Antibiotic Therapy for Adults Hospitalized With Community-Acquired Pneumonia
A Systematic Review

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IMPORTANCE Antibiotic therapy is the cornerstone of medical management for community-acquired pneumonia.

OBJECTIVE To assess the associations between 3 key aspects of antibiotic therapy (optimal time to antibiotic initiation, initial antibiotic selection, and criteria for the transition from intravenous to oral therapy) and short-term mortality in adults hospitalized with community-acquired pneumonia.

EVIDENCE REVIEW Bibliographic databases of MEDLINE, EMBASE, and the Cochrane Collaboration were searched for studies of adults hospitalized with radiographically confirmed community-acquired pneumonia published from January 1, 1995, until November 5, 2015.

FINDINGS Twenty studies (17 observational and 3 randomized trials) met eligibility criteria. Among 8 observational studies identified, the 4 largest (study populations of 2878 to 1 170 022) found that antibiotic initiation within 4 to 8 hours of hospital arrival was associated with relative reductions of 5% to 43% in mortality; the 4 smallest studies (study populations of 451 to 2076) found no associations between the timing of antibiotic initiation and mortality. One cluster randomized trial (n = 1737) demonstrated noninferiority of β-lactam monotherapy (n = 506) vs β-lactam plus macrolide combination therapy (n = 566), with an absolute adjusted difference of 2.5% (90% CI, −0.6% to 5.2%) in 90-day mortality favoring β-lactam monotherapy. A second randomized trial (n = 580) failed to demonstrate noninferiority of β-lactam monotherapy vs β-lactam plus macrolide combination therapy, with an absolute difference of 7.6% (1-sided 90% CI upper limit, 13.0%) in attainment of clinical stability on hospital day 7 favoring β-lactam plus macrolide combination therapy. Six of 8 observational studies (study populations of 1188 to 24 780) found that β-lactam plus macrolide combination therapy was associated with relative reductions of 26% to 68% in short-term mortality and all 3 observational studies (study populations of 2068 to 24 780) reported that fluoroquinolone monotherapy was associated with relative reductions of 30% to 43% in mortality compared with β-lactam monotherapy. One randomized trial (n = 302) reported significantly reduced hospital length of stay (absolute difference, 1.9 days; 95% CI, 0.6 to 3.2 days), but no differences in treatment failure when objective clinical criteria were used to decide when to transition patients from intravenous to oral therapy.

CONCLUSIONS AND RELEVANCE In adults hospitalized with community-acquired pneumonia, antibiotic therapy consisting of β-lactam plus macrolide combination therapy or fluoroquinolone monotherapy initiated within 4 to 8 hours of hospital arrival was associated with lower adjusted short-term mortality, supported predominantly by low-quality observational studies. One randomized trial supports the use of objective clinical criteria to guide the transition from intravenous to oral antibiotic therapy.

Take-Home Points

- Antibiotic therapy should be initiated within 4 to 8 hours of hospital arrival for patients with radiographically confirmed pneumonia and moderate to high levels of illness severity at presentation.
- Initial first-line antibiotic therapy should consist of β-lactam plus macrolide combination therapy or fluoroquinolone monotherapy for hospitalized patients with community-acquired pneumonia treated outside an intensive care unit setting.
- Patients meeting all of the following criteria for at least 24 hours can be transitioned from intravenous to oral therapy:
  1. Absence of mental confusion
  2. Ability to take oral medication
  3. Temperature lower than 38.3°C
  4. Hemodynamic stability (heart rate <100 beats/min and systolic blood pressure >90 mm Hg)
  5. Respiratory rate lower than 25 breaths/min
  6. Oxygen saturation higher than 90%, arterial oxygen partial pressure higher than 60 mm Hg while breathing in normal room air or low-flow supplemental oxygen by nasal cannula, or return to baseline oxygen level for patients receiving long-term oxygen therapy.