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Albert RK, Connett J, Bailey WC, et al. Azithromycin for prevention of exacerbations of COPD. N Engl J Med. 2011;365:689-98.

Acute exacerbations of chronic obstructive pulmonary disease (COPD) are a major cause of morbidity and the major cost of COPD care. Chronic use of macrolide antibiotics have been shown to benefit patients with cystic fibrosis, bronchiectasis and COPD by preventing exacerbations presumably by their anti-inflammatory rather than their antibiotic effects. Albert et al. performed a randomized, placebo-controlled, double-blinded trial to determine whether azithromycin decreased the frequency of exacerbations in participants with COPD. A total of 1577 subjects were screened; 1142 (72%) were randomly assigned to receive azithromycin, at a dose of 250 mg daily (570 participants), or placebo (572 participants) for 1 year in addition to their usual care. Azithromycin improved the median time to the first exacerbation (266 days vs. 174 days, $p < 0.001$); the frequency of exacerbations was (1.48 vs. 1.83 per patient-year, $p = 0.01$); scores on the St. George's Respiratory Questionnaire (2.8 ± 12.8 vs. 0.6 ± 11.4 , $p = 0.004$); and the percentage of participants with more than the minimal clinically important difference of -4 units (43% vs. 36% $p = 0.03$). Hearing decrements were slightly more common in the azithromycin group than in the placebo group (25% vs. 20%, $p = 0.04$). Colonization with respiratory pathogens was lower in the azithromycin group (12 vs. 31%, $p < 0.001$) although when present colonization with macrolide resistant organisms was more frequent (81 vs. 41%, $p < 0.001$). Mortality was low and did not differ between the groups.

This study confirms a previous study by Seemungal et al. (1) who also performed a randomized, double-blind, placebo-controlled study of another macrolide, erythromycin, administered at 250 mg twice daily to 109 patients with COPD over 12 months. Exacerbations for the erythromycin-treated patients were reduced compared with placebo-treated patients ($p < 0.003$). These two well done, randomized studies lend strong support to chronic use of macrolide antibiotics in COPD. In both studies complications were low and antibiotic resistance remained mostly a laboratory observation rather than a clinical problem. Details such as the optimal doses and frequency of antibiotic administration will need further investigation. Other antibiotics such as the tetracyclines also have anti-inflammatory effects and may be alternatives to macrolides (2). It now seems that the concept of chronic use of some antibiotics as anti-inflammatories is well established in respiratory disease and I would urge consideration of their usage in patients who have had or are likely to have a COPD exacerbation.

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References

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2. Rempe S, Hayden JM, Robbins RA Hoyt JC. Tetracyclines and pulmonary Inflammation. *Endocrine, Metabolic & Immune Disorders - Drug Targets* 2007;4:232-6.