVC is a major risk factor for BSI.^{4,11-13} Critically ill patients often require extended use of CVCs and have a high risk of developing a BSI.^{38,39} Increases of 4%-37% in attributable mortality have been reported in several studies of CVC-associated BSI,^{2,5,9,40,41} although this association has not been a consistent finding.^{42,43}

In our study, we found that CVC-associated BSI was related

to a median excess costs of \$11,591 and an extra LOS of 6.1 days per episode. In contrast, almost all studies that evaluated the impact of CVC-associated BSI on patient outcomes have found significantly increased healthcare costs and excess LOS for patients who developed this type of nosocomial infection (Table 2). The excess healthcare costs reported from developed countries are significantly higher than costs found in our study^{5,7,14} and higher than costs reported from Argentina, where the extra costs were reported to be \$4,888.¹⁰

Our study may underestimate the true costs of CVC-associated BSI in other countries where expensive medical technologies not yet available in Mexico are routinely used. For example, the mean cost per day of hospitalization in most US centers is more than 5 times that in Mexico. Also, the real attributable mortality might be higher in Mexico, because patients whose care was prohibitively expensive might have died early during their hospital stay. Notwithstanding these possibilities, our data demonstrated that CVC-associated BSIs significantly increased the cost of treatment for these patients.

Studies of nosocomial infection have revealed that the use of antibiotics is increasing. Our study, for example, revealed a mean of 10 additional antibiotic DDDs for patients with CVC-associated BSI, which accounted for \$589 of the mean excess healthcare costs per episode. The excess use of antibiotics has important consequences for patients in the ICU setting, for whom the risk of acquiring drug-resistant nosocomial pathogens may be higher than that for patients hospitalized in other settings.⁴⁴ Thus, prevention of CVC-associated BSI may reduce healthcare costs through reducing LOS, antibiotic use, and the antibiotic pressure that is driving the selection of resistant microorganisms in hospitals.⁴⁵

Finally, our discoveries are concordant with those of other studies that have found an increased mortality among patients with CVC-associated BSI.^{2,5,9,40,41} It is possible that the 20% attributable mortality found in this and other studies is an artificial product of the measurement techniques used (ie, mean severity of illness score or other severity of illness scores calculated at ICU admission rather than at the moment of onset of CVC-associated BSI).⁴³ In our study, we were unable to find statistically significant differences in mortality between case and control patients. The main reason for this was probably our small sample size (55 case patients and 55 control patients).

This study has a number of limitations. In Mexico, laboratory resources are expensive and scarce, and frequently the only BSI criterion we can use is the presence of clinical sepsis. The number of matching variables used might not account for all of the variation in LOS and cost outcomes. A weakness of case-control studies is that it is only possible to match subjects on the basis of a relatively small number of variables before selection bias arises. The inability to measure severity of illness scores on a daily basis in our study hospitals was another limitation of our study. Future studies must use more-rigorous analytic methods, such as time series analysis,⁴⁶ to assess the true impact of CVC-associated BSI on mortality.

However, the preponderance of current evidence suggests that CVC-associated BSI is associated with excess patient mortality, and our data are consistent with this body of evidence.

Multifaceted programs developed for preventing CVC-associated BSI have proved to be useful. Examples of these measures are rigorous hand washing compliance, improved care of vascular catheter-insertion sites, judicious use of antimicrobial therapy, and use of antimicrobial-impregnated catheters. Our data suggest that successful implementation of such programs would not only significantly reduce patient mortality but also result in considerable cost savings and reduced LOS.

Address reprint requests to Victor D. Rosenthal, MD, Medical College of Buenos Aires, Arengreen 1366, Buenos Aires, 1405, Argentina (victor_rosenthal@fibertel.com.ar).

ACKNOWLEDGMENT

General Hospital and Specialties IMSS Hospital were supported by a grant from Baxter Healthcare International.

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