



Cystic Fibrosis Research News

Title:

Impact of azithromycin on the clinical and antimicrobial effectiveness of tobramycin in the treatment of cystic fibrosis

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What was your research question?

Our goal with this study was to determine if individuals with CF who take a preventative dose of oral azithromycin have more beneficial results when paired with one of two inhaled antibiotics – aztreonam or tobramycin. Additionally, we wanted to determine if azithromycin affected the ability of either antibiotic to kill the germ *Pseudomonas aeruginosa*, a significant problem in CF.

Why is this important?

We estimate that up to half of the CF patient population in the US will be prescribed azithromycin and inhaled tobramycin at the same time. If azithromycin is found to reduce the beneficial impact of tobramycin, then this practice may need to be revised.

What did you do?

We reanalysed data from a completed clinical trial in which participants received 4 weeks of inhaled tobramycin immediately followed by 4 weeks of inhaled aztreonam. We evaluated

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how well these antibiotics worked during the study for participants who were regularly taking oral azithromycin. Germs such as *P. aeruginosa* can develop abilities to counter the antibiotics used in treatment, known as 'antibiotic resistance'. So we also tested in the laboratory whether or not the addition of azithromycin to the antibiotic treatment can cause *P. aeruginosa* to develop antibiotic resistance. Finally, we investigated how azithromycin affected the ability of *P. aeruginosa* to resist tobramycin therapy in patients.

What did you find?

We found that participants in the trial who listed azithromycin as one of their routine preventative medications typically observed less benefit from inhaled tobramycin compared to inhaled aztreonam. Adding azithromycin to the cultures of *P. aeruginosa* in the laboratory also reduced the ability of tobramycin to kill this germ. This undesirable effect was not observed when adding azithromycin to cultures with several other antibiotics commonly used to treat people with CF. Exposing *P. aeruginosa* to azithromycin increased the ability of the germ to survive exposure to tobramycin and this may explain how combining these two common therapies can be problematic for some individuals.

What does this mean and reasons for caution?

Our findings add to previous studies with similar results and suggest that the common practice of recommending oral azithromycin in conjunction with tobramycin may be less effective than originally anticipated. However, the approach of our study and prior studies that assessed azithromycin treatment in humans has been to re-analyse data from already completed research studies, that were conducted to test different questions (*i.e. post-hoc* analysis). So whilst our research in the laboratory showed azithromycin can make bacteria more resistant to tobramycin, which is an important step toward explaining how this unexpected drug interaction may occur, new research studies involving humans and designed to specifically test the effect of azithromycin in the clinic are necessary. Until then the evidence is not strong enough to recommend a change in clinical practice.

What's next?

A clinical trial is underway to address the potential drug interaction between azithromycin and inhaled tobramycin. The results of this ongoing study in people with CF should allow us to determine with greater confidence whether these two drugs are effective when used in combination or if they may work better when used separately.



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