The attributable cost and length of hospital stay because of nosocomial pneumonia in intensive care units in 3 hospitals in Argentina: A prospective, matched analysis

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Background: No information is available on the financial impact of nosocomial pneumonia in Argentina. To calculate the cost of nosocomial pneumonia in intensive care units, a 5-year, matched cohort study was undertaken at 3 hospitals in Argentina.

Setting: Six adult intensive care units (ICU).

Methods: Three hundred seven patients with nosocomial pneumonia (exposed) and 307 patients without nosocomial pneumonia (unexposed) were matched for hospital, ICU type, year admitted to study, length of stay more than 7 days, sex, age, antibiotic use, and average severity of illness score (ASIS). The patient's length of stay (LOS) in the ICU was obtained prospectively in daily rounds, the cost of a day was provided by the hospital's finance department, and the cost of antibiotics prescribed for nosocomial pneumonia was provided by the hospital's pharmacy department.

Results: The mean extra LOS for 307 cases (compared with controls) was 8.95 days, the mean extra antibiotic defined daily doses (DDD) was 15, the mean extra antibiotic cost was $996, the mean extra total cost was $2255, and the extra mortality was 30.3%.

Conclusions: Nosocomial pneumonia results in significant patient morbidity and consumes considerable resources. In the present study, patients with nosocomial pneumonia had significant prolongation of hospitalization, cost, and a high extra mortality. The present study illustrates the potential cost savings of introducing interventions to reduce nosocomial pneumonia. To our knowledge, this is the first study evaluating this issue in Argentina. (Am J Infect Control 2005;33:157-61.)

Nosocomial pneumonia (NP) is the leading cause of death in critically ill patients. The most important risk factor for development of NP is mechanical ventilation.[1] Once NP develops, it is associated with prolongation of hospital stay and morbidity.[2,3] Some studies have also reported a high attributable mortality, although that is still a subject of controversy.[4] Infection control programs are important in the prevention of NP by implementing strategies that modify the risk factors for NP, such as use of hand hygiene, elevation of the head of the bed to 45° to prevent aspiration, and aspiration precautions.[5]

Many countries in Latin America, such as Argentina, lack mandatory infection control programs. As a result, many cases of NP occur in health care facilities that lack caregivers who are familiar with published infection control guidelines. We report the results of a multicenter, prospective, matched cohort study to determine the attributable cost and mortality of NP in patients from 6 cardiac and medical/surgical intensive care units (ICUs) in 3 Argentinean medical centers.

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METHODS

Setting

The study was conducted in 3 medical centers in Buenos Aires, Argentina. Each center has an infection control team composed of a medical doctor with formal education and background in internal medicine,

Table 1. Baseline characteristics of patients with and without nosocomial pneumonia

	Cases, N = 307 (%)	Control, N = 307 (%)	*P* value
LOS (7 or more days)	307 (100)	307 (100)	NS
Age, mean, SD, years	73.79 SD 11.97	69.90 SD 11.48	NS
Sex (male)	157/307 (51.1)	157/307 (51.1)	NS
ICU (Ms ICU)	247/307 (80.5)	247/307 (80.5)	NS
Average severity of illness score, mean, SD	3.34 SD 0.95	3.11 SD 0.83	NS
Year	1998 (5.2)	1998 (6.8)	NS
	1999 (20.5)	1999 (18.9)	
	2000 (24.4)	2000 (22.8)	
	2001 (43.0)	2001 (44.6)	
	2001 (6.8)	2001 (6.8)	

ICU, Intensive care unit; *LOS*, length of stay; *Ms ICU*, Medical Surgical Intensive care unit.

infectious diseases, and hospital epidemiology and an infection control nurse.[6]

Hospital A is a public 250-bed hospital situated in the province of Buenos Aires with 1 medical/surgical ICU (10 beds) and 1 coronary ICU (10 beds). Hospital B is a private 150-bed hospital situated in the province of Buenos Aires with 1 medical/surgical ICU (17 beds) and 1 coronary ICU (15 beds). Hospital C is a private 180-bed hospital situated in the city of Buenos Aires with 1 medical/surgical ICU (10 beds) and 1 coronary ICU (10 beds). All ICUs in the study centers care for patients who have undergone open heart, neurosurgical, and orthopedic surgery as well as patients with severe medical illness. The institutional review board at each center approved the study protocol. All the hospital teams are trained, coordinated, and supervised by the same hospital epidemiologist, using the same methodology.

Study population

All patients admitted to the study ICUs from July 1998 to June 2002 were included in the study.

Nosocomial infection surveillance and data collection

All patients with a nosocomial pneumonia detected by prospective nosocomial surveillance applying the National Nosocomial Infections Study (NNIS) surveillance system[7] and who were admitted to the study ICUs were enrolled. An infection control nurse at each study center extracted patient data prospectively from charts. The principal investigator (V.D.R.) trained the data collectors at each center before initiation of the study. The patient's age, sex, hospital name, type of ICU, average severity illness score (ASIS), length of stay (LOS), year of admission, and antibiotic use were recorded on each study patient. Study center data collection sheets were checked for potential errors and missing items by the study coordinator to confirm each diagnosis of nosocomial pneumonia.

Active surveillance for nosocomial pneumonia care began in 1998 and was continued through 2002.[8] This study was performed for the period between July 1998 and August 2000 in hospital A, between April 1999 and June 2002 in hospital B, and between September 2000 and June 2002 in hospital C.

Definitions

Definitions for nosocomial pneumonia were adapted from the Centers for Disease Control and Prevention.[9] Nosocomial pneumonia was defined as (1) presence of rales or dullness to percussion on physical examination of the chest and at least 1 of the following: (a) new onset of purulent sputum or change in character of sputum; (b) organism cultured from blood; and/or (c) isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy; (2) chest radiograph that shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion and at least 1 of the following: (a) new onset of purulent sputum or change in character of sputum; (b) organism cultured from blood; (c) isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy; (d) histopathologic evidence of pneumonia.

Culture techniques

Decisions to take respiratory samples and obtain blood cultures were made independently by the patient's attending physicians. Specimens not immediately cultured were refrigerated at 4°C. Standard laboratory methods were used to identify microorganisms in respiratory samples.

Case and control selection and matching

Patients with NP (exposed) and patients without NP (unexposed) who were hospitalized for at least 7 days following the Halley methodology were matched for hospital to which they were admitted, ICU type, year they were admitted to the study ICU, length of stay at least 7 days, sex, age, and average severity of illness score (ASIS) at admission.[8] Each NP patient was matched to 1 unexposed patient (ie, patient without NP).[10]

Cost estimation

The patient's LOS in the ICU was obtained prospectively on daily rounds. Each hospital's finance department provided the fixed cost per bed-day. The pharmacy department provided the defined daily doses (DDD)[11] of antibiotic use for patients in each ICU and

Table 2. Extra expenditures of nosocomial pneumonia

	Case (N = 307)	Control (N = 307)	Attributable extra expenditures
Total days	6043	3295	Total extra days: 2748
LOS	19.68	10.73	Mean extra days: 8.95
	SE 0.794	SE 0.308	*T* test *P* value ≤0.000
	SD 13.90	SD 5.39	
	Percentile 25% 11	Percentile 25% 8	
	Percentile 75% 24	Percentile 75% 11	
	Median 16	Median 9	
Total fixed cost	$1,510,750 (SE 0.794)	$823,750	Fixed Extra Cost: $687,000
Mean fixed cost	$4,921 (SE 198,43)	$2,683 (SE 76.97)	Mean extra cost: $2,238
Total antibiotic DDD	7815	3181	Antibiotic extra DDD: 4,634
Mean antibiotic DDD	25.45 (SE 1.4)	10.36 (SE 0.64)	Mean extra antibiotic DDD: 15.09
Total antibiotic cost	$515,790	$209,946	Antibiotic extra cost: $305,844
Mean antibiotic cost	$1,680.09 (SE 93.85)	$683.86 (SE 42.73)	Mean extra antibiotic cost: $996.22
Total global cost	$1,518,565	$826,931	Total extra global cost: $691,634
Mean Global Cost	$4,946.46	$2,693.58 (SE 77.3)	Mean total extra global cost: $2,252.88
	SE 199.57	SE 77.3	
	SD 3,496.79	SD 1,354.55	*T* test *P* value 0.0000
	Percentile 25% 2751	Percentile 25% 2000	
	Percentile 75% 6049	Percentile 75% 2780	
	Median 4010	Median 2257	

DDD, Defined daily dose; *LOS*, length of stay.

Table 3. Extra mortality of nosocomial pneumonia

	Case (N = 307)	Control (N = 307)	Attributable extra expenditures
Total mortality	195	102	Total extra dead: 90
Percentage mortality	63.51%	33.22%	Extra attributable mortality: 30.3%
			Kruskal Wallis 56.31
			P value ≤0.000

their associated costs. A list of fixed costs for each study patient was obtained from each study center's finance department, which calculated the actual cost-to-charge ratio for each patient or their average daily cost. Extra cost attributable to NP was defined as the estimated median difference in direct costs between an infected patient and his or her matched uninfected patient. The length of stay and the direct costs were compared.

Outcomes

The primary outcomes evaluated in this study included additional days of hospitalization, extra cost, and extra ICU mortality of NP.

Statistical methods

EpiInfo version 6.04b (CDC, Atlanta, GA) was used for data analysis. Baseline differences between treatment groups were analyzed using χ^2 analyses or Fisher exact test for dichotomous variables and Student *t* test for continuous variables. Differences between costs and length of stay for both groups were compared using Student paired *t* test; mortality was compared using χ^2 derivation adapted for use with a 2×2 table of matched data. *P* values were determined for all primary and secondary outcomes: $<.05$ was considered statistically significant.

RESULTS

During the study period (July 1998 to June 2002), 7230 adult patients were admitted to the study ICUs, and 419 (5.79%) were found to have nosocomial pneumonia.

Three hundred seven patients with nosocomial pneumonia had a LOS of 7 days or more and were incorporated into the analysis. Matching for more than 7 days of ICU stay, hospital, year of admission, type of ICU, sex, age, and average severity of illness score at admission was done. After matching for the 7 described characteristics, we chose 307 unexposed patients; if more than 1 unexposed patient met the matching criteria, the selection was done randomly. The key features of patients with NP and the matched unexposed patients are presented in Table 1.

Patients with NP were in the ICU for a total of 6043 days, whereas the patients without NP spent 3295 days in ICU, a mean of 19.68 versus 10.73 days, respectively. The extra LOS for 307 cases (compared with the controls) was 2748, with a mean per patient with NP of 8.95 days. The fixed costs of NP were $ 1,510,750 and without NP, $823,750, resulting in $687,000 extra fixed costs; the mean extra fixed cost was $2238.

Patients with NP received much more antimicrobial use, with a mean of 15 extra antibiotic DDD. One

hundred ninety-two of the patients with NP and 102 of the matched unexposed patients died, for an extra mortality of 30%. The extra ICU cost and length of ICU stay of the study population are shown in Table 2. The extra ICU mortality of NP is shown in Table 3.

DISCUSSION

NP is the leading cause of death from hospital-acquired infection; the incidence in ICUs varies from 7% to 40% of patients.[4] Critically ill patients often require prolonged mechanical ventilation, which is the most important risk factor for NP.[1] Several recent studies have found that nosocomial infections are emerging as an important problem in many developing countries.[12-18] When infection, including NP, does occur, studies have repeatedly demonstrated an increased length of hospitalization[19] and excess costs, and some studies have shown an increased attributable mortality ranging from 33% to 72%,[3,4,20,21] whereas others have failed to find a difference in mortality.[22,23] Many studies evaluating attributable mortality have included only patients with ventilator-associated pneumonia, and these may not be directly comparable with studies attempting to characterize the attributable mortality of NP overall. These differences may in part be explained by differences in diagnostic criteria for pneumonia and study design using different matching criteria. We found an extra mortality of 30% associated with NP.

Our study has several limitations. We defined NP using clinical criteria in some of the cases, which may have resulted in misclassification of the exposure. Sometimes our limited resources made it difficult to use invasive techniques for confirmation of NP. We only assessed the severity illness score at admission. We did not use other severity illness score as APACHE because of our lack of resources to calculate this more expensive and labor-intensive score. We did not stratify ventilator-associated pneumonia and so cannot comment on the extra mortality (if any) of the subset of patients with ventilator-associated pneumonia.

Limited literature exists on the cost of nosocomial pneumonia and the attributable length of stay associated with it. Dietrich et al investigated the incremental cost of nosocomial pneumonia, using a matched case control study; they found an excess cost of $14,890 and 14 extra days of intensive care stay.[22] Kappstein et al investigated the incremental cost of nosocomial pneumonia, using a matched case control study; they found an excess cost of $8800 and 10.13 extra days of intensive care stay.[24] In an earlier, matched case control study, the same investigators found a mean additional stay of 10 days and $8800 extra cost of VAP in the ICU.[25] A matched case control study from China found an excess cost of 31,940 Chinese Yuan Renminbi ($3858).[26] We found excess costs of nosocomial pneumonia to be $2252 and an extra length of stay of 9 days. Some of these differences may be attributable to the infecting species of bacteria causing nosocomial pneumonia, with more virulent species associated with longer hospitalization and more cost.

The development of NP results in a great deal of antimicrobial therapy; we found a mean of 15 extra antibiotic defined daily doses (DDD), associated with $996 excess cost. This has important implications in the ICU for development of antibiotic-resistant organisms, which flourish under antibiotic pressure. Prevention of NP is necessary to control antimicrobial usage in the ICU, which is one of the most frequently prescribed classes of drugs in hospitalized patients.[27]

Multifaceted nosocomial pneumonia and ventilator-associated pneumonia prevention programs that emphasize application of interventions shown to be useful,[28] such as rigorous handwashing,[29,30] focused education programs,[31] ventilator circuit maintenance,[32] keeping the head of the patient's bed elevated to 45 degrees,[33,34] continuous aspiration of subglottic secretions,[35] and judicious and appropriate antimicrobial use,[27,36] are needed in Argentina to reduce the mortality, financial burden, and prolonged hospitalization associated with nosocomial pneumonia.

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