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Cystic Fibrosis Research News

Title:

Long-term azithromycin use is not associated with QT prolongation in children with cystic fibrosis

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What was your research question?

Chronic use of azithromycin is a common treatment for lung infection. We investigate whether chronic use of azithromycin increased the risk of unwanted events in heart and/or blood vessels in children. The study period was longer than previously studied: 18 months of continuous, 3-times weekly use of azithromycin.

Why is this important?

Among adults at risk of heart disease, azithromycin use has been previously associated with increased risk for harm. Harm from azithromycin use has been identified in two ways: 1) as an increase in the QT interval (an interval of time used to assess healthy heart rhythms) and 2) as development of a cardiac arrythmia called torsades des pointes. When we began our study in 2014, there had been no evidence of harm from azithromycin use on heart rhythms in children.

What did you do?

We conducted a secondary evaluation of a completed clinical trial in children with cystic fibrosis. The study tested whether azithromycin reduced the risk of pulmonary exacerbations (a clinical worsening) in children with a new *Pseudomonas aeruginosa* infection. Participants were randomly assigned to take either azithromycin or placebo 3-times-weekly for up to 18 months. They underwent heart rhythm measurement via electrocardiogram at study enrollment, and then after 3 weeks and 18 months of participation. The randomized study ended early after about a third of participants had completed the planned 18 months of participation, when azithromycin was found to be very effective at reducing pulmonary

exacerbations; and after that time most participants took azithromycin for the remainder of the study period.

What did you find?

Among 221 study participants with a median of 18 months follow-up, no persons experienced abnormally high QT intervals (defined as longer than 500 milliseconds). However, 10 persons experienced a QT prolongation, or an abnormal rise in the QT interval (defined as an increase of at least 30 milliseconds relative to at a previous visit): 3 of these persons were taking azithromycin at the time, and 7 of these persons were taking placebo tablets. The occurrence of QT prolongation was not found to be more frequent among those taking azithromycin.

What does this mean and reasons for caution?

We found no evidence of cardiovascular harm in children with cystic fibrosis taking 3-times-weekly azithromycin for up to 18 consecutive months. During much of our study, participants were required to pause azithromycin use if QT-prolonging drugs were needed. Therefore, few other drugs known to cause QT-prolongation were taken simultaneously with azithromycin. Relatedly, only 17% of persons took cystic fibrosis modulator therapy during the study.

What's next?

Chronic use of azithromycin in children with cystic fibrosis should not be considered to increase risk of cardiovascular harm in the absence of other medications that can prolong QT; but it should continue to be evaluated for safety when it is taken in combination with other therapies.

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