Outpatient Treatment of Community Acquired Pneumonia: Macrolide or β-lactam?

Community acquired pneumonia (CAP) is a common, but serious respiratory disease that occurs most often during the winter months and costs in excess of $10 billion per year in the US. The majority of CAP cases are bacterial in nature with *Streptococcus pneumoniae* being the most common (20-60%) pathogen. Others include *Haemophilus influenzae*, respiratory viruses, and atypical organisms such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and, uncommonly, *Legionella* species.

During the last decade bacterial resistance to macrolides (e.g. Zithromax®, Biaxin®), β-lactams (e.g. Amoxil®, Augmentin®), and fluoroquinolones (e.g. Cipro®, Levaquin®) has increased worldwide. *S. pneumoniae* resistance in the US is reportedly 21.5% for macrolides, 8.6% for β-lactams, and 1.2% for fluoroquinolones. Even higher percentages of macrolide resistance have been reported in Europe.

Key Points

- ***S. pneumoniae* remains the most common causative organism of CAP.**
- **Macrolide antibiotics (e.g. Zithromax® and Biaxin®) are considered effective first-line treatment for outpatient CAP in the US.**
- **An important concern is the increasing resistance of *S. pneumoniae* to macrolide antibiotics in the US and worldwide and the potential for losing this unique class of antibiotics for empiric outpatient treatment.**
- **Most patients with symptoms of mild to moderate CAP (i.e. do not have risk factors for drug-resistant pathogens, Table 1) can be successfully treated with high-dose β-lactam monotherapy (e.g. amoxicillin 1000 mg PO tid or Augmentin® XR 2000 mg PO bid).**
- **Fluoroquinolone (Levaquin®, Avelox®) use for outpatient CAP is discouraged unless risk factors for drug-resistant pathogens are present (Table 1).**
- **Patients with symptoms of severe CAP (Table 2), or if *Legionella* species is suspected, should be hospitalized and treated with an antibiotic that covers atypical organisms.**

The true incidence of CAP caused by atypical organisms in the US remains unknown but has been reported as low as 7.5% and as high as 50% or more. While North American treatment guidelines recommend macrolides first-line for the treatment of uncomplicated CAP and places more emphasis on covering atypical organisms, in contrast, European guidelines favor β-lactam agents. Reasons for this include high macrolide resistance and the debate regarding the importance of therapy for *Mycoplasma* and *Chlamydia* infections, as many of the cases caused by these organisms are self-limiting. High-dose β-lactam monotherapy likely remains an effective treatment for outpatient CAP, as these agents cover the most common causative pathogen, *S. pneumoniae.*

(Available online at http://idahodur.isu.edu, information current as of December 2008)

An analysis of recent Idaho Medicaid cases of uncomplicated outpatient CAP revealed that initial antibiotic failure (a change in antibiotic or admission to the hospital for pneumonia within 14 days) was actually higher for patients prescribed macrolides compared to those receiving β-lactams (12.7% vs 4.7%, p=0.021).

The rising resistance of *S. pneumoniae* to macrolides worldwide, including the US, is a major cause of concern. β-lactam antibiotics, if dosed appropriately (e.g. amoxicillin 1000 mg PO tid or Augmentin® XR 2000 mg PO bid for 7-10 days), are still a reasonable alternative for treating non-hospitalized patients with CAP. If patients have signs and symptoms of severe CAP (Table 2), or if *Legionella* species are suspected, hospitalization and selection of an antibiotic that covers atypical organisms is recommended.

Table 1: Risk factors for drug-resistant pathogens in CAP

Age <2 or >65 years	Immunosuppresive illness or therapy
Antibiotic therapy in previous 3 months	Alcoholism
Hospitalization in previous 3 months	Exposure to a child in a day care center
Medical comorbidities (chronic heart, lung, liver, or renal disease, diabetes, malignancies, asplenia)	

Table 2: Identifying patients with signs of severe CAP (CURB-65)

Criteria	Value
Confusion	1
B**U**N > 19.6 mg/dL	1
Respiration ≥ 30/min	1
Blood pressure low (< 90mm/Hg systolic OR ≤ 60mmHg diastolic)	1
65 years or older	1
A score of 2 or more is associated with increased mortality and represents symptoms of severe CAP	

References

1. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. Clin Infect Dis. 2007 44(2):S27-72.
2. File TM Jr, Tan JS. International guidelines for the treatment of community-acquired pneumonia in adults: the role of macrolides. Drugs. 2003;63(2):181-205.
3. Hoare Z, Lim WS. Pneumonia: update on diagnosis and management. BMJ. 2006 May 6;332(7549):1077-9.
4. Mandell LA, Marrie TJ, Grossman RF, et al. Canadian guidelines for the initial management of community-acquired pneumonia: an evidence-based update by the Canadian Infectious Diseases Society and the Canadian Thoracic Society. The Canadian Community-Acquired Pneumonia Working Group. Clin Infect Dis. 2000 Aug;31(2):383-421.
5. British Thoracic Society. Guidelines for the management of community-acquired pneumonia in adults. Thorax 2001;56(suppl):1-64.
6. Dorcar J. Guidelines for community-acquired pneumonia in spain: another perspective. Clin Pulm Med 2000;7:1-8.
7. French Society of Infectious Diseases (SPILF). What should the initial antibiotherapy for acute community-acquired pneumonia be? How should it be reassessed in case of failure, given the evolution of responsible pathogens and the resistance of pneumococci? Should combined treatment be used? Med Mal Infect 2001;31:357-368.
8. Working Group of the South African Thoracic Society. Management of community-acquired pneumonia in adults. S Afr Med J. 2007 Dec;97(12 Pt 2):1296-306.