New Treatment for Asthma - Frankly Speaking EP 46

Transcript Details

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Dr. Frank Domino:

Aaron is a 19-year-old college student who has persistent asthma. He is currently on budesonide and formoterol, two puffs twice a day, and uses albuterol on a PRN basis. Despite this, he continues to have symptoms three to four times a week that require use of his rescue inhaler. He is not waking up during the night with asthma symptoms and describes that his asthma only bothers him a little bit during the day with activities. He has previously had an allergy evaluation and there is no obvious trigger to his asthma. Recently, a friend on Facebook sent him a link to a story about People's Pharmacy using azithromycin for hard-to-treat asthma. He asked you today if this would help. How do you respond? Joining me today is Dr Alan Ehrlich, Clinical Associate Professor in the Department of Family Medicine and Community Health at the University of Massachusetts Medical School, and Executive Editor at DynaMed. Welcome to the show, Alan.

Dr. Alan Ehrlich:

Thanks, Frank.

Dr. Domino:

So Aaron's got pretty significant asthma. What are his treatment options at this point and how do we classify his asthma?

Dr. Ehrlich:

Aaron's having symptoms three to four times a week and that would qualify him as having

persistent asthma. He doesn't really have a lot of problems with nighttime awakenings and there's only a limited impact on his functioning, but he still is symptomatic despite the use of long-term controller medications. He's classified as persistent asthma. And additional add-on options, there's quite a variety at this point, now that he's using controller medications. One option would be to consider giving him some type of anti-leukotriene medication such as montelukast or zafirlukast. He also could be given a medication like tiotropium, that would add to the long-term bronchodilation. There are the IGE and IL5 monoclonal antibodies, but those are reserved usually for people who have very specific identified allergic etiologies, and that's not really the case with him. And then, finally, there's still people who might use theophylline or things like that, but for him, probably the most likely next step would be just to give him a higher dose of his inhaled corticosteroid.

Dr. Domino:

Yeah, he's got pretty significant asthma. He's still having three to four episodes a week where he needs assistance, and he's already on both an inhaled corticosteroid, and a long-acting beta agonist. What does this new study tell us about using azithromycin for patients with moderate to persistent asthma?

Dr. Ehrlich:

This is the AMAZES trial that was published recently. And in the AMAZES trial, what they did was they... This was for adults of 18 or over who... They had 420 who had persistent asthma, and they were all on an inhaled corticosteroid, and some type of long-acting bronchodilator, and they were randomized to azithromycin, 500 mg three times a week, or placebo, and then followed for almost a year. What they found was that in the group that was treated with azithromycin, they had a significant decrease in the number of acute exacerbations, and they also had improvement in asthma quality of life scale. This is a little surprising, but again, the basis for it is that macrolides, azithromycin in particular, have anti-inflammatory properties. There's some evidence that they may have some anti-viral properties, and so there may be any number of ways in which it's acting to prevent these flare-ups.

The difference between the two groups, in the group that got azithromycin, they were averaging about one exacerbation per year, and these are exacerbations that require you to go to the emergency room, or get put on a short course of corticosteroids. And in the group that had placebo, it was closer to about 1.8 per person a year, so about half. And they also analyzed it along the basis of how many patients had at least one exacerbation, and that was 44% in the group with the azithromycin, and 61% in the placebo group.

Dr. Domino:

So maybe a 15% absolute risk reduction?

Dr. Ehrlich:

Yeah.

Dr. Domino:

That's significant, but you know me, I'm always cynical about chronic use of antibiotics. What were the downsides of using azithromycin, 500 mg three times a week?

Dr. Ehrlich:

This won't surprise too many people. Diarrhea was the most common side effect and that was significantly greater with the azithromycin. Other than that, there weren't any clinical adverse effects between the two groups. There was some suggestion on testing that maybe there was some anti-microbial resistance building up in the normal bacteria that were being cultured, but at a clinical level, there wasn't any other difference. That being said, they did exclude from the trial anyone who had a hearing loss, or who had prolonged QT intervals, because azithromycin can aggravate both of those conditions, or can cause ototoxicity, and so this is not meant that it can be used willy-nilly with anyone. In fact, actually, Frank, the reality is, this is something, because of the potential for problems with antibiotics, that probably should only be used after you've tried most other things.

Dr. Domino:

Well, I was going to ask you, is if you had this patient in your practice, he's already taking an inhaled corticosteroid, a long-acting beta agonist, using PRN rescue inhalers, what would you do? Would you increase the dose of his corticosteroid? Would you try another agent? Where should we be placing azithromycin chronically in our step-wise care of this patient?

Dr. Ehrlich:

I would definitely increase this patient's inhaled corticosteroid dose as the next step, and then I probably would go with something like tiotropium or montelukast as the next add-on therapy. I think that you really want to use this in a very select group where you really have tried most other things first.

Dr. Domino:

So a little bit about an acute exacerbation in this patient. Let's say he's on your azithromycin and he's been pretty controlled, but he comes in febrile, short of breath, wheezing. What would you use to treat him, in particular, in the form of an antibiotic?

Dr. Ehrlich:

For the majority of patients who have acute asthma exacerbation, even if they've got a fever, I'm not going to use an antibiotic. Most of those are caused by viruses. The use of azithromycin had previously been looked at in that setting in the AZALEA trial and they found no benefit. Now, the proponents of using azithromycin all the time will tell you that, while the study was underpowered, and maybe if we had a bigger study, we might find some benefit. But at least to date, there's been no benefit shown for the use of azithromycin in acute asthma exacerbations, unless you have proven pneumonia. Just the fact that someone's wheezing, or they're short of breath, and they have a fever doesn't mean that azithromycin or any other antibiotic is going to be helpful.

Dr. Domino:

Well, Alan, thank you so much for helping put this study in its place in our armamentarium. I

think we've heard a bit about it, but we didn't realize that using azithromycin chronically was something that was possibly third or fourth choice down the line. Additionally, hearing about the AZALEA trial really reminds us all that antibiotic resistance is increasing and we have to be very, very careful in how we use these medications.

Dr. Ehrlich:

Thanks, Frank.

Dr. Domino:

Practice pointer: Adding azithromycin to your current regimen for a patient with persistent asthma may be helpful, but likely only after you have maximized other methods of care. And remember, use of azithromycin in an acute exacerbation of asthma is only beneficial when you have clinical findings, and/or X-ray findings consistent with pneumonia. Join us next time where we will be discussing the new varicella-zoster vaccine for the prevention of shingles.