Title: THE FATE OF INHALED ANTIBIOTICS AFTER DEPOSITION IN CYSTIC FIBROSIS: HOW TO GET DRUG TO THE BUG?

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What was your research question? How do the local conditions in the airways of people with cystic fibrosis (CF) influence the effectiveness of antibiotics after inhalation?

Why is this important? In people with CF chronic (long-lasting) airway infections are an important factor in progressive lung disease. These chronic infections are most often treated with inhaled antibiotics. How inhaled antibiotics are deposited within the lung has been extensively studied. However, the journey of inhaled antibiotic particles does not end after they have been deposited within the airways; but continues through thick sputum layers and slime generated by the bacteria. What happens to antibiotic particles after being deposited in the airways of people with CF and how local conditions affect the clinical effectiveness of different types of inhaled antibiotics is not well described.

What did you do? We systematically searched in the available literature for relevant articles related to our research question. We included all studies describing the effect of CF sputum on antibiotic effectiveness or describing the effect of bacterial factors on antibiotic effectiveness. We also included studies on formulations of antibiotics that might increase effectiveness. The results of the included studies were combined to describe what is known about the effectiveness of inhaled antibiotics after they have been deposited in the airways.
What did you find?
Out of 2669 articles that were screened by 2 researchers, 35 articles were included in this review. Unfortunately, none of the studies described research in humans, but most studies were performed in laboratories. These studies showed that many factors in CF sputum can reduce the effectiveness of inhaled antibiotics in the airways of people with CF. For example; the slime layer surrounding bacteria in the lungs has a negative impact on the effectiveness of inhaled antibiotics. Some available drugs, like dornase alfa and mannitol, might be able to improve the local effectiveness of inhaled antibiotics.

What does this mean and reasons for caution?
To be able to kill bacteria, an antibiotic needs to overcome the barriers in CF sputum and slime layer surrounding bacteria. Higher concentrations of inhaled antibiotics may allow more antibiotic particles to reach the bacteria. More research in people with CF is required to establish the effect of higher doses of inhaled antibiotics and the effect of combining this inhalation with other drugs to improve the penetration of the inhaled antibiotic into the sputum and slime.

What’s next?
For people with CF, the next step would be to study if higher doses of inhaled antibiotics, combined with other drugs are more effective in treating lung infections.

Original manuscript citation in PubMed
N/A 13 November 2016