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## Rationale for Performing Airway Clearance for Patients with Cystic Fibrosis

Narrator:

Welcome to CME on ReachMD. This segment: Rationale for Performing Airway Clearance for Patients with CF, is sponsored by Prova Education. Your host is Dr. Jennifer Caudle, who welcomes Dr. Robert Zanni, Section Chief of Pediatric Pulmonary Medicine; and, Director of the Cystic Fibrosis Center at Unterberg Children's Hospital at Monmouth Medical Center in Long Branch, New Jersey. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements, as well as the learning objectives, or if you're listening to this as a podcast, go to this activity on ReachMD.com/Prova on your computer, Smartphone, or tablet device.

Dr. Caudle:

Airway clearance is the primary therapy for patients with cystic fibrosis. Today, we will discuss the rationale for performing airway clearance, as well as current mechanical and pharmacologic choices for patients. We will also discuss airway clearance therapies that are making their way through the pipeline. You're listening to CME on ReachMD, and I'm your host, Dr. Jennifer Caudle. Dr. Robert Zanni, welcome to ReachMD.

Dr. Zanni:

Thank you very much, Jennifer.

Dr. Caudle:

Let's start off with understanding what is the primary rationale for performing airway clearance in patients with cystic fibrosis?

Dr. Zanni:

Cystic fibrosis is a genetic disease, caused by the mutation of the cystic fibrosis transmembrane regulator gene, we often call that the CFTR gene, and that creates a dysfunctional protein, which leads to abnormal salt and fluid transport in many organs, and that's especially marked in the lungs and the digestive system. So, I would say that CF is characterized by dehydration of airway surface liquid. The airway secretions become viscid and thick and this ultimately impairs mucociliary clearance, and then the clearance of airway secretions has been a primary therapy for those with cystic fibrosis, and a variety of airway clearance therapies have been developed to achieve mobilization of the viscous secretions out of the airways.

Dr. Caudle:

So, if untreated or poorly treated, what are the ultimate clinical consequences in the cystic fibrosis lung?

Dr. Zanni:

Well, the thick secretions within the airways cause impairment of mucociliary clearance, which leads to chronic infection and neutrophil-predominant airway inflammation. Structural damage of the airways caused by the chronic infection and inflammation ultimately leads to bronchiectasis. Chronic infection with staph aureus, and that can be methicillin-sensitive staph aureus or methicillin-resistant S. aureus, and pseudomonas organisms predominantly infect the airways and are not cleared by the natural defense mechanisms of the lung. So, in essence, this vicious cycle of impaired airway clearance, chronic infection, and chronic inflammation lead to the progressive lung damage and chronic respiratory failure that we see in endstage disease in cystic fibrosis.

Dr. Caudle:

Dr. Zanni, what are the mechanical therapy choices for patients?

Dr. Zanni:

There's various therapies which exist for patients in CF, primarily to begin with, I would like to just talk about the chest physiotherapy which, historically, has been the gold standard for airway clearance and, as you know, this includes therapies such as postural drainage, percussion and vibration on the chest to mobilize secretions. But over the past 3 decades, various devices have been developed, and those have been made to improve on the concept of chest physiotherapy, and I will discuss these by categories, if you will.

The first category would be the high frequency chest wall oscillation techniques. The examples of these are the various vest garment devices, which basically cause the vibration technique on the chest wall to mobilize secretion.

The second group of devices are incorporated under the positive expiratory pressure therapies, or PEP therapies, and this is a technique where patients breathe against the resistance, which causes an increase in back pressure in the airways, which will help mobilize secretions throughout the airways. An example of this is the device called TheraPEP®. Now, there have been improvements on that particular type of therapy, called oscillatory PEP therapy, so basically, this is PEP therapy, but now in this wave-like form or oscillation form, which enters the airways and helps mobilize secretions. Examples of these have been the Acapella® device or the flutter device, and now there is further advancements on that particular concept, utilizing the old concept of IPPB or intrapulmonary positive pressure breathing. These devices are called intrapulmonary percussive ventilation devices. Examples of these are the MetaNeb® or the Percussionaire® devices, again, which causes oscillatory movement of air into the airways, causing pressure, which helps mobilize secretions out of the airways.

Another technique is acoustical wave therapy, which utilizes different frequencies on the chest wall; these are frequencies of sound waves, and they will help mobilize secretions within the airways. Examples of that particular therapy are the Frequencer™ device and then there is the Vibr Lung® device, which has recently become available for patients.

And then there are non-device-oriented therapies, which are taught therapies; I call these breathing techniques. We utilize our respiratory therapists and our physical therapists to teach patients how, number one, to cough effectively. The huff cough is a common example of that particular type of maneuver. And then, there are more involved types of therapies called autogenic drainage or active cycle of breathing. Again, you need experts in those areas to help teach patients those techniques, but they're quite effective and they don't need devices to mobilize secretions, they do it all on their own.

And I'll end with the last piece of this, and that is aerobic exercise. It is very helpful as adjunct therapy to airway clearance therapies. So, although, by itself it is probably not enough to mobilize the large content of secretions, but certainly in conjunction with, or as an adjunct therapy to all the therapies I've mentioned previously, exercise can be a great help to patients.

Dr. Caudle:

Thank you for that overview. Now, can you review the pharmacologic choices?

Dr. Zanni:

Discussing this, I would say that it's important to know that these are used in conjunction with many of the forms of airway clearance that I've previously mentioned. So, this is an adjunct therapy to airway clearance, and the types of therapies that we routinely use come under the headings of bronchodilators, something that is inhaled to help mobilize secretions. There is also dornase alfa, which is a mucolytic agent, which will liquefy the secretions and help patients expectorate the secretions more efficiently. There is hypertonic saline, anywhere from 3 to 7% of saline, as a hydrator of the thick mucus to help mobilize secretions. I would also include in this inhaled antibiotics, since patients are chronically infected, although these are not necessarily mechanisms that are going to mobilize secretions. In essence, if you think about that vicious cycle that I talked about before, if we can help control the chronic infections, we can, in essence, hopefully interrupt the inflammatory response that the bacteria causes.

And ultimately, on the forefront are some of the new modulation therapies which restores CFTR function. These therapies are based on patient's underlying genetics. The two products that have come available recently have been ivacaftor and a combination of lumacaftor and ivacaftor. Again, these will help restore the CFTR function in patients, which will interrupt this cycle of increased secretions in patients.

Dr. Caudle:

Finally, can you share with us what's in the clinical research pipeline that may improve airway clearance?

Dr. Zanni:

Well, I think that this is the most exciting part of what we have coming into the future of CF care, and that is the research that continues

to move forward in terms of improvements, even in this particular one specific area. So, for mucociliary clearance, there is an agent that is in Phase 3 trials called inhaled mannitol, which will be another component to help hydrate secretions and hopefully the trials will show that this will be an additional therapeutic agent that patients can use to enhance the movement of mucus out of the airways. There's the area of antiinflammatory therapies. We've had ibuprofen for years that has shown, in studies that were done years ago, that it can decrease the inflammatory response in the airways, and there is additional products that are in the pipeline right now that will be utilized in patients, hopefully, if it shows true in the clinical trials that it has efficacy, that we would have more agents to use that decrease the inflammatory response.

Again, the most exciting area of this is the explosion of the modulation therapies that are on the horizon that will restore CFTR function. So, as I mentioned before, we have two agents already. There are two additional agents that are in Phase 3 trials; there's the VX-661 and the ataluren product, which will be specific for patients with the particular mutations. So we're getting to the basic defect of CF and, hopefully, that will be the agents that will ultimately turn off the inflammatory response and the infection response and the increased mucus production response.

Dr. Caudle:

Dr. Robert Zanni, thank you for joining us today and sharing your insights on airway clearance for patients with cystic fibrosis and their treatment options.

Dr. Zanni:

Great, thank you.

Dr. Caudle:

I'm your host, Dr. Jennifer Caudle for ReachMD.

Narrator:

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