Inpatient Notes: Optimal Treatment Duration for Patients Hospitalized With Pneumonia–The Benefits of Less

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Traditionally, community-acquired pneumonia (CAP) has been treated with a total of 7 to 14 days of antibiotic therapy. Contemporary guidelines recommend shorter courses, but overtreatment remains common. A recent evaluation of pneumonia treatment in 43 diverse hospitals in Michigan showed that two thirds of patients received antibiotics for longer than the shortest effective duration consistent with guidelines (1). Reasons for the widespread excess are unclear. However, an overwhelming body of evidence shows that shorter durations of antibiotic treatment lead to favorable clinical outcomes with fewer antibiotic-associated adverse effects and reduce the selective pressure that drives antibiotic resistance.

Short- Versus Long-Course Treatment for CAP

Several meta-analyses have compared short courses with longer courses of antibiotic therapy for pneumonia. The most recent of these identified 5 randomized controlled trials (RCTs) comparing short-course treatment (≤7 days) with longer treatment and found no difference in rates of clinical success, relapse, adverse events, or mortality (2). There were similar findings in a subset analysis comparing patients receiving no more than 5 days of therapy with those receiving 7 or more days. Most studies excluded "severe" pneumonia, and many of the 5-day treatment groups received fluoroquinolones. A recent RCT, however, compared 5-day treatment with "usual care" and included more severely ill patients (40% with Pneumonia Severity Index class IV or V). Compared with usual care, in which patients received a median 10 days of treatment, 5-day courses were associated with similar clinical outcomes and a reduced rate of readmission at 30 days (3). In a cohort study of more than 6000 patients hospitalized with pneumonia, only 24% of patients received a mean of 5 days (SD, 1) of antibiotic treatment. However, this group had rates of mortality, readmission, and postdischarge emergency visits similar to those treated with longer courses. Of note, each excess day of therapy was associated with a 5% increase in the odds of patient-reported antibiotic-associated adverse events after discharge (1). Most studies evaluating short-course therapy have required a minimum of 5 days of therapy and demonstration of clinical stability (assessed by objective criteria) before antibiotics are discontinued. Clinical stability is often defined as being afebrile (≤37.8 °C) and having no more than 1 sign of instability (systolic blood pressure <90 mm Hg, heart rate >100 beats/min, respiratory rate >24 breaths/min, and oxygen saturation <90% on room air). Patients treated with short-course therapy who tolerate oral medications, are at baseline mental status, and demonstrate clinical stability have been shown to have a very low rate of relapse after antibiotic discontinuation. Evidence is mounting that the best clinical outcomes, with the fewest adverse effects, are achieved by treating pneumonia with no more than 5 days of antibiotics.

Patients at Risk for Resistant Organisms

Many of the studies evaluating 5-day antibiotic courses for pneumonia have excluded severely ill patients or those with risk factors for resistant organisms. Patients with ventilator-associated pneumonia (VAP) and hospital-acquired pneumonia (HAP) are often severely ill and have been shown to be at increased risk for resistant organisms. Recent VAP/HAP guidelines summarize the evidence comparing 7-day therapy with 8 to 15 days of therapy. In patients with VAP, shorter courses of therapy have been associated with reduced rates of recurrent pneumonia with drug-resistant organisms and no differences in treatment failure, recurrence, or mortality (4). These data have been extrapolated to support 7-day therapy for patients with HAP as well as those with CAP who have risk factors for resistant organisms (often referred to as health care–associated pneumonia). As long as objective criteria for stability are used, there is no reason to extend treatment beyond 5 to 7 days, even in patients with severe pneumonia or those with suspected or proven drug-resistant organisms (e.g., methicillin-resistant *Staphylococcus aureus*, or *Pseudomonas aeruginosa).* Patients who do not achieve clinical stability by day 5 or patients with complications (including bacteremia, meningitis, endocarditis, or deep-seated infections) may require longer antibiotic courses.

The Role of Procalcitonin in Reducing Treatment Duration

Serum procalcitonin is an inflammatory biomarker that increases with bacterial infection and is associated with disease severity and prognosis. When tested serially and incorporated into management pathways, it has been shown to provide evidence of when antibiotic duration can be safely reduced in patients with suspected respiratory infections. As such, it is an appealing tool and has the potential to improve antibiotic stewardship. However, there are several limitations to its diagnostic use. First, up to one quarter of patients hospitalized with pneumonia may have procalcitonin levels that are discordant with their ultimate diagnosis (as determined by adjudicated physician review). Second, levels of procalcitonin in patients with bacterial pneumonia may be low if they present early in the disease course, necessitating repeated testing in 12 to 24 hours. This limits the usefulness of the test to inform initial treatment recommendations. Third, many of the studies demonstrating reductions in antibiotic treat-

ment duration with procalcitonin were done in Europe, where treatment durations in control groups often exceeded guideline recommendations. Whether it will have an effect in institutions treating patients in a manner consistent with current guidelines is less clear. In fact, a recent randomized trial of procalcitonin-guided treatment for lower respiratory tract infections in 14 U.S. hospitals with high levels of guideline adherence did not reduce antibiotic treatment duration or overall antibiotic use (5). Nonetheless, procalcitonin testing may be useful in patients with a documented viral infection and no obvious signs of bacterial infection. Low levels of procalcitonin in such patients might be used to facilitate discontinuation of antibiotics after 48 to 72 hours of treatment.

SUMMARY

Ample data show that antibiotic treatment durations for patients with pneumonia often exceed guideline recommendations. Emerging evidence suggests that shorter courses are effective and have the advantage of reducing the adverse consequences of antibiotic exposure. For most patients that achieve clinical stability, treatment duration of 5 days is safe and effective. Small subsets may warrant a slightly longer duration, whereas use of procalcitonin, in limited settings, might facilitate even shorter durations.

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