Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Three versus Five Days of Azithromycin

Azithromycin is a macrolide antibiotic with activity against many respiratory tract organisms, including *Streptococcus pneumoniae, Haemophilus influenzae*, *Moraxella catarrhalis*, and atypical pneumonia pathogens.[1] Given its spectrum of activity, it is commonly used for the treatment of community-acquired pneumonia (CAP). The Infectious Diseases Society of America/American Thoracic Society CAP Guidelines recommend a β-lactam antibiotic with azithromycin for a minimum of 5 days.[2]

The recommended 5 day course of azithromycin is typically dosed 500 mg on day 1, then 250 mg on days 2-5 (Z-Pak).[3] This dosing can be inconvenient, particularly for inpatients, as it requires multiple antibiotic orders and failure to enter orders correctly may result in greater unintended antibiotic exposure (e.g. 500 mg daily x 5 days). Alternative dosing of 500 mg x 3 days has been used in pneumonia. Can azithromycin 500 mg daily x 3 days routinely be administered in the treatment of CAP?

How do pharmacokinetics compare?

Azithromycin maximum serum concentration in the serum and the area under the curve have been found to be similar between 3-day regimen and a 5-day regimen.[3] Azithromycin has a long half-life of ~ 70 hours[1], resulting in therapeutic concentrations that extend well beyond the duration of antibiotic administration.

How do clinical outcomes compare?

A retrospective study compared the efficacy of azithromycin given over 3 days (500 mg daily) versus 5 days (500 mg on day 1, then 250 mg daily on days 2-5) for the treatment of atypical pneumonia.[4] Across both groups, all patients were clinically cured, with significant improvement in signs and symptoms within 5 days of the start of treatment. Tolerability was also similar between the two groups. These results suggest that a 1.5 g cumulative dose of azithromycin is equally effective when given over either a course of 3 days versus 5 days for the treatment of atypical pneumonia.

Longer durations of azithromycin with total doses > 1500 mg may be warranted in some pulmonary infections such as severe legionella pneumonia or pneumonia due to non-tuberculous mycobacteria.[5-6]

Key Takeaway: Azithromycin 500 mg x 3 days is interchangeable with azithromycin 500 mg on day 1 followed by 250 mg on days 2–5 in the treatment of most CAP. Azithromycin 500 mg x 3 days may be logistically easier for inpatient treatment (e.g. automatic stop date) and limit unintended overuse of azithromycin.

References

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