FPIN's Clinical Inquiries

Antibiotic Prophylaxis for COPD Exacerbations

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Clinical Question

Are prophylactic antibiotics effective in reducing chronic obstructive pulmonary disease (COPD) exacerbations?

Evidence-Based Answer

Prophylactic antibiotics may be used to reduce the overall rate of COPD exacerbations and delay their onset. (Strength of Recommendation: A, based on a high-quality systematic review of randomized controlled trials [RCTs].) However, the appropriate antibiotic regimen and target population are unclear.

Evidence Summary

A 2013 Cochrane review of seven RCTs (N = 3,170) examined whether the use of prophylactic antibiotics in patients with COPD reduces exacerbations or improves quality of life.[1] The trials compared prophylactic oral antibiotics with placebo over three to 36 months. Five trials (N = 1,438) studied continuous prophylaxis with oral macrolide antibiotics (azithromycin [Zithromax], erythromycin, or clarithromycin [Biaxin]) vs. placebo. Two trials (N = 1,732) studied pulsed prophylaxis with oral moxifloxacin (Avelox) or azithromycin vs. placebo. Both regimens demonstrated an overall reduction in the number of treated patients who had one or more COPD exacerbations (four trials; N = 2,411; odds ratio [OR] = 0.64; 95% confidence interval [CI], 0.45 to 0.90; number needed to treat [NNT] = 13). Continuous prophylaxis with macrolides resulted in a decrease in the number of patients with one or more exacerbations (three trials; N = 1,262; OR = 0.55; 95% CI, 0.39 to 0.77; NNT = 8). Pulsed prophylaxis with moxifloxacin did not reduce the risk of exacerbations compared with placebo (one trial; n = 1,149; OR = 0.87; 95% CI, 0.69 to 1.09). Continuous prophylaxis with macrolide antibiotics resulted in a significant reduction in the rate of COPD exacerbations per patient-year (three trials; N = 1,262; rate ratio [RR] = 0.73; 95% CI, 0.58 to 0.91). One trial of azithromycin found that macrolide resistance was significantly higher in the treatment group (81% vs. 41%, $P < .001$), although only 15% of participants were able to give sputum for a culture. There were no significant differences in all-cause mortality or serious adverse events between the treatment and placebo groups. One trial found that daily azithromycin for 12 months was associated with a statistically significant increase in hearing impairment (n = 1,117; OR = 1.39; 95% CI, 1.05 to 1.85; number needed to harm = 18). However, a significant number of patients in both groups reportedly discontinued the medication secondary to hearing loss.

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A 2014 RCT compared pulsed prophylaxis with azithromycin (500 mg three times weekly for 12 months) with placebo in 92 adults with COPD who had at least three exacerbations in the preceding year.[2] The rate of exacerbations over the 12-month follow-up period was significantly lower in patients receiving pulsed azithromycin compared with placebo (RR = 0.58; 95% CI, 0.42 to 0.79). Patients in the azithromycin group also delayed their median time to first exacerbation compared with the placebo group (130 days vs. 59 days, $P = .001$).

A 2015 RCT examined antibiotic prophylaxis with the macrolide roxithromycin (not available in the United States). The study compared roxithromycin, 300 mg per day for 12 weeks; a combination of roxithromycin and doxycycline, 300/100 mg per day for 12 weeks; and placebo.[3] Study participants had a history of frequent COPD exacerbations, including at least three moderate or severe exacerbations within the preceding two years, and serologic evidence of prior *Chlamydia pneumoniae* infection. Over a 48-week post-treatment period, there was no statistically significant difference in exacerbation rate or time to first exacerbation between the treatment groups and the placebo group.

Recommendations from Others

A 2014 joint statement from the American Thoracic Society and the European Respiratory Society states that it is not clear which patients benefit from antibiotic prophylaxis for COPD exacerbations, and that the optimal dosing strategy and duration of use are unknown.[4] Macrolides are recommended for use on a case-by-case basis after considering the risk vs. benefits for each patient.

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