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Nosocomial bloodstream infections caused by *Streptococcus pneumoniae*

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ABSTRACT

A retrospective study of *Streptococcus pneumoniae* bacteraemia among adult patients in two large teaching hospitals in Spain identified 108 (10.6%) of 1020 episodes as nosocomial pneumococcal bloodstream infections (NPBIs). Seventy-seven clinical records with sufficient data were available for analysis. The interval between admission and a positive blood culture was 3–135 days (median 17 days; interquartile range 8–27). The main underlying and predisposing conditions for NPBI were malignancy (31%), chronic obstructive pulmonary disease (28.6%), heart failure (16.9%), chronic renal failure (15.6%), liver cirrhosis (13%) and infection with human immunodeficiency virus (13%). Overall, 31.2% of patients developed severe sepsis, 11.7% septic shock, and 3.9% multi-organ failure. The main portals of entry were pneumonia (70.1%), meningitis (5.2%) and primary peritonitis (5.2%). Of the responsible serogroups, 78% were included in the 23-valent polysaccharide vaccine. Thirty-five (45.5%) patients died, with death considered to be related to the NPBI in 21 (27.3%) cases. Following multivariate analysis, factors that independently predicted death after adjusting for age were: ultimately fatal underlying disease (OR, 8.9; 95% CI, 0.8–94.3; $p < 0.001$); rapidly fatal underlying disease (OR, 15.0; 95% CI, 2.8–81.3; $p < 0.001$); heart failure (OR, 8.11; 95% CI, 1.1–60.8; $p < 0.03$); inadequate empirical therapy (OR, 10.6; 95% CI, 1.2–97; $p < 0.003$); a severe sepsis score (OR, 9.5; 95% CI, 1.9–47.0; $p < 0.001$); and septic shock or multi-organ failure (OR, 63.7; 95% CI, 4.9–820.7; $p < 0.001$). Adequate empirical therapy was an independent protective factor (OR, 0.05; 95% CI, 0.04–0.58; $p < 0.005$), but the use of more than one antimicrobial agent was not.

Keywords Bacteraemia, bloodstream infection, nosocomial infection, pneumococci, risk factors, *Streptococcus pneumoniae*

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INTRODUCTION

Nosocomial pneumococcal bloodstream infections (NPBIs) are reported infrequently in the literature, despite the fact that they represent 8.9–41% of all pneumococcal bloodstream infections [1–8]. This study describes the incidence, clinical manifestations, treatment and outcome of NPBI in two large teaching hospitals in Spain.

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PATIENTS AND METHODS

Study design and settings

The study was a retrospective cohort study carried out in two large teaching hospitals located in the city of Madrid, Spain. The study was performed during the 8-year period from January 1995 to December 2002, and included all adult patients (aged >16 years) with one or more blood cultures from which *Streptococcus pneumoniae* was isolated, and who were considered to have acquired the infection in the hospital (see below). Charts were reviewed according to a pre-established protocol.

Microbiological identification and susceptibility testing

S. pneumoniae was identified using standard and well-recognised procedures. Capsular serotyping of isolates was performed at the Centro Nacional de Microbiología (Instituto de Salud Carlos III, Majadahonda, Madrid). Antimicrobial susceptibility tests were performed using a microdilution technique (Sensititre; Trek Diagnostic Systems, East Grinstead, UK) and interpreted according to NCCLS recommendations [9].

Definitions and classifications

Nosocomial infections were defined according to CDC recommendations [10]. NPBIs were defined as infections that were demonstrated ≥72 h after admission, excluding those patients who were suspected of having pneumococcal disease present or in incubation at admission [11]. The underlying condition of each patient before pneumococcal disease was rated according to the McCabe and Jackson criteria [12], and categorised according to the Charlson co-morbidity index [13]. The severity of the clinical condition of each patient with NPBI was assessed by the APACHE II score for those admitted to the intensive care unit (ICU) [14]. The maximum severity of septic illness until the moment of discharge or death of each patient was assessed according to Bone's score [15]. The following potential predisposing conditions for nosocomial bloodstream infections were recorded: tracheal intubation, upper or lower gastrointestinal endoscopy, bronchoscopy, nasogastric tube insertion, central catheter line, indwelling bladder catheter, surgery (in the previous 7 days), use of antimicrobial agents (within 30 days before the episode) or corticosteroids (at least 10 mg of prednisone or equivalent for at least 7 days in the 2-week period before the episode), hospitalisation within the preceding 3 months, liver cirrhosis, diabetes mellitus, total parenteral nutrition (before the episode), low serum albumin (< 3 g/dL), solid or haematological malignancy, heart failure, alcoholism (> 50 g of alcohol ingestion/day), splenectomy (at any time in the past), infection with human immunodeficiency virus, chronic obstructive pulmonary disease, and chronic renal failure (creatine > 1.5 mg/dL). The clinical origin of NPBI was defined on the basis of clinical data or as a consequence of the isolation of *S. pneumoniae* from a focus of infection.

Treatment parameters

Treatment parameters recorded were: number of active antimicrobial agents received simultaneously for a minimum of 2 days, length of days on active antimicrobial therapy (receiving at least one active drug), and treatment with penicillins, cephalosporins (third and fourth generation), macrolides, cotrimoxazole, fluoroquinolones and other drugs (carbapenems, other cephalosporins, aminoglycosides and glycopeptides). Antimicrobial therapy during the first 24 h of treatment was considered to be adequate when the patient received at least one active antimicrobial agent during this period.

Outcome

Patients were finally classified as deceased or as having been discharged. Death was classified as related to the NPBI when persistence of a clinical picture of sepsis at death could be attributed to pneumococcal infection, or when death occurred during the first week after blood cultures were taken.

Statistical analysis

Quantitative variables were calculated as a mean and standard deviation (SD). Median and interquartile range were calculated when appropriate. Categorical data were analysed using the chi-square test or Fisher's exact test, as appropriate, with statistical significance set at $p \leq 0.05$. All p values were two-tailed. A logistic regression model was used to examine the effects of multiple risk-factors on mortality. Variables included in the model were those found to reach a significance level of $p < 0.1$ in the univariate analysis, together with the age of the patients, since age is known to be a variable that has an important impact on mortality.

RESULTS

The population served by the two institutions between 1995 and 2002 remained stable, at close to 1 175 000 inhabitants. Between January 1995 and December 2002, there were 1092 episodes of pneumococcal bloodstream infections in patients of all ages, of which 1020 (93.4%) occurred in the adult population. Overall, the estimated incidence of pneumococcal bloodstream infections in adults was 10.7 episodes/100 000 inhabitants/year. Of the 1020 episodes of pneumococcal bloodstream infections in adults, 108 (10.6%) were considered to be nosocomial. Clinical charts with adequate information were available for 77 of these 108 patients.

Of the 77 patients analysed, 55 were male and 22 were female, with a mean age of 64.34 years (SD, 16.89 years). The interval between admission and the day of positive blood cultures for *S. pneumoniae* ranged from 3 to 135 days (median, 17 days; interquartile range, 8–27 days). Patients with NPBI were located mainly in medical units (76.6%), followed by surgical departments (13%) and ICUs (10.4%). There was no evidence of nosocomial outbreaks or in-hospital transmission. The main underlying and predisposing conditions of the patients with NPBI are summarised in Table 1.

The severity of the underlying condition was: rapidly fatal, 8 (10.4%); ultimately fatal, 34 (44.2%); and non-fatal, 35 (45.5%). Co-morbidity was variable and ranged from 0 to 11 (median 2; interquartile range 2–7), according to Charlson's index. The mean APACHE II score of the 17 patients who were admitted to the ICU ranged from 6 to 25 (mean, 13.18; SD, 6.19). The percentages of patients who developed different degrees of sepsis were: sepsis only, 53.2%; severe sepsis, 31.2%; septic shock, 11.7%; and multi-organ failure, 3.9%.