Title: Azithromycin and Tezacaftor/Ivacaftor is associated with first-degree heart block in an adult with Cystic Fibrosis

Authors: Yang Song 1,2, Alexandra Coronel Palacios 1,2, Aravinda Thiagalingam 3,4, Peter G Middleton 1,2,4

Affiliations:  
1 Department of Respiratory and Sleep Medicine, Westmead Hospital, NSW  
2 Ludwig Engel Centre for Respiratory Research, The Westmead Institute of Medical Research, NSW  
3 Department of Cardiology, Westmead Hospital, NSW  
4 Sydney Medical School, University of Sydney at Westmead Hospital, NSW

What was your research question?  
We present a case report of a subject who experienced a rare heart complication associated with the combination of azithromycin and tezacaftor/ivacaftor. The complication was first degree heart block, where the electrical impulse from the atria at the top of the heart was delayed in transmission to the ventricles at the bottom of the heart.

Why is this important?  
This highlights the importance of heart monitoring in long term follow-up of people with CF taking this combination therapy as leaving this condition untreated could cause more severe cases of heart block. Furthermore, ECGs are not routinely performed as part of standard of care.

What did you do?  
Consistent monitoring of subject’s ECG throughout her time on combination therapy of azithromycin and tezacaftor/ivacaftor. In addition, the tezacaftor/ivacaftor was ceased for 6 months and her heart block returned to normal. Then she recommenced tezacaftor/ivacaftor and remained well for the first 9 months. After this she developed heart block again. This time the azithromycin was ceased and the tezacaftor/ivacaftor continued. The heart block again resolved. The person has remained on tezacaftor/ivacaftor, but not azithromycin, without any issues.
What did you find?
Taking either medication alone was not associated with heart block. Only the combination of azithromycin and tezacaftor/ivacaftor caused heart block. The important changes in her electrocardiogram (ECG) only became evident after 8 months of combination treatment. Whilst the subject felt perfectly well, her ECG showed heart block. The subject again remained well for the first 9 months but then started to develop heart block again. We have other patients on this combination who have not developed any heart block.

What does this mean and reasons for caution?
This case shows that neither azithromycin nor the tezacaftor/ivacaftor alone would cause heart block but the combination was associated with changes in the ECG.

What’s next?
ECG monitoring for people with CF on this combination therapy should be considered.

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