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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Meeting the Needs of Uncontrolled Asthma Patients

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This series is produced in partnership with the American College of CHEST Physicians. Today's podcast will focus on unmet need in uncontrolled asthma.

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And, here is your host Dr. Xavier Soler, who is an Associate Professor of Medicine at University of California, San Diego. And, a respiratory medical expert in US medical affairs at GlaxoSmithKline.

Dr. Soler:
Even with a timely diagnosis of asthma and good adherence to standard therapy, a significant number of patients remain symptomatic or uncontrolled while being treated. It is important to recognize those patients because of the potential severe consequences impacting the quality of life or even death[1]. Currently, there is a lack of awareness of uncontrolled or symptomatic patients[2]. But how and why does this happen? And what else can we offer our patients to turn things around when it does?

Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Xavier Soler, and joining me today is Dr. Nick Hanania, Associate Professor of Pulmonary Medicine and Director of the Airway Clinical Research Center at Baylor College of Medicine in Houston, Texas. Together we'll be discussing the unmet needs of patients with uncontrolled asthma.

Dr. Hanania, welcome to the program.

Dr. Hanania:
Thanks, Dr. Soler, for having me. It's a pleasure.

Dr. Soler:
Just to start us off, can you give us a brief snapshot on how effective standard therapies with inhaled corticosteroids, ICS, and long-acting beta agonists, LABAs, have been for asthma patients?

Dr. Hanania:
Well, Xavier, about a quarter of patients with asthma are estimated to be receiving inhaled steroid/long-acting beta agonist therapy in combination[3]. We have several of those available. In fact, when you look at the GINA step 4 and 5, these are the patients who are on ICS/LABA[4]. Almost 25% of the total asthmatics fall in this category[3], but about a quarter of those patients remain uncontrolled despite the fact that they're taking or at least we know they're on these agents[5-7]. Among those, about 3–5% have severe asthma[4]. So it is an unmet need where we have good drugs but still see patients who continue to be uncontrolled despite being prescribed these agents.

Dr. Soler:
So, with that being said, what are the factors into this uncontrolled asthma despite being on these ICS, inhaled corticosteroids, and long-acting beta agonist therapy? What are your thoughts on that?

Dr. Hanania:
Well, I'm glad, Xavier, you're bringing this up, because one thing I want my colleagues who are listening to understand is that asthma is a bit complex. The fact that patients are prescribed ICS/LABA does not, first of all, mean they have asthma, but it also doesn't mean

that they're taking the drug, or if they're taking it correctly.

There is a checklist which I go through. One is: Am I dealing with an asthmatic? Because the fact that a patient is prescribed ICS/LABA does not automatically make him or her an asthma patient, so we have to confirm the diagnosis and also rule out mimickers of the diagnosis or other diagnoses that may actually complicate the course of the disease. Second is: Is the patient taking their inhaler? I mean, it's very well-known in any chronic disease, but particularly in asthma, that adherence problem exists, both intentional and nonintentional. Patients may forget to take their inhalers, but some patients are worried about it; they don't believe that the drug is helping, so they intentionally don't take it. The third and very important step is to make sure the patient is taking their inhaler correctly[4]. Of course, there are other issues. One is exposure to triggers and continuous comorbidities like GERD and upper airway disease, rhinitis, sinusitis, psychosocial issues. All these have to be treated to achieve control. It's not enough to give the drug and expect the patient to get better, so we have to minimize triggers.

Now, having looked at all these, if a patient is adherent, the morbidities and triggers are dealt with, he or she knows how to use the inhaler device and it's confirmed asthma and they still are uncontrolled, that's when you start scratching your head and saying, "Okay, what else can I offer them?"

Dr. Soler:
Yes, I think that what you said is extremely important because reviewing the managing cycle to reassure the patients are taking the medications, consider alternate diagnoses, the patient owning the disease and the treatment, and being sure that he/she is engaged in the conversation is extremely important for treatment success[4]. So, when you have considered that in your clinics, are there any other treatment strategies available for patients with uncontrolled asthma?

Dr. Hanania:
Of course. The nice thing about it is that over the last few years we've had a plethora of new medications for asthma and different delivery systems. Obviously, inhaled steroids remain the backbone in treatment of uncontrolled disease, so if the patient is taking their inhaled steroid, you might want to reassess the dose and see if increasing the dose may be helpful. Sometimes you double-up the inhaled steroid dose[4]. It may not work all the time, and there are pros and cons of doing this. Obviously, exposure to steroids can have systemic effects over time, but that's one thing you can look at. The other option is adding other therapies on top of the inhaled steroid. And we all agree inhaled steroids should be there as a platform. Adding a leukotriene modifier, an oral agent, especially if they have upper airway disease, may be helpful in some patients with asthma—not in all. Adding another bronchodilator and long-acting antimuscarinic agent, as an add-on in GINA step 4 and 5 in addition to ICS LABA[4].

Obviously, there are others. If the patients continue to have symptoms, then you need to phenotype them and decide, "Do I need a biologic?[4]" And that's another step forward where it's a big step, but it is an important one. If a patient continues to have severe disease, then one of the biologics available—if he or she is a candidate—can be entertained. And then there are other options, maybe not for everyone, but using chronic azithromycin therapy in those with recurrent exacerbation, and then bronchoscopic approaches like bronchial thermoplasty[4].

Obviously, we sometimes seek advice from our allergy colleagues. Looking at allergen desensitization is something that can be helpful in patients with significant upper airway disease, and that may actually help control the asthma in some patients[4]. So there are options there, and it's not just a magic bullet. Sometimes it's a trial and see how the patient responds to these agents, and sometimes more than one option can be used at the same time.

Dr. Soler:
For those joining us, this is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Xavier Soler, and today I'm speaking with Dr. Nick Hanania about improving our recognition and treatment approaches for uncontrolled asthma.

So, Nick, you just mentioned some additional therapies available to help these patients. Let's focus on a long-acting muscarinic agent for a moment since it is a relatively new player in the therapeutic landscape. What do we need to know about this treatment?

Dr. Hanania:
Well, Xavier, the bronchodilators are very important in managing asthma[4]. We know that short-acting agents like beta agonists are used for rescue, and long-acting beta agonists have been used for a while now as add-on therapies to inhaled steroid, but more recently we've gone back to looking at anticholinergic agents, particularly tiotropium bromide, which was tested in large clinical trials in asthma as add-on therapy. Now, the importance of anticholinergics in general is actually historic. If you remember, anticholinergics were first used for treatment of asthma many years ago, were actually smoked in cigarettes that contain atropine leaves. Atropine was used many years ago[8], but obviously it's not the best. More recently the role of anticholinergics in asthma has emerged, and these agents

have been used for many years in COPD and partly because they target smooth muscle and they can relax the smooth muscles[9].

The pathophysiology of asthma is complex. It's not just airway inflammation, but bronchoconstriction is important[4], and smooth muscles are controlled by both beta 2 receptor, and so that's why beta 2 agonists work[10]; but also, the muscarinic receptors and the anticholinergic blocks mainly the M3 receptor on the smooth muscle, so it does cause bronchodilation, and thus, as add-on to ICS LABA, it may have a beneficial effect based on clinical trials[4], both in improving lung function and reducing exacerbations. It's not something new in a way historically, but certainly the role of long-acting antimuscarinic agents is emerging right now in asthma. They may have other roles, such as effect on mucociliary clearance, but that needs to be further evaluated[11]. Currently, we believe the main role is the bronchodilation.

The biggest homework we have as clinicians is to decide, "Okay, who would respond to one or the other bronchodilator?" And when we add bronchodilators, of course both groups can be used together, but also, there may be some subgroup of patients that may respond more to an anticholinergic agent versus another group that would respond to a beta agonist[12], and I think that needs to be worked up in future studies.

Dr. Soler:
Absolutely, I couldn't agree more. So, before we close, Nick, let's look ahead to some of the developments in the research arena. Is there anything up and coming that you are excited about that help address our current needs?

Dr. Hanania:
I think as a clinician and a researcher I would like to identify subgroups who would best benefit from an anticholinergic agent as an add-on therapy. Is it all asthmatics? As we know, asthma does not have one face, and there are multiple phenotypes and even endotypes[4]. And these are bronchodilators, so they may work in all phenotypes, but we don't know. I think that's a big important question.

I like to have a more personalized approach to therapy in asthma, and certainly, I'd like to use the best drug for the patient who would respond. The other thing is we want long-term studies with anticholinergics in asthma and see if there's any effect on decline in lung function. It's something that we know asthmatics have. Whether they smoke or whether they don't, the lung function declines with time[4], and we have no idea what happens if they're treated with a long-acting anticholinergic like tiotropium. And eventually we would like to see the role or the effect of combination therapies—is there a beneficial effect when you combine more than one group of bronchodilator in these patients with an inhaled corticosteroid, which is the backbone of therapy. I think these are some of the things that I'm looking forward to seeing or at least studying in the future so that we can have a more precise approach for this problem.

Dr. Soler:
Thank you very much, Nick, for giving us where we are going with addressing the current needs for uncontrolled or difficult-to-control asthma. Clearly, these are exciting directions to look forward to, but for now, I want to thank my guest, Dr. Nick Hanania, for joining me today. Dr. Hanania, it was great having you on the program.

Dr. Hanania:
Dr. Soler, it was great to chat with you. Thank you for having me.

Announcer:
This was *Deep Breaths: Updates from CHEST* produced in partnership with the American College of Chest Physicians. To access other episodes of this series, visit ReachMD.com/CHEST, where you can be part of the knowledge. Thanks for listening!

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