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[Intervention Review]

Combination antimicrobial susceptibility testing for acute exacerbations in chronic infection of Pseudomonas aeruginosa in cystic fibrosis

Valerie Waters[1], Felix Ratjen[2]

[1]Department of Pediatrics, Division of Infectious Diseases, Hospital for Sick Children, Toronto, Canada. [2]Department of Pediatrics, The Hospital for Sick Children, Toronto, Canada

Contact address: Valerie Waters, Department of Pediatrics, Division of Infectious Diseases, Hospital for Sick Children, 555 University Avenue, Toronto, ON, M5G 1X8, Canada. valerie.waters@sickkids.ca.

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ABSTRACT

Background

Antibiotic therapy for acute pulmonary exacerbations in people with cystic fibrosis is usually chosen based on the results of antimicrobial susceptibility testing of individual drugs. Combination antimicrobial susceptibility testing assesses the efficacy of drug combinations including two or three antibiotics in vitro and can often demonstrate antimicrobial efficacy against bacterial isolates even when individual antibiotics have little or no effect. Therefore, choosing antibiotics based on combination antimicrobial susceptibility testing could potentially improve response to treatment in people with cystic fibrosis with acute exacerbations. This is an updated version of a previously published review.

Objectives

To compare antibiotic therapy based on conventional antimicrobial susceptibility testing to antibiotic therapy based on combination antimicrobial susceptibility testing in the treatment of acute pulmonary exacerbations in people with cystic fibrosis and chronic infection with *Pseudomonas aeruginosa*.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Cystic Fibrosis Trials Register which comprises of references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. Date of latest search: 19 December 2016.

We also searched ongoing trials registries. Date of latest search: 08 March 2017.

Selection criteria

Randomised and quasi-randomised controlled studies of antibiotic therapy based on conventional antimicrobial susceptibility testing compared to antibiotic therapy based on combination antimicrobial susceptibility testing in the treatment of acute pulmonary exacerbations in cystic fibrosis due to chronic infection with *Pseudomonas aeruginosa.*

Data collection and analysis

Both authors independently selected studies, assessed their quality and extracted data from eligible studies. Additionally, the authors contacted the study investigators to obtain further information.

Main results

The search identified one multicentre study eligible for inclusion in the review. This study prospectively assessed whether the use of multiple combination bactericidal antibiotic testing improved clinical outcomes in participants with acute pulmonary exacerbations of cystic fibrosis who were infected with multiresistant bacteria. A total of 132 participants were randomised in the study. The study investigators provided data specific to the 82 participants who were only infected with *Pseudomonas aeruginosa* for their primary outcome of time until next pulmonary exacerbation. For participants specifically infected with only *Pseudomonas aeruginosa*, the hazard ratio of a subsequent exacerbation was 0.82, favouring the control group (95% confidence interval 0.44 to 1.51) (P = 0.52). No further data for any of this review's outcomes specific to participants infected with *Pseudomonas aeruginosa* were available. The risk of bias for the included study was deemed to be low. The quality of the evidence was moderate for the only outcome providing data solely for individuals with infection due to *Pseudomonas aeruginosa*. For other outcomes, we were unable to judge the quality of the evidence as no data were available for the relevant subset of participants.

Authors' conclusions

The current evidence, limited to one study, shows that there is insufficient evidence to determine effect of choosing antibiotics based on combination antimicrobial susceptibility testing compared to choosing antibiotics based on conventional antimicrobial susceptibility testing in the treatment of acute pulmonary exacerbations in people with cystic fibrosis with chronic *Pseudomonas aeruginosa* infection. A large international and multicentre study is needed to further investigate this issue.

The only study included in the review was published in 2005, and we have not identified any further relevant studies up to March 2017. We therefore do not plan to update this review until new studies are published.

PLAIN LANGUAGE SUMMARY

Testing antibiotics in combination for acute infections of *Pseudomonas aeruginosa* in cystic fibrosis

Review question

We reviewed the evidence about the effect of testing antibiotics in combination for acute airway infections in people with long-term (chronic) infection with *Pseudomonas aeruginosa*.

Background

The main cause of death in people with cystic fibrosis is chronic lung infection. People with cystic fibrosis now live longer due to the aggressive use of antibiotics to treat lung infections. Traditionally, antibiotics are chosen based on the results of laboratory testing of each antibiotic separately against the bacterium (or bug) that is found in the lungs of the person with cystic fibrosis. Antibiotics tested in combination may work effectively against a bacterium even if not effective when tested alone. However, when choosing antibiotics to treat lung infections caused by *Pseudomonas aeruginosa* in people with cystic fibrosis, it is unclear whether basing the choice of antibiotics on the results of combination testing is better than basing choice on the results of testing antibiotics separately.

This is an updated version of a previously published review.

Search date

The evidence is current to: 19 December 2016.

Study characteristics

The search identified one study that tried to answer this question and was eligible for inclusion in the review. The study enrolled 132 people with cystic fibrosis, most of whom (82 people) had acute lung infections with *Pseudomonas aeruginosa*, and randomly put them into two treatment groups. In the first group two antibiotics were selected following the testing of combinations of antibiotics and in the second group the two antibiotics were chosen after testing individual antibiotics to see how effective the drugs were against the bacterium. The study was run across several centres and assessed the clinical outcomes in the participants after a 14-day course of treatment.

Key results

The study investigators were only able to provide us with data for those who were infected with *Pseudomonas aeruginosa* for their main outcome (the time until the next acute lung infection). Choosing antibiotics based on the results of combination antibiotic testing did not lead to a longer time until the next lung infection compared to choosing antibiotics based on results of separate testing. They could not provide us with any results people infected with *Pseudomonas aeruginosa* for other outcomes in our review.

Quality of the evidence

We are satisfied that the people taking part were divided into the different treatment groups completely at random and no one could have foreseen which group any individual would be in. We are also satisfied that during the study, neither the individuals or clinic personnel

knew which treatment group each individual was in. There were no missing data from the study. The quality of the evidence for the only outcome for which we have data (time to the next lung infection) is moderate, but we could not judge the quality of the evidence for other outcomes as there were no separate results available for people infected with *Pseudomonas aeruginosa*.