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Impact of pre-hospital antibiotic use on community-acquired pneumonia

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Abstract

Information on the influence of pre-hospital antibiotic treatment on the causative organisms, clinical features and outcomes of patients with community-acquired pneumonia (CAP) remains scarce. We performed an observational study of a prospective cohort of non-immunosuppressed adults hospitalized with CAP between 2003 and 2012. Patients were divided into two groups: those who had received pre-hospital antibiotic treatment for the same episode of CAP and those who had not. A propensity score was used to match patients. Of 2179 consecutive episodes of CAP, 376 (17.3%) occurred in patients who had received pre-hospital antibiotic treatment. After propensity score matching, *Legionella pneumophila* was more frequently identified in patients with pre-hospital antibiotic treatment, while *Streptococcus pneumoniae* was less common ($p < 0.001$ and $p < 0.001$, respectively). Bacteraemia was less frequent in pre-treated patients (p 0.01). The frequency of positive sputum culture and the sensitivity and specificity of the pneumococcal urinary antigen test for diagnosing pneumococcal pneumonia were similar in the two groups. Patients with pre-hospital antibiotic treatment were less likely to present fever (p 0.02) or leucocytosis (p 0.001). Conversely, chest X-ray cavitation was more frequent in these patients (p 0.04). No significant differences were found in the frequency of patients classified into high-risk Pneumonia Severity Index classes, in intensive care unit admission, or in 30-day mortality between the groups. In conclusion, *L. pneumophila* occurrence was nearly three times higher in patients who received pre-hospital antibiotics. After a propensity-adjusted analysis, no significant differences were found in prognosis between study groups. Pre-hospital antibiotic use should be considered when choosing aetiological diagnostic tests and empirical antibiotic therapy in patients with CAP.

Keywords: Clinical features, community-acquired pneumonia, aetiology, pre-hospital antibiotic use, prognosis
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Introduction

Although a large number of patients with community-acquired pneumonia (CAP) require hospitalization, the majority are treated as outpatients [1,2]. However, studies report that around 10% of CAP patients initially treated as outpatients require subsequent hospitalization [3,4]. Moreover, the frequency of pre-hospital antibiotic use in hospitalized patients with CAP ranges between 12 and 27% [5,6].

Recent studies have suggested that outpatient antibiotic treatment for CAP may be associated with increased disease severity and hospital complications, and may affect the predictive value of inflammatory biomarkers [6,7]. Despite this, however, the few studies published to date have been limited by their exclusive use of database records [3,7], retrospective analysis [8] or by the fact that they report the effects of previous antibiotic treatment as a secondary finding [6,9]. Moreover, they do not specify the type of antibiotic used or state whether other confounding factors were considered. Therefore, the information about the influence of pre-hospital antibiotic treatment on the causative organisms, clinical

features and outcomes of hospitalized patients with CAP remains limited.

In this study we sought to determine the impact of pre-hospital antibiotic treatment for the same episode of CAP on causative organisms, clinical features and outcomes.

Methods

Setting, patients and study design

This observational study was conducted at a 700-bed teaching hospital for adults in Barcelona, Spain. All non-severely immunosuppressed patients admitted to the hospital with CAP via the emergency department from 1 January 2003 to 31 December 2012 were prospectively recruited and followed. Immunosuppressed patients (those with neutropenia, HIV infection, transplantation, splenectomy, receiving immunosuppressants and/or >20 mg/day of prednisone or its equivalent) and nursing home residents were excluded. The study was approved by the Ethics Committee of the hospital. Written informed consent was obtained from all patients before enrolment.

For the purposes of this study, patients hospitalized with CAP were divided into two groups: patients who had received pre-hospital antibiotic treatment for the same episode of CAP and patients who had not. The use of pre-hospital antibiotics was recorded on admission, and three classes of antibiotic drugs were investigated: β-lactams, macrolides and quinolones.

Follow-up

Patients were seen daily during the hospital stay by one or more of the investigators, who recorded clinical data in a computer-assisted protocol. Data were collected on demographic characteristics, comorbidities, causative organisms, antibiotic susceptibilities, biochemical analysis, empirical antibiotic therapy, and outcomes, including mortality. The Pneumonia Severity Index (PSI) and CURB-65 were used to stratify patients according to risk [10,11].

Definitions

Pre-hospital antibiotic treatment was defined as the oral intake of antibiotic drugs >24 h before hospitalization for the same episode of acute disease. Patients were classified as receiving antibiotics if they self-reported prescription of any of these medications or by reviewing the prescriptions from their general practitioner at the SAP Healthcare Database of the Catalan Health Service (Institut Català de la Salut).

Community-acquired pneumonia was defined as an acute illness associated with two or more of the following signs and symptoms: new cough with or without sputum production, pleuritic chest pain, dyspnoea, fever or hypothermia, altered breath sounds on auscultation, leucocytosis, plus the presence of a new infiltrate on a chest radiograph. Pneumococcal pneumonia was diagnosed as defined elsewhere [12].

The diagnosis of septic shock was based on a systolic blood pressure of <90 mmHg and peripheral hypoperfusion with the need for vasopressors. Time to clinical stability was defined as described elsewhere [13]. Early case-fatality rate and overall case-fatality rate were defined as death from any cause within 72 h and 30 days after hospital admission, respectively. All patients were prospectively followed up during hospitalization. In addition, a long-term follow-up visit took place 1 month after discharge.

Microbiological studies

Pathogens in blood, pleural effusion, sputum and other samples were investigated using standard microbiological procedures. The *Streptococcus pneumoniae* antigen in urine was detected by using a rapid immunochromatographic assay (NOW Assay; Binax Inc., Portland, ME, USA). *Legionella pneumophila* Serogroup 1 antigen in urine was detected by an immunochromatographic method (NOW Legionella Urinary Antigen Test; Binax Inc.) or by ELISA (ELISA-Bartels, Bartels, Trinity Biotech, Wicklow, Ireland). Serological methods were used both on admission and 3–4 weeks thereafter, to determine antibodies against the following pathogens: *Mycoplasma pneumoniae*, *Chlamydophila psittacci*, *Chlamydophila pneumoniae*, *Coxiella burnetii*, *L. pneumophila*, respiratory syncytial virus, parainfluenza virus and influenza A virus [14]. Real-time PCR was performed to identify influenza A (H1N1)pdm09 virus.

Statistical analysis

Categorical variables were described using counts and percentages from the available data. Continuous variables were expressed as the mean and SD or median and interquartile range for abnormally distributed data (Kolmogorov–Smirnov test). To detect significant differences between study groups, we used the chi-square test or Fisher's exact test for categorical variables and the Student's *t*-test or Mann–Whitney *U*-test for continuous variables, as appropriate.

To evaluate propensity, the probability that a patient had received an antibiotic before hospital admission was assessed with multivariate analysis. The variables included in this multivariate analysis were the ones considered as factors that might influence the decision to give outpatient antibiotic treatment to patients with CAP. This multivariate model was used to create a propensity score for each patient, representing the probability that a patient had received antibiotic treatment during pre-hospital care. We then matched patients who had received antibiotics before hospital admission and