Cochrane Database of Systematic Reviews - - Cochrane Review

Strategies to prevent kidney injury from antibiotics in people with cystic fibrosi

Code: CD013032 **Year:** 2018 **Date:** 2009 - updated: 6 APR 2022 **Author:** Ditchfield N

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

Randomised controlled trials (RCTs) of people with CF, in whom Pseudomonas aeruginosa had recently been isolated from respiratory secretions.

List of included studies (11)

Gibson 2003; Proesmans 2013; Ratjen 2010; Taccetti 2012; Treggiari 2011; Valerius 1991; Wiesemann 1998

Participants

Children and adults with CF, diagnosed clinically and by sweat or genetic testing (or both) with a first positive microbiological isolate of P. aeruginosa from a lower respiratory tract specimen. Participants should be enrolled into a trial within two months from first isolation of P. aeruginosa. People with CF of all ages and disease severity will be included.

Interventions

Inhaled tobramycin; Oral ciprofloxacin and inhaled colistin. Combinations of inhaled, oral or intravenous antibiotics with placebo, usual treatment or other combinations of inhaled, oral or intravenous antibiotics.

Outcome measures

Adverse events; Change in modified Shwachmann score from baseline; Change in weight from baseline; Positive respiratory culture for P. aeruginosa (combined available case analysis); Positive respiratory culture for P. aeruginosa (combined) - best case; Positive respiratory culture for P. aeruginosa (combined) - worst case; Positive respiratory culture for P. aeruginosa (Gibson 2003); Positive respiratory culture for P. aeruginosa (Wiesemann 1998); Positive respiratory culture for P.aeruginosa; Proportion colonised with P. aeruginosa

Main results

We included 11 trials (1449 participants) lasting between 28 days and 27 months; some had few participants and most had relatively short followâ€•up periods. Antibiotics in this review are: oral â€“ ciprofloxacin and azithromycin; inhaled â€“ tobramycin nebuliser solution for inhalation (TNS), aztreonam lysine (AZLI) and colistin; IV â€“ ceftazidime and tobramycin. There was generally a low risk of bias from missing data. In most trials it was difficult to blind participants and clinicians to treatment. Two trials were supported by the manufacturers of the antibiotic used. - TNS versus placebo - TNS may improve eradication; fewer participants were still positive for P aeruginosa at one month (odds ratio (OR) 0.06, 95% confidence interval (CI) 0.02 to 0.18; 3 trials, 89 participants; lowâ€•certainty evidence) and two months (OR 0.15, 95% CI 0.03 to 0.65; 2 trials, 38 participants). We are uncertain whether the odds of a positive culture decrease at 12 months (OR 0.02, 95% CI 0.00 to 0.67; 1 trial, 12 participants). - TNS (28 days) versus TNS (56 days) - One trial (88 participants) comparing 28 days to 56 days TNS treatment found duration of treatment may make little or no difference in time to next isolation (hazard ratio (HR) 0.81, 95% CI 0.37 to 1.76; lowâ€•certainty evidence). - Cycled TNS versus cultureâ€•based TNS - One trial (304 children, one to 12 years old) compared cycled TNS to cultureâ€•based therapy and also ciprofloxacin to placebo. We found moderateâ€•certainty evidence of an effect favouring cycled TNS therapy (OR 0.51, 95% CI 0.31 to 0.82), although the trial publication reported ageâ€•adjusted OR and no difference between groups. - Ciprofloxacin versus placebo added to cycled and cultureâ€•based TNS therapy - One trial (296 participants) examined the effect of adding ciprofloxacin versus placebo to cycled and cultureâ€•based TNS therapy. There is probably no difference between ciprofloxacin and placebo in eradicating P aeruginosa (OR 0.89, 95% CI 0.55 to 1.44; moderateâ€•certainty evidence). - Ciprofloxacin and colistin versus TNS - We are uncertain whether there is any difference between groups in eradication of P aeruginosa at up to six months (OR 0.43, 95% CI 0.15 to 1.23; 1 trial, 58 participants) or up to 24 months (OR 0.76, 95% CI 0.24 to 2.42; 1 trial, 47 participants); there was a low rate of shortâ€•term eradication in both groups. - Ciprofloxacin plus colistin versus ciprofloxacin plus TNS - One trial (223 participants) found there may be no difference in positive respiratory cultures at 16 months between ciprofloxacin with colistin versus TNS with ciprofloxacin (OR 1.28, 95% CI 0.72 to 2.29; lowâ€•certainty evidence). - TNS plus azithromycin compared to TNS plus oral placebo - Adding azithromycin may make no difference to the number of participants eradicating P aeruginosa after a threeâ€•month treatment phase (risk ratio (RR) 1.01, 95% CI 0.75 to 1.35; 1 trial, 91 participants; lowâ€•certainty evidence); there was also no evidence of any difference in the time to recurrence. - Ciprofloxacin and colistin versus no treatment - A single trial only reported one of our planned outcomes; there were no adverse effects in either

group. - AZLI for 14 days plus placebo for 14 days compared to AZLI for 28 days - We are uncertain whether giving 14 or 28 days of AZLI makes any difference to the proportion of participants having a negative respiratory culture at 28 days (mean difference (MD) â€•7.50, 95% CI â€•24.80 to 9.80; 1 trial, 139 participants; very lowâ€•certainty evidence). - Ceftazidime with IV tobramycin compared with ciprofloxacin (both regimens in conjunction with three months colistin) - IV ceftazidime with tobramycin compared with ciprofloxacin may make little or no difference to eradication of P aeruginosa at three months, sustained to 15 months, provided that inhaled antibiotics are also used (RR 0.84, 95 % CI 0.65 to 1.09; P = 0.18; 1 trial, 255 participants; highâ€•certainty evidence). The results do not support using IV antibiotics over oral therapy to eradicate P aeruginosa, based on both eradication rate and financial cost.

Authors' conclusions

Nebulised antibiotics, alone or with oral antibiotics, were better than no treatment for early infection with P aeruginosa. Eradication may be sustained in the short term. There is insufficient evidence to determine whether these antibiotic strategies decrease mortality or morbidity, improve quality of life, or are associated with adverse effects compared to placebo or standard treatment. Four trials comparing two active treatments have failed to show differences in rates of eradication of P aeruginosa. One large trial showed that intravenous ceftazidime with tobramycin is not superior to oral ciprofloxacin when inhaled antibiotics are also used. There is still insufficient evidence to state which antibiotic strategy should be used for the eradication of early P aeruginosa infection in CF, but there is now evidence that intravenous therapy is not superior to oral antibiotics.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD013032/abstract

See also

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Keywords

Adult; Anti-Bacterial Agents; Bacterial Infections; Child; Ciprofloxacin; Infection; Inhalation OR nebulised; Oral; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Tobramycin; Colistin; Aminoglycosides; Quinolones; other anti-bacterial agents;