

## Can an azithro a day keep COPD exacerbation away?

**The clinical issue:** Inhaled glucocorticoids, long-acting beta<sub>2</sub>-agonists, and anticholinergics decrease the frequency of COPD exacerbations, but these still occur frequently in patients taking all of these medications. Macrolide antibiotics such as azithromycin have both antibacterial and anti-inflammatory properties, and have been proposed as an adjunct to commonly used COPD medications.

**The new evidence:** Albert and colleagues studied COPD patients at high risk of exacerbation, defined as using home oxygen or systemic steroids in the prior year, or being treated in an ER or hospital for a COPD flare. Patients were randomized to receive azithromycin (250 mg daily) or placebo for one year, in addition to their usual COPD medications. Patients with a long QTc interval (>450 ms), taking QTc prolonging medications, or with hearing loss were excluded.

**COPD exacerbations occurred less frequently (1.48 vs. 1.83 per year,  $p=0.01$ ) and longer after randomization (266 vs. 174 days,  $p<0.001$ ) in azithromycin-treated patients than in those randomized to placebo.** This meant a 27% relative reduction in the risk of COPD exacerbation and a number needed to treat (NNT) over a year of less than 3 (lower is better). Azithromycin also improved subjective quality of life ( $p=0.004$ ) as measured by severity of respiratory symptoms.

Rates of adverse outcomes were equal in the two groups except for hearing loss, which occurred in 25% of patients receiving azithromycin and 20% of the placebo group ( $p=0.04$ ). Patients given azithromycin whose respiratory tracts were not colonized with bacteria at the beginning of the study were less likely to become colonized during the year of treatment (12% vs. 31%,  $p<0.001$ ). However, if patients became colonized, the bacteria isolated were more likely to be resistant to macrolides (81% vs. 41%,  $p<0.001$ ), although this was not associated with an increased risk of pneumonia. There were no differences in mortality between the two groups.

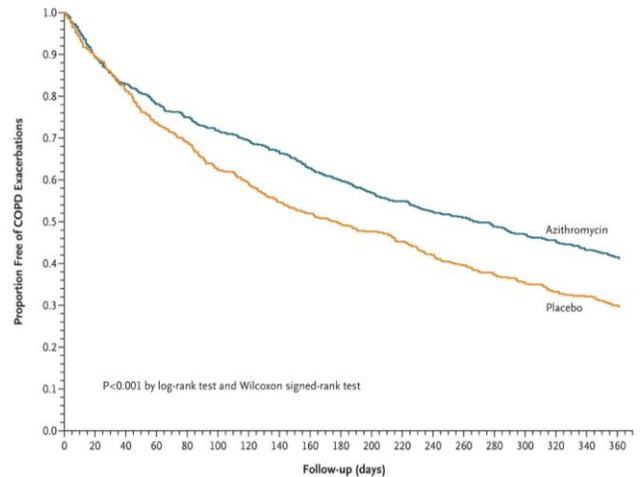
**Limitations:** This study lasted only one year, though azithromycin might be used longer in actual practice. The effects of using daily azithromycin for longer than a year in patients with COPD remain unknown. Additionally, only one treatment protocol was tested; azithromycin has a long half-life and other dosing frequencies could also be effective.

**Bottom line:** Daily azithromycin significantly reduced the frequency of COPD exacerbations and may be a useful preventive therapy in patients with COPD who are at high risk of an acute exacerbation. Review concurrent medications and check a baseline EKG before starting treatment, to identify those who have or are at risk of a prolonged QTc interval. Order audiology testing for patients with hearing complaints, and reassess treatment if hearing worsens.

**References:** 1. Albert RK, Connett J, Bailey WC, et al. COPD Clinical Research Network. Azithromycin for prevention of exacerbations of COPD. *N Engl J Med.* 2011 Aug 25;365(8):689-98.

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**These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.**



**Figure 1.** Proportion of Participants Free from Acute Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) for 1 Year, According to Study Group. Acute exacerbations were experienced by 57% of patients in the azithromycin group and 68% of patients in the placebo group.<sup>1</sup>