Cochrane Database of Systematic Reviews - - Cochrane Review

Antibiotic adjuvant therapy for pulmonary infection in cystic fibrosis

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

Randomised controlled trials and quasi-randomised controlled trials of a therapy exerting an antibiotic adjuvant mechanism of action compared to placebo or no therapy for people with cystic fibrosis.

List of included studies (8)

Abdulhamid 2008; Milla 2013; Renner 2001; Smyth 2010

Participants

Adults and children with CF, diagnosed using the Cystic Fibrosis Foundation consensus statement (Rosenstein 1998). Therefore, a diagnosis of CF should be based on: â€¢ presence of one or more characteristic phenotypic features; â€¢ or a positive newborn screening test result; â€¢ or a history of CF in a sibling and laboratory evidence of an abnormality in the cystic fibrosis transmembrane regulator (CFTR) as documented by: â—¦ elevated sweat chloride concentration; or â—¦ identification of mutations in each CFTR gene known to cause CF; or â—¦ in vivo demonstration of characteristic abnormalities in ion transport across the nasal epithelium. As no standardised, validated definitions of acute exacerbation or chronic infection exists, we have employed the definitions employed by the CF Trust Antibiotic Working Group (UK Cystic Fibrosis Trust Antibiotic Working Group) alongside those identified by Rosenfeld (Rosenfeld 2001). An acute exacerbation will be defined as at least four of the following (UK Cystic Fibrosis Trust Antibiotic Working Group): â€¢ increased productive cough or breathlessness; â€¢ changes in the appearance or volume of sputum; â€¢ new signs on auscultation; â€¢ new chest radiograph signs; â€¢ loss of appetite; â€¢ fall in respiratory function; â€¢ fever requiring treatment with intravenous antibiotics. Or by the following score meeting or exceeding 2.6 (Rosenfeld 2001) - Antibiotic adjuvant therapy for pulmonary infection in cystic fibrosis (Review). A chronic P. aeruginosa infection will be defined by more than 50% of months in a year when samples had been taken being P. aeruginosa culture-positive (Lee 2004).We previously had used the UK Cystic Fibrosis Trust definition of two or more occasions of P. aeruginosa isolation over six months (UK Cystic Fibrosis Trust 2004); however the definition cited above more closely replicates current clinical practice. In the case of studies including both clinical scenarios or less defined criteria, we shall aimtomanage these separately using a pragmatic approach.

Interventions

beta -carotene supplementation; garlic supplementation; zinc supplementation

Outcome measures

Antibiotic consumption (days iv antibiotics); Antibiotic consumption (days of oral and iv antibiotics); Antibiotic consumption (days oral antibiotics); Days of antibiotic consumption; Mild adverse events; Mortality; Respiratory function (% change FEV1); Respiratory function (FEV1 % predicted); Respiratory function (FVC %predicted)

Main results

We identified 42 trials of which eight (350 participants) that examined antibiotic adjuvant therapies are included. Two further trials are ongoing and five are awaiting classification. The included trials assessed Î²â€•carotene (one trial, 24 participants), garlic (one trial, 34 participants), KB001â€•A (a monoclonal antibody) (two trials, 196 participants), nitric oxide (two trials, 30 participants) and zinc supplementation (two trials, 66 participants). The zinc trials recruited children only, whereas the remaining trials recruited both adults and children. Three trials were located in Europe, one in Asia and four in the USA. Three of the interventions measured our primary outcome of pulmonary exacerbations (Î²â€•carotene, mean difference (MD) â€•8.00 (95% confidence interval (CI) â€•18.78 to 2.78); KB001â€•A, risk ratio (RR) 0.25 (95% CI 0.03 to 2.40); zinc supplementation, RR 1.85 (95% CI 0.65 to 5.26). Î²â€•carotene and KB001â€•A may make little or no difference to the number of exacerbations experienced (lowâ€•quality evidence); whereas, given the moderateâ€•quality evidence we found that zinc probably makes no difference to this outcome. Respiratory function was measured in all of the included trials. Î²â€•carotene and nitric oxide may make little or no difference to forced expiratory volume in one second (FEV1) (lowâ€•quality evidence), whilst garlic probably makes little or no difference to FEV1 (moderateâ€•quality evidence). It is uncertain whether zinc or KB001â€•A improve FEV1 as the certainty of this evidence is very low. Few adverse events were seen across all of the different interventions and the adverse events that were reported were mild or not treatmentâ€•related (quality of the evidence ranged from very low to moderate). One of the trials (169 participants) comparing KB001â€•A and placebo, reported on the time to the next

course of antibiotics; results showed there is probably no difference between groups, HR 1.00 (95% CI 0.69 to 1.45) (moderateâ€•quality evidence). Quality of life was only reported in the two KB001â€•A trials, which demonstrated that there may be little or no difference between KB001â€•A and placebo (lowâ€•quality evidence). Sputum microbiology was measured and reported for the trials of KB001â€•A and nitric oxide (four trials). There was very lowâ€•quality evidence of a numerical reduction in Pseudomonas aeruginosa density with KB001â€•A, but it was not significant. The two trials looking at the effects of nitric oxide reported significant reductions in Staphylococcus aureus and nearâ€•significant reductions in Pseudomonas aeruginosa, but the quality of this evidence is again very low.

Authors' conclusions

We could not identify an antibiotic adjuvant therapy that we could recommend for treating of lung infection in people with cystic fibrosis. The emergence of increasingly resistant bacteria makes the reliance on antibiotics alone challenging for cystic fibrosis teams. There is a need to explore alternative strategies, such as the use of adjuvant therapies. Further research is required to provide future therapeutic options.

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See also

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Keywords

Anti-Bacterial Agents; Bacterial Infections; Infection; pharmacological_intervention; Respiratory Tract Diseases; Respiratory Tract Infections; Colonization; Exacerbation; Pseudomonas aeruginosa; Pseudomonas; Garlic; Zinc; Food; non pharmacological intervention - diet; Minerals; Supplementation; non pharmacological intervention - complement med;