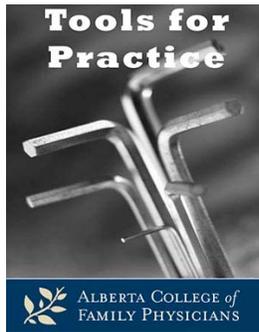


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Daily Prophylactic Antibiotics in COPD

Clinical Question: Are daily prophylactic antibiotics a reasonable option in preventing acute exacerbation of COPD (and if so, which patients)?

Evidence:

Three recent randomized controlled trials (RCT)

- 1142 severe COPD patients (60% on O₂, 48% on all 3 puffers), randomized to azithromycin 250mg QD or placebo.¹
 - At one year, azithromycin
 - Decreased exacerbations, hazard ratio 0.73 (0.63-0.84).
 - Decreased patients ≥ 1 exacerbation: 57% versus 68%, Number Needed to Treat (NNT) 10
 - Clinically important improved quality of life, NNT 15
 - Harms: 5% more had decreased hearing and macrolide resistance from nasopharyngeal swabs increased (81% versus 41%)
- 109 COPD patients, 35% had ≥ 3 exacerbations last year, randomized to erythromycin 250mg BID or placebo.²
 - Erythromycin reduced exacerbations, rate ratio 0.65 (0.49-0.86)
 - No difference in adverse events.
- 1157 COPD patients with ≥ 2 exacerbations last year, randomized to moxifloxacin 400mg QD x 5 days every 8 weeks or placebo for 48 weeks.³
 - Non-significant trend to reduced exacerbation (odds ratio 0.81, 0.65-1.01)
 - No impact on other endpoints (hospitalization, mortality, or quality of life).
 - Harms: More adverse events (primarily GI) arising from treatment, 9.3% versus 3.8%, Number Needed to Harm (NNH) 19

Context:

- A systematic review of 9 old trials (before 1970), also suggest a reduction in exacerbation rate, relative risk 0.91 (0.84-0.99).⁴
- Most recent COPD guidelines and review articles do not include the use of prophylactic antibiotics⁵ or indicate that benefits do not exceed risk⁶⁻⁸ (although only one⁶ includes the most recent RCT¹).

- The reduction in exacerbation is similar to that seen with long-acting inhaled therapies.^{9,10}
- Macrolide antibiotics are used chronically in respiratory disorders such as cystic fibrosis and diffuse panbronchiolitis.¹¹
 - Effect may be anti-inflammatory more than antimicrobial.

Bottom-line: In selective patients with severe COPD and recurrent exacerbations, prophylactic antibiotics may reduce exacerbations for about 1 in 10. Balanced against possible increased resistance and adverse events, present use should be very limited. The long term benefits and impacts on antimicrobial resistance remain to be seen.

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