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[Intervention Review]

Single versus combination intravenous anti-pseudomonal antibiotic therapy for people with cystic fibrosis

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ABSTRACT

Background

Choice of antibiotic, and the use of single or combined therapy are controversial areas in the treatment of respiratory infection due to *Pseudomonas aeruginosa* in cystic fibrosis (CF). Advantages of combination therapy include wider range of modes of action, possible synergy and reduction of resistant organisms; advantages of monotherapy include lower cost, ease of administration and reduction of drug-related toxicity. Current evidence does not provide a clear answer and the use of intravenous antibiotic therapy in cystic fibrosis requires further evaluation. This is an update of a previously published review.

Objectives

To assess the effectiveness of single compared to combination intravenous anti-pseudomonal antibiotic therapy for treating people with cystic fibrosis.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register, comprising references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings.

Most recent search of the Group's Trials Register: 14 October 2016.

Selection criteria

Randomised controlled trials (RCTs) comparing a single intravenous anti-pseudomonal antibiotic with a combination of that antibiotic plus a second anti-pseudomonal antibiotic in people with CF.

Data collection and analysis

Two authors independently assessed trial quality and extracted data.

Main results

We identified 45 trials, of which eight trials (356 participants) comparing a single anti-pseudomonal agent to a combination of the same antibiotic and one other, were included.

There was a wide variation in the individual antibiotics used in each trial. In total, the trials included seven comparisons of a beta-lactam antibiotic (penicillin-related or third generation cephalosporin) with a beta-lactam-aminoglycoside combination and three comparisons of an aminoglycoside with a beta-lactam-aminoglycoside combination. These two groups of trials were analysed as separate subgroups.

There was considerable heterogeneity amongst these trials, leading to difficulties in performing the review and interpreting the results. The meta-analysis did not demonstrate any significant differences between monotherapy and combination therapy, in terms of lung function; symptom scores; adverse effects; and bacteriological outcome measures.

These results should be interpreted cautiously. Six of the included trials were published between 1977 and 1988; these were single-centre trials with flaws in the randomisation process and small sample size. Overall, the methodological quality was poor.

Authors' conclusions

The results of this review are inconclusive. The review raises important methodological issues. There is a need for an RCT which needs to be well-designed in terms of adequate randomisation allocation, blinding, power and long-term follow up. Results need to be standardised to a consistent method of reporting, in order to validate the pooling of results from multiple trials.

PLAIN LANGUAGE SUMMARY

A comparison of single and combined intravenous drug therapy for people with cystic fibrosis infected with *Pseudomonas aeruginosa*

Review question

We reviewed the evidence about the different effects of using a single intravenous (given directly into a vein) antibiotic compared to using a combination of intravenous antibiotics in people with cystic fibrosis infected with *Pseudomonas aeruginosa*.

Background

Cystic fibrosis is a serious genetic disease that affects cells in the exocrine glands (sweat glands and others). People with cystic fibrosis have a greater risk of chronic lung infections, often due to bacteria called *Pseudomonas aeruginosa*. They receive antibiotics, either a single drug or a combination of different drugs, by injection to treat these infections. Both the choice of antibiotic and the use of single or combined therapy vary. We looked for randomised controlled trials which compared a single intravenous antibiotic with a combination of that antibiotic plus another one in people with cystic fibrosis. This is an updated version of the review.

Search date

The evidence is current to: 14 October 2016.

Study characteristics

We included eight trials with a total of 356 people. Six of these were published before 1988, were each based in a single centre and used a range of different drugs. These factors made it difficult to combine and analyse the results.

Key results

We did not find any differences between the two therapies for lung function, symptom scores, side effects or bacteriological outcome measures. We conclude that there is not enough evidence to compare the different therapies. More research is needed, particularly looking at side effects of treatment.

Quality of the evidence

Six of the included trials were quite old (published between 1977 and 1988). They did not include many people and had flaws in the way the people taking part were put into the different treatment groups. Overall, the quality of the trials' design was poor.