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Chronic Care Challenges with Cystic Fibrosis

Narrator:

Welcome to the ReachMD activity: *Chronic Care Challenges with Cystic Fibrosis.* This segment is sponsored by Prova Education. Your host is Dr. Barry Mennen, who welcomes Dr. Peter Mogayzel, Professor of Pediatrics. Vice Chair for Pediatric Health System coordination, the Director of the Cystic Fibrosis Center and Medical Director of the Pediatric Specialty Clinic at Johns Hopkins Cystic Fibrosis Center in Baltimore, Maryland. Prior to beginning the activity please be sure to review the goals of this educational activity, or if you are listening to this as a podcast, go to this activity on ReachMD.com/Prova, on your computer, Smartphone, or tablet device.

Dr. Mennen:

We will be discussing the etiology of pulmonary disease in cystic fibrosis, the role of CFTR modulator therapy in its treatment, and the relationship between lung function and the nutritional status in CF. You are listening to ReachMD, and I am your host, Dr. Barry Mennen. Dr. Mogayzel, welcome to ReachMD.

Dr. Mogayzel:

Thank you for having me.

Dr. Mennen:

Our pleasure. Let's start off with describing the effects of cystic fibrosis on the lungs.

Dr. Mogayzel:

So, cystic fibrosis is a disease that causes problems with salt going in and out of cells, so it leads to abnormal mucus that blocks the small airways in the lungs and leads to obstruction. This is combined with a defect in mucociliary clearance which causes infections to develop in the lungs when bacteria can't be cleared properly. The ongoing infection and inflammation leads to destruction of the lung over time and a loss of lung function.

Dr. Mennen:

So, infection plays an important role in the progression of lung disease in CF. Can infection be prevented?

Dr. Mogayzel:

You are right, infection plays a very important role. We work very hard to instruct people on infection control, to try to prevent exposure

to bacteria in the environment, but everyone with cystic fibrosis eventually becomes colonized with certain bacteria. Some bacteria are more problematic than others. Pseudomonas aeruginosa is a bacteria that is often associated with a more rapid decline in lung function, so we see patients routinely in clinic, do throat or sputum cultures to identify what bacteria might be there and we find infections such as pseudomonas aeruginosa, we treat with inhaled or oral antibiotics to try to eradicate that therapy and push off colonization. Eventually everyone does become colonized with some bacteria and in the case of pseudomonas aeruginosa, that's when the transition is made to using chronic antibiotic therapy, typically inhaled antibiotics, to suppress the infection and minimize inflammation.

Dr. Mennen:

So, can you describe the challenges that patients face in trying to reach this goal of being infection-free or at least having the infection modulated down?

Dr. Mogayzel:

The goal in all therapy for cystic fibrosis lung disease is to try to minimize the decline in lung function that happens in CF patients. So all of us have a decline in our lung function naturally as we age, and in cystic fibrosis this just happens faster because of the ongoing inflammation and infection in the lungs. So we ask patients to, on a routine basis, do airway clearance with either manual percussion or high frequency chest oscillation of a device that you wear, a vest that you wear that inflates and shakes the chest to mobilize the mucus or other devices to help mobilize mucus and keep the lungs as free of excess mucus as possible. In addition, we ask patients often to use mucolytic therapies and nebulize therapies that would thin out the mucus, dornase alpha or hypertonic saline, for example, and this allows more mucus clearance and, hopefully, less obstruction. That, in addition with the antibiotics as I mentioned earlier, hopefully will prevent the decline of lung function. The difficulty is, is this is a very time consuming regimen, often taking 30 minutes to an hour twice a day when people are healthy and more frequently needs to be used when they are not. So, adherence is a significant challenge for people because of the time commitment involved.

Dr. Mennen:

Now, there are new therapies available that affect the basic defect of CF. How do these fit into the current treatment of cystic fibrosis?

Dr. Mogayzel:

There are several new drugs that have been developed over the past few years that treat the underlying defect in cystic fibrosis. As I mentioned earlier, the problem in cystic fibrosis is that salt doesn't go in and out of cells the way it should normally, and that's because there is a defect in a chloride channel called CFTR. The new drugs known as CFTR modulators actually work at the basic defect. They fix, to some extent, the function of the CFTR protein and they allow chloride transport to be reinstituted in the cells, thereby getting at the basic problem, rehydrating the mucus and hopefully preventing the downstream symptoms of infection and airway obstruction.

Dr. Mennen:

Now, could you talk about the various CFTR mutations and their incidence?

Dr. Mogayzel:

Understanding CFTR mutations is very important. These new therapies, the CFTR modulators are directed at particular problems with the cell and the way CFTR is abnormal in certain cases and this is based on the mutations. CFTR mutations can lead to different problems at a cellular level that all result in cystic fibrosis but affects CFTR differently and, therefore, the modulator drugs, these new oral medications, only work for people with certain mutations. Cystic fibrosis mutations that are identified through genetic testing, through blood screening and there have been over two thousand mutations found at this point. Not all of them cause cystic fibrosis, but many of them lead to significant disease but they can be grouped into certain categories. I think you can think of them in three broad groups. One group is where the CFTR is never made, it never is produced at all. Another group is where the CFTR is made but

doesn't get to the cell surface, and a third group is where the CFTR is made, it gets to the cell surface and it just doesn't work the way it is supposed to. So the drugs that are available right now are to treat the CFTR defect, that basic problem in cystic fibrosis, or ivacaftor, and ivacaftor treats certain mutations where the CFTR is made and gets to the cell surface, and those are known as Class 3, 4 and 5 mutations, if you look at a more detailed diagram of the molecular biology. That's about 10 percent of the people with cystic fibrosis. The other drug that is now available is a combination of ivacaftor and lumacaftor. That combination drug is a combination of one medication, lumacaftor that gets abnormal CFTR to the cell surface, combined with ivacaftor that will activate it. So that medication works for people where the CFTR is made, but it doesn't get to the surface. So one component helps it get to the surface, the other component then activates it. That works for the people that have a particular mutation known as F508del. It's the most common mutation in cystic fibrosis, and if you have two copies of that then, this medication is effective and that is about 50 percent of the population. There are, however, a number of people that don't have these mutations and there are drugs under development for those as well.

Dr. Mennen:

But based on what you said about 60 percent of CF patients can be handled by these drugs?

Dr. Mogayzel:

Yes, right now about 60 percent of people with cystic fibrosis have the opportunity to use these drugs and they have been shown to be safe and effective. In the case of ivacaftor, down to children 2 and older. The problem with these drugs, although they are very effective, they don't reverse damage. So people that have damage to their lungs, who have bronchiectasis or scarring from this chronic infection and inflammation that's been going on for some time, that scarring and bronchiectasis won't be reversed. That's why it is so important to use the other therapies that I spoke about earlier to try to minimize lung damage and preserve lung function over time, so when newer therapies become available that really do treat the basic defect, the best advantage can be obtained from those drugs, and really, the ultimate goal is to have these sorts of drugs available right at diagnosis when we diagnosis people in infancy.

Dr. Mennen:

Excellent discussion, thank you. Now, are there other aspects of CF care that are important to lung health?

Dr. Mogayzel:

There are. We talked a lot about medications and therapies for the lungs themselves. We know other aspects of CF impact lung disease. So about 80 percent of patients with cystic fibrosis are pancreatic insufficient, meaning they don't make pancreatic enzymes. This is for the same reason that there is problems in the lungs; in the pancreatic duct there isn't CFTR, therefore there is obstruction of those ducts early in life, often times in utero that leads to pancreatic insufficiency. So it is very difficult for patients to gain weight because of that, because of high calorie needs and because of a number of other issues that can develop over time with complications of cystic fibrosis and medication use like as use of steroids and the complication of diabetes that can develop. But we know that people that have better BMIs, whose body mass index is closer to normal, or closer to what the average person would be, have better lung function. So, therefore, it is very important that nutrition be considered a pulmonary therapy. We work very hard to help patients to understand the importance of nutrition and to be able to work with them to gain weight and be able to have an optimum nutrition status as well.

Dr. Mennen:

Now, as you mentioned earlier, the therapies required by families to preserve lung function create a tremendous burden for people with cystic fibrosis. What are some of the practical suggestions that you might give the families to lighten this burden?

Dr. Mogayzel:

You are absolutely right. There is a tremendous burden for therapy. As I mentioned earlier, we ask patients to perform airway clearance twice a day for 20 to 30 minutes. We oftentimes prescribe nebulized therapies that can take an additional 15 to 30 minutes twice a day, and that's when people are healthy and don't have additional symptoms. When they are sick they oftentimes have to perform these therapies more often. So part of our strategy is to work with families to identify barriers to adherence. Time is obviously the biggest barrier with the idea that if you can work these therapies into a routine from diagnosis and make it part of daily living, to try to strategize around other activities because we don't want to have cystic fibrosis be the burden that doesn't allow children or adults to participate in regular activities, to prevent them from going to school, or playing sports or having a job. So it really does depend a lot on working on an individual basis to figure out strategies for fitting all of them in to a, what we hope is going to be, a normal lifestyle.

The other aspect is to make sure that this doesn't create a financial burden for families and to help families have the opportunity or the resources to be able to have all the therapies they need and all the nutritional supplements they may need to really lead a healthy life.

Dr. Mennen:

Well, Dr. Mogayzel, any final thoughts?

Dr. Mogayzel:

I think that this is a very hopeful time for people with cystic fibrosis. This is a time where we have therapies that have been proven to extend people's lives and we are at the cusp of having therapies that really treat the basic defect. So when I talk to new families with children with cystic fibrosis, I am very positive in the way I approach this, saying, "This really is a time where your child is going to do much better than people in the past and where we really have the opportunity to change the disease itself."

Dr. Mennen:

Dr. Mogayzel, thank you so much for joining us today.

Dr. Mogayzel:

Thank you.

Dr. Mennen:

I am your host, Dr. Barry Mennen for ReachMD.

Narrator:

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