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Intravenous antibiotics for pulmonary exacerbations in people with cystic fibrosis

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

Randomised controlled trials and the first treatment cycle of cross-over studies

List of included studies (45)

Agostini 1983; Black 1990; Blumer 2005; Bosso 1988; Bosso 1989; BTS 1985; Caplan 1984; Church 1997; Conway 1985; Conway 1997; Cooper 1985; Costantini 1982; De Boeck 1989; De Boeck 1999; Elborn 1992; Gold 1985; Gold 1987; Hodson 1987; Huang 1983; Hyatt 1981; Knowles 1988; Macfarlane 1985; Master 2001; McCarty 1988; McLaughlin 1983; Padoan 1987; Penketh 1983; Penketh 1984; Regelmann 1990; Richard 1997; Salh 1992; Schaad 1986; Schaad 1987; Schaad 1989; Semykin 2010; Smith 1999; Stephens 1983; Wang 1988; Wesley 1988; Wientzen 1980

Participants

CF patients with cystic fibrosis of all ages and all degrees of disease severity, experiencing a pulmonary exacerbation

Interventions

single intravenous antibiotic versus placebo; combination of intravenous antibiotics versus placebo; one regimen of intravenous antibiotics versus another intravenous regimen of antibiotics (with or without placebo); intravenous antibiotic regimen versus nebulised antibiotics; intravenous antibiotic regimen versus oral antibiotics

Outcome measures

Primary outcomes: FEV1, FVC, time to next exacerbation, QoL

Main results

We included 45 studies involving 2810 participants. The included studies were mostly small, and inadequately reported, many of which were quite old. The certainty of the evidence was mostly low. Combined intravenous antibiotics versus placebo: data reported for absolute change in % predicted FEV1 and FVC suggested a possible improvement in favour of IV antibiotics, but the evidence is very uncertain (1 study, 12 participants; very lowâ€•certainty evidence). The study did not measure time to next exacerbation or quality of life. Intravenous versus nebulised antibiotics: 5 studies (122 participants) reported FEV1, with analysable data only from one study (16 participants). We found no difference between groups (moderateâ€•certainty evidence). 3 studies (91 participants) reported on FVC, with analysable data from only one study (54 participants). We are very uncertain on the effect of nebulised antibiotics (very lowâ€•certainty evidence). In one study, the 16 participants on nebulised plus IV antibiotics had a lower mean number of days to next exacerbation than those on combined IV antibiotics (lowâ€•certainty evidence), but we found no difference in quality of life between groups (lowâ€•certainty evidence). Intravenous versus oral antibiotics: 3 studies (172 participants) reported no difference in different measures of lung function. We found no difference in analysable data between IV and oral antibiotic regimens in either FEV1 % predicted or FVC % predicted (1 study, 24 participants; lowâ€•certainty evidence) or in the time to the next exacerbation (1 study, 108 participants; very lowâ€•certainty evidence). No study measured quality of life. Intravenous antibiotic regimens compared: 1 study (analysed as two data sets) compared the duration of IV antibiotic regimens between two groups (split according to initial antibiotic response). The first part was a nonâ€•inferiority study in 214 early treatment responders to establish whether 10 days of IV antibiotic treatment was as effective as 14 days. Second, investigators looked at whether 14 or 21 days of IV antibiotics were more effective in 705 participants who did not respond early to treatment. We found no difference in FEV1 % predicted with any duration of treatment (919 participants; highâ€•certainty evidence) or the time to next exacerbation (information later taken from registry data). Investigators did not report FVC or quality of life. Other comparisons: authors also found little or no difference in lung function when comparing single IV antibiotic regimens to placebo (2 studies, 70 participants), or in lung function and time to next exacerbation when comparing different single antibiotic regimens (2 studies, 95 participants). There may be a greater improvement in lung function in participants receiving combined IV antibiotics compared to single IV antibiotics (6 studies, 265 participants; lowâ€• to very lowâ€•certainty evidence), but probably no difference in the time to next exacerbation (1 study, 34 participants; lowâ€•certainty evidence). Four studies compared a single IV antibiotic plus placebo to a combined IV antibiotic regimen with high levels of heterogeneity in the results. We are very uncertain if there is any difference between groups in lung function (4 studies, 214 participants) and there may be little or no difference to being reâ€•admitted to hospital for an exacerbation (2 studies, 104 participants). Nine studies (417 participants) compared combined

IV antibiotic regimens with a great variation in drugs. We identified no differences in any measure of lung function or the time to next exacerbation between different regimens (lowâ€• to very lowâ€•certainty evidence). There were mixed results for adverse events across all comparisons; common adverse effects included elevated liver function tests, gastrointestinal events and haematological abnormalities. There were limited data for other secondary outcomes, such as weight, and there was no evidence of treatment effect.

Authors' conclusions

The evidence of benefit from administering IV antibiotics for pulmonary exacerbations in cystic fibrosis is often poor, especially in terms of size of studies and risk of bias, particularly in older studies. We are not certain whether there is any difference between specific antibiotic combinations, and neither is there evidence of a difference between the IV route and the inhaled or oral routes. There is limited evidence that shorter antibiotic duration in adults who respond early to treatment is not different to a longer period of treatment. There remain several unanswered questions regarding optimal IV antibiotic treatment regimens.

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See also

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Keywords

Exacerbation; Respiratory Tract Infections; Respiratory Tract Diseases; Infection; Bacterial Infections; Anti-Bacterial Agents; pharmacological_intervention; Intravenous;