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Cystic Fibrosis Research News

Title:

Pharmacokinetics of oral antimycobacterials and dosing guidance for *Mycobacterium avium* complex treatment in cystic fibrosis

Lay Title:

Drug levels and dosing recommendations for antibiotics used to treat *Mycobacterium avium* complex in people with cystic fibrosis.

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What was your research question?

Azithromycin, ethambutol, and rifampin are common oral antibiotics used to treat lung infections caused by *Mycobacterium avium* complex bacteria. We wondered whether people with cystic fibrosis (CF) absorb and breakdown these antibiotics differently when taken with or without food and digestive enzymes and compared to people without CF.

Why is this important?

Mycobacterium avium complex are drug-resistant bacteria that can lead to long-term lung infections and a worsening of disease in people with CF. Despite treating these infections with multiple antibiotics over a long period of time (months to years), in many people these bacteria remain in their lungs. One possible reason for these treatment failures are low drug levels. Research has already shown that people with CF have different levels of other antibiotics compared to people who don't have CF. We wanted to see whether levels of

azithromycin, ethambutol and rifampin are low in people with CF and to help develop dosing guidelines to better treat *Mycobacterium avium* complex infections.

What did you do?

People with CF and people without CF took part in the study. They did *not* have *Mycobacterium* infection, to avoid partially treating an infection. People with CF were tested at two different times, once after taking the antibiotics on an empty stomach, and again after taking the antibiotics with digestive (pancreatic) enzymes and food. People without CF were tested just once after taking the antibiotics on an empty stomach. We measured drug levels after they took a single dose of the three antibiotics: azithromycin, ethambutol, and rifampin.

What did you find?

Levels of ethambutol were similar between people with CF and people without CF while azithromycin levels were slightly higher and rifampin levels were low in people with CF. Taking these antibiotics with food and enzymes did not improve drug levels in people with CF. While differences were found, we could not see a consistent pattern among people with CF. Our findings suggest that standard dosing of these antibiotics should be given to people with CF and drug levels should be checked in people with CF being treated for *Mycobacterium avium* complex infections to make sure levels are in the normal range.

What does this mean and reasons for caution?

Although current guidelines recommend that drug level monitoring be reserved for people experiencing treatment failure, our results suggest that drug levels should be monitored for all people with CF being treated for *Mycobacterium avium* complex to prevent the possibility of treatment failing due to drug levels not being high enough.

What's next?

Our results could be useful for doctors treating people with CF with *Mycobacterium avium* complex lung infections. We are currently performing a study to test drug levels in a larger group of people with CF actively being treated for *Mycobacterium avium* complex lung disease.

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