Stopping antibiotics after 5 days in clinically stable community-acquired pneumonia was noninferior to usual care

Uranga A, España PP, Bilbao A, et al. ***Duration of antibiotic treatment in community-acquired pneumonia: a multicenter randomized clinical trial.*** *JAMA Intern Med. 2016;176:1257-65.*

Clinical impact ratings: EM ★★★★★☆☆ HO ★★★★★★☆ ID ★★★★★☆☆

Question

In adults hospitalized with community-acquired pneumonia (CAP), is stopping antibiotic treatment after 5 days in clinically stable patients noninferior to usual care?

Methods

Design: Randomized, controlled, noninferiority trial. Clinicaltrialsregister.eu 2011-001067-51.

Allocation: {Concealed}*.†

Blinding: Blinded† {data analysts}*.

Follow-up period: 30 days.

Setting: 4 teaching hospitals in the Basque Country, Spain.

Patients: 312 adults (mean age 65 y, 63% men) who were hospitalized with CAP (no previous pulmonary infiltrate on chest radiograph and ≥ 1 of cough, fever, dyspnea, or chest pain). Exclusion criteria included HIV, chronic immunosuppression, nursing home residence, discharge from acute care hospital or unit, palliative care in the past 14 days, antibiotic therapy in the 30 days before admission, uncommon cause of CAP needing longer treatment duration, or need for a chest tube.

Intervention: Antibiotic treatment stopped after a minimum of 5 days if body temperature ≤ 37.8 °C for 48 hours and ≤ 1 CAP-associated sign of clinical instability (systolic blood pressure < 90 mm Hg, heart rate > 100/min, respiratory rate > 24/min, arterial oxygen saturation < 90%, or PaO_2 < 60 mm Hg in room air) according to Infectious Diseases Society of America/American Thoracic Society (IDSA/ITS) guidelines (n = 162) or usual care, with duration of antibiotic treatment determined by physicians (n = 150). Antibiotics were chosen by physicians according to local guidelines.

Outcomes: Primary outcomes were clinical success (resolution or improvement in pneumonia signs and symptoms without further antibiotic treatment) at 10 and 30 days from admission, and symptoms (CAP symptom questionnaire; 18-items, score range 0 to 90, higher scores = higher symptom severity). Secondary outcomes included duration of antibiotic treatment.

Patient follow-up: 95% (intention-to-treat analysis).

Main results

Median duration of antibiotic treatment was 5 days in the early stopping group and 10 days in the usual care group (P < 0.001). The main results are in the Table.

Early stopping of antibiotics in stable patients vs usual care in patients with community-acquired pneumonia (CAP)‡

Outcomes	Follow-up	Event rates		RBI (95% CI)
		Early stopping§	Usual care	
Clinical success‖	10 d	56%	47%	17% (−5 to 46)
	30 d	91%	88%	3% (−5 to 12)
		Mean		P value
CAP symptom questionnaire¶	5 d	27.2	24.7	0.10
	10 d	17.9	18.6	0.69

‡Abbreviations defined in Glossary. RBI and CI calculated from event rates in article.

§Stopped after 5 d if body temperature ≤ 37.8 °C for 48 h and ≤ 1 CAP-associated sign of clinical instability present.

‖Resolution or improvement in pneumonia signs and symptoms without further antibiotic treatment.

¶18-items, score range 0 to 90, higher scores = higher symptom severity; noninferiority margin = 3 points.

Conclusion

In adults hospitalized with community-acquired pneumonia, stopping antibiotic treatment after 5 days in clinically stable patients was noninferior to usual care.

**Information provided by author.*

†See Glossary.

Sources of funding: Health Department of Basque Country; Pharmacy Department of the Spanish government; Spanish Pulmonary and Thoracic Surgery Society.

For correspondence: Dr. A. Uranga, Galdakao-Usansolo Hospital, Galdakao, Bizkaia, Spain. E-mail ane.urangaecheverria@osakidetza.eus.

Commentary

The optimal treatment duration for infections is hard to pinpoint because it depends on patient-, microbe-, and location-specific variables. IDSA/ITS 2007 guidelines indicate that 5 days is a reasonable duration of treatment for CAP and shorter courses may be possible (1). In this pragmatic, unblinded Spanish trial by Uranga and colleagues, longer courses of antibiotic treatment (10 vs 5 d) had no discernible benefit on CAP outcomes. The trial was large enough and had sufficient power to show equivalence in this population and supports efforts to reduce antibiotic exposure in patients with CAP.

Is there a catch? First, patients who are hospitalized for pneumonia should be sicker than those treated at home, but in this trial about 60% of patients had Pneumonia Severity Index (PSI) class I to III (predicted mortality < 1%), suggesting a low threshold for admission. Second, 80% of patients received quinolones, which, while effective and inexpensive, are not optimal for stewardship or safety (2). Third, the level of comorbid disease was low, which could limit generalizability to patients with more comorbidity and those excluded for such factors as HIV infection or steroid use.

With these caveats, we can confidently proceed in applying the 5-day treatment for CAP in patients who are improving, afebrile, and clinically stable. By 5 days, most "surprises" will already have occurred. In this trial, about 30% of patients received additional antibiotics and the rest had a low risk for relapse or readmission. This crucial day-5 assessment makes it possible for an order set to include a 5-day treatment regimen. Can treatment stop on day 5 in patients who are doing well even if they have complicated infections or comorbid conditions? In this trial, patients with higher PSI scores (IV to V) showed equivalent outcomes to healthier patients (PSI I to III), indicating that the day-5 assessment may even protect patients with higher predicted mortality.

Thomas Fekete, MD
Temple University School of Medicine
Philadelphia, Pennsylvania, USA

References

1. **Mandell LA, Wunderink RG, Anzueto A, et al; Infectious Diseases Society of America; America Thoracic Society.** Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44 Suppl 2:S27-72.
2. **U.S. Food and Drug Administration.** FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. www.fda.gov/Drugs/DrugSafety/ucm511530.htm (accessed 29 Aug 2016).

doi:10.7326/ACPJC-2016-165-10-050