Sequential administration of beta-lactams and macrolides on the outcomes of hospitalized patients with community-acquired pneumonia (CAP)

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INTRODUCTION

Even though we currently have newer broad-spectrum antibiotics and better treatment regimens, the mortality rate from pneumonia remains high (32,33). Appropriate antibiotic regimen is crucial for the outcome of hospitalized patients with CAP. According to the American Thoracic Society 2007 guidelines, recommended empiric antibiotics for CAP according to the setting are as follows, for inpatients, non-ICU (treatment [beta-lactam plus a macrolide or a respiratory fluoroquinolone]), for inpatients, ICU (treatment [beta-lactam plus either a macrolide or a respiratory fluoroquinolone]) and if Pneumococcus is a consideration (or amoxicillin-clavulanate/beta-lactam (pipercillin-tazobactam, sulpenem, imipenem, or management plus either ciprofloxacin or levofloxacin or the above beta-lactam plus an anti-microtubule and an anti-arrhythmics and in the case of the fluoroquinolones, linezolid). The most commonly used antimicrobial regimen is a beta-lactam antibiotic in combination with a macrolide. Beta-lactam agents on the bacterial cell wall causing bacteriostasis while macrolides act at the level of bacterial ribosome and also have anti-inflammatory effects. As a result, the beta-lactam antibiotics by themselves are effective against pneumococcal and streptococcal infections and the combination of beta-lactam agents with macrolides enhances their in vitro and in vivo activity. However, the simultaneous use of both agents is associated with an increase in the risk of adverse drug reactions. This is because the combination is not synergistic against most pathogens, but the anti-inflammatory effects of macrolides may minimize some of these adverse reactions. It has been hypothesized that the sequential administration of beta-lactam followed by macrolides (βlactam-macrolide de-sequencing) might be a more effective strategy to reduce the risk of adverse drug reactions while maintaining the anti-inflammatory effects of macrolides.

OBJECTIVES

The objective of this study was to compare clinical outcomes when macrolides are used before or after administration of beta-lactams.

METHODS

This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPRO) International Cohort Study database. Patients receiving a combination of beta-lactams plus macrolides for empiric therapy were included. Patients given beta-lactams and macrolides within 1 hour or more than 24 hours apart were excluded.

RESULTS

A total of 555 patients were included, 63 with a macrolide first and 492 with a beta-lactam first. The adjusted percent in hospital mortality was 16% for patients receiving a macrolide first and 8% for patients receiving a beta-lactam first (P = 0.158).

CONCLUSIONS

These data suggest that, although not statistically significant, there is a clinically relevant decrease in in-hospital mortality if a macrolide is given before a beta-lactam. Since macrolides may decrease mortality only when given prior to or concurrently with beta-lactams, their activity is likely due to anti-inflammatory effects as opposed to coverage of atypical pathogens.

METHODS

-Study design and study population

The data was obtained from a cohort study enrolled in the Community-Acquired Pneumonia Organization (CAPRO) international cohort study. Data were collected between 2001 and 2014. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website (www.caponline.org). Validation of data quality was performed at the study center before the case was entered into the CAP database. Institutional Review Board approval was obtained by each participating center.

-Study definitions:

CAP: Diagnosis of CAP required the presence of criteria A, B, and C:

A. New pulmonary infiltrates on imaging (CT or chest x-ray) at the time of admission to the hospital.
B. Signs and Symptoms of CAP (at least one of the following)
   1. Fever >38.3°C (101.0°F) or hypothermia <35.5°C (95.9°F)
   2. Changes in WBC (leukopenia <4,000 cells/mm³; left shift >10% band forms/micron; leukopenia >4,000 cells/mm³)
C. Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

REFERENCES