Systematic review of antistaphylococcal antibiotic therapy in cystic fibrosis

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Authors' objectives
To determine the efficacy of antistaphylococcal therapy, as assessed by clinical outcomes, in patients with cystic fibrosis.

Searching
MEDLINE was searched from 1966 to 1995 using a Cochrane Collaboration strategy; EMBASE and MEDLINE Express searches were also conducted. Details of the search strategy were given. Additional material was obtained by examining bibliographies of identified papers and relevant review articles, and by contacting all cystic fibrosis physicians in the UK.

Study selection
Study designs of evaluations included in the review
RCTs, non-randomised non-controlled trials, randomised non-controlled, and randomised controlled crossover trials of antistaphylococcal treatment in cystic fibrosis were included. Duration of RCTs ranged from 2 months to 2 years.

Specific interventions included in the review
The following antibiotics were used either alone or in combination: trimethoprim; sulphamethoxazole; cefadroxil; dicloxacillin; cephalaxin; fluclaxacinil; cloxacillin; ampicillin; amoxycillin (with and without clavulanic acid); penicillin V; erythromycin; cotrimoxazole; cephalosporin; ciprofloxacin; fusidic acid; lincomycin; chloramphenicol; novobiocin; carbenicillin; gentamycin; clindamycin; oxacillin; rifampicin; methicillin; cephuroxime; and macrolide. Drugs were given either continuously or intermittently using oral, intravenous and inhalation administration methods.

Participants included in the review
Patients with cystic fibrosis, including children under the age of 5, were studied.

Outcomes assessed in the review
The following outcomes were assessed in the randomised controlled trials (RCTs): pulmonary function tests, chest radiography score, clearance of Staphylococcal aureus from sputum, cough frequency, respiratory exacerbations, antibiotic courses, erythrocyte sedimentation rate, serum immunoglobulin, weight, height, and hospital admissions.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Studies were combined by a narrative review.
How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Thirteen clinical trials were included, of which 3 were RCTs (91 patients). One of the RCTs was reported as 2 studies with different outcomes on the same population.

Substantial heterogeneity was noted among trials. Nineteen different pharmacological treatments used 11 clinical and 6 laboratory outcome measures in 13 clinical trials. There was a large variation in the clinical outcomes assessed in the 3 RCTs; the only outcomes common to all 3 studies were weight and sputum clearance of S. aureus. The 3 RCTs studied continuous cephalexin versus continuous dicloxacillin (duration 2 months), or continuous versus intermittent therapy with a variety of antibiotics (duration 1 to 2 years). Clearance of S. aureus from sputum: 1 RCT with a maximum of 42 patients reported an increased clearance of S. aureus with continuous flucloxacillin, compared to intermittent use of a variety of antibiotics. One RCT used multiple antibiotics for both treatment arms and was considered to be difficult to interpret. The other RCT compared continuous cephalexin and continuous dicloxacillin and had a short-term follow-up (2 months). All 9 non-randomised trials reporting this outcome showed improved sputum clearance with antistaphylococcal therapy.

There was limited evidence on clinical and pulmonary function.

Authors’ conclusions
Antistaphylococcal treatment achieves sputum clearance of S. aureus in patients with cystic fibrosis. Prophylactic antistaphylococcal treatment in young children with cystic fibrosis is likely to be of benefit. It remains to be determined whether the use of prophylactic versus intermittent antistaphylococcal therapy is associated with improved lung function and/or chest radiography scores, an increase in bacterial resistance, or earlier acquisition of Pseudomonas aeruginosa.

CRD commentary
The aims were stated. Full details of the search strategy were given. A narrative review was appropriate in view of the heterogeneity among studies. Inclusion criteria for studies were not clearly defined and it was unclear whether language restrictions were applied to primary studies. No details were given of the methods used to select primary studies or extract data. Validity was not assessed. More comprehensive details of the included studies would have been helpful, such as criteria used for diagnosis of cystic fibrosis, characteristics of participants, and methods used to ascertain outcomes. Results were not reported clearly, and were classified as ‘positive’ or ‘no difference’ without qualification. The evidence reported was not adequate to assess antistaphylococcal antibiotic therapy in cystic fibrosis. The authors’ conclusion that further research is urgently required was supported by the review.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors consider that a large randomised clinical trial lasting approximately 2 years is urgently required to determine whether the use of prophylactic versus intermittent antistaphylococcal therapy is associated with improved lung function and/or chest radiography scores, an increase in bacterial resistance, or earlier acquisition of Pseudomonas aeruginosa.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.