Combination Antibiotic Therapy for Patients Hospitalized with Community-Acquired Bacterial Pneumonia

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Background: Combination antibiotic therapy is advocated for severe community-acquired bacterial pneumonia (CABP) that requires hospitalization and has been shown to achieve better outcomes compared with monotherapy. This study describes combination antibiotic treatment patterns in a hospital setting and evaluates their effect on the risk of adverse events, rehospitalizations and mortality.

Methods: This was a retrospective observational study using a database derived from the billing systems of approximately 600 US based hospitals. Patients were aged ≥18 years, hospitalized with CABP between January 1, 2007 and December 31, 2012, and requiring treatment with intravenous or oral antibiotics. Patterns of initial combination antibiotic therapy (within 48 hours of admission) are described for fluoroquinolone + beta-lactam (FQ/BL) and macrolide + beta-lactam (M/BL) and their effects on risk of adverse events or mortality during index CABP admission, and pneumonia-related rehospitalization visits within 30 days of admission were estimated after adjusting for demographics, index length of stay (LOS) and health using multivariate regression models. Analyses were conducted separately by ward and ICU settings.

Results: Out of a total of 299,602 CABP hospital admissions, 90% were admitted to the ward. FQ/BL patients were older, sicker and had longer index LOS compared to M/BL patients in both settings. In the ward, FQ/BL v. M/BL initiation was associated with increased risk of *Clostridium difficile* (OR=1.25 [95% CI: 1.04-1.50]), peripheral neuropathy (OR=1.17 [1.04-1.31]), digestive effects (OR=1.14 [1.09-1.20]), hematologic toxicity (OR=1.13 [1.09-1.17]) and mortality (OR=1.68 [1.48-1.90]), and increased odds of pneumonia-related rehospitalization (OR=1.24 [1.16-1.32]). FQ/BL v. M/BL initiation, in the ICU setting was associated with an increased risk of *Clostridium difficile* (OR=1.62 [1.03-2.53]), hematologic toxicity (OR=1.10 [1.01-1.20]) and mortality (OR=1.67 [1.26-2.22]), and increased odds of pneumonia-related rehospitalization (OR=1.35 [1.13-1.63]).

Conclusion: Combination therapy of FQ/BL is associated with worse outcomes compared to M/BL. One limitation of these results is the difficulty in properly accounting for disease severity, which is unavailable in a database derived from billings systems.