*Cochrane Database of Systematic Reviews - - Cochrane Review*

# Macrolide antibiotics (including azithromycin) for cystic fibrosis

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### Study design (if review, criteria of inclusion for studies)

Randomised controlled trials of macrolide antibiotics compared to: placebo; another class of antibiotic; another macrolide antibiotic; or the same macrolide antibiotic at a different dose.

### List of included studies (14)

Clement 2006, Equi 2002, Kabra 2010, McCormack 2007, O'Connor 2009, Rotschild 2005, Saiman 2003, Saiman 2010, Steinkamp 2007, Wolter 2002

### Participants

People included in the analysis fulfilled strict criteria for the diagnosis of CF. If two disease-causing genetic mutations were not recognised, participants were required to have a positive sweat test and clinical features consistent with CF.

### Interventions

Macrolide antibiotics (including azithromycin)

### Outcome measures

Adverse effects of antibiotic treatment; Percentage change in FEV1; Percentage change in FVC

### Main results

We included 14 studies (1467 participants) lasting 28 days to 36 months. All the studies assessed azithromycin: 11 compared oral azithromycin to placebo (1167 participants); one compared a high dose to a low dose (47 participants); one compared nebulised to oral azithromycin (45 participants); and one looked at weekly versus daily dose (208 participants). Oral azithromycin versus placebo: There is a slight improvement in forced expiratory volume (FEV1 % predicted) in one second in the azithromycin group at up to six months compared to placebo (mean difference (MD) 3.97, 95% confidence interval (CI) 1.74 to 6.19; highâ€•certainty evidence), although there is probably no difference at three months, (MD 2.70%, 95% CI â€•0.12 to 5.52), or 12 months (MD â€•0.13, 95% CI â€•4.96 to 4.70). Participants in the azithromycin group are probably at a decreased risk of pulmonary exacerbation with a longer time to exacerbation (hazard ratio (HR) 0.61, 95% CI 0.50 to 0.75; moderateâ€•certainty evidence). Mild side effects were common, but there was no difference between groups (moderateâ€•certainty evidence). There is no difference in hospital admissions at six months (odds ratio (OR) 0.61, 95% CI 0.36 to 1.04; highâ€•certainty evidence), or in new acquisition of P aeruginosa at 12 months (HR 1.00, 95% CI 0.64 to 1.55; moderateâ€•certainty evidence). Highâ€•dose versus lowâ€•dose azithromycin: We are uncertain whether there is any difference in FEV1 % predicted at six months between the two groups (no data available) or in the rate of exacerbations per child per month (MD â€•0.05 (95% CI â€•0.20 to 0.10)); very lowâ€•certainty evidence for both outcomes. Only children were included in the study and the study did not report on any of our other clinically important outcomes. Nebulised azithromycin versus oral azithromycin: We were unable to include any of the data into our analyses and have reported findings directly from the paper; we graded all evidence as being of very low certainty. The authors reported that there was a greater mean change in FEV1 % predicted at one month in the nebulised azithromycin group (P

### Authors' conclusions

Azithromycin therapy is associated with a small but consistent improvement in respiratory function, a decreased risk of exacerbation and longer time to exacerbation at six months; but evidence for treatment efficacy beyond six months remains limited. Azithromycin appears to have a good safety profile (although a weekly dose was associated with more gastrointestinal side effects, which makes it less acceptable for longâ€•term therapy), with a relatively minimal treatment burden for people with CF, and it is inexpensive. A wider concern may be the emergence of macrolide resistance reported in the most recent study which, combined with the lack of longâ€•term data, means we do not feel that the current evidence is strong enough to support azithromycin therapy for all people with CF. - Future research should report over longer time frames using validated tools and consistent reporting, to allow for easier synthesis of data. In particular, future trials should report important adverse events such as hearing impairment or liver disease. More data on the effects of azithromycin given in different ways and reporting on our primary outcomes would benefit decisionâ€•making on whether and how to give macrolide antibiotics. Finally, it is important to assess azithromycin therapy for people with CF who are established on the relatively

new cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies which correct the underlying molecular defect associated with CF (none of the trials included in the review are relevant to this population).

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### See also

Southern KW, Solis-Moya A, Kurz D, Smith S. Macrolide antibiotics (including azithromycin) for cystic fibrosis. Cochrane Database of Systematic Reviews 2024, Issue 2. Art. No.: CD002203. DOI: 10.1002/14651858.CD002203.pub5. Accessed 28 February 2024.

### Keywords

Anti-Bacterial Agents; Bacterial Infections; Infection; Macrolides; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Staphylococcus aureus; Azithromycin; Anti-Inflammatory Agents; Anti-Inflammatory Agents - excl Steroids;