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Latest Treatment Guidelines for Uncontrolled Asthma

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And, here is your host Dr. Tom Corbridge, who is an Emeritus physician and Adjunct Professor of Medicine at Northwestern in Chicago, IL. And, a respiratory medical expert in US medical affairs at GlaxoSmithKline.

Dr. Corbridge:
Uncontrolled asthma represents a tremendous burden for our patients and society resulting in reduced quality of life, increased emergency department visits, missed days at work and school, and US healthcare costs of more than $80 billion per year, but there are ways we can help alleviate this burden, and today we're going to dive into treatment strategies that can help.[1]

Hello, my name is Tom Corbridge, and this is Deep Breaths on ReachMD. Joining me today to discuss new and emerging treatments for uncontrolled asthma is a friend and colleague, Dr. Matt Hegewald. Matt is a pulmonary and critical care physician at Intermountain Medical Center and Associate Professor of Medicine at the University of Utah.

Matt, welcome to the program.

Dr. Hegewald:
Thank you, Dr. Corbridge. I'm looking forward to an interesting discussion.

Dr. Corbridge:
Me too. So, Matt, just to start off, could you just walk us through kind of the available treatment options that we have for patients with uncontrolled asthma?

Dr. Hegewald:
Well, first, let's define uncontrolled asthma. Asthma control is assessed in 2 domains. Number one, symptom control, and number 2, risk, which includes the risk of future adverse outcomes, primarily exacerbations, but also physiologic worsening, such as progressive reduction in lung function over time.[2] Symptom control can be assessed in many different ways, including the asthma control test, which I think is probably most likely used by physicians in the United States, and also the Asthma Control Questionnaire, and both of these are well-validated tools for assessing asthma control.

The GINA 2020 guidelines define asthma symptom control based on 4 key questions, which are also components of the Asthma Control Test and Asthma Control Questionnaire.[2] So these questions are: In the last 4 weeks, has the patient had, first of all, daytime daily symptoms more than twice a week? Second, any nighttime awakenings due to asthma? Third, short-acting beta agonist reliever use for symptoms more than twice a week? And fourth, any activity limitation due to asthma? So, if none of these are present, the patient is considered to be well-controlled. If 1 or 2 of these are present, the patient is partly controlled. And if 3 or 4 are present, the patient is deemed to be uncontrolled. In addition to symptoms, control is assessed by exacerbation frequency, and the goal of that is none, and lung function with a goal of FEV1 greater than the lower limit of normal or generally 80 percent of predicted.

So, before we discuss treatment options for asthma control, we need to, first of all, assess asthma control based on those domains of symptoms and risk; second, address comorbidities, inhaler technique and adherence; and then third, the GINA guidelines use a stepwise approach to asthma management.[2] We'll focus on step 3, which are patients that are treated with a low-dose ICS and LABA, long-acting beta agonist. So, if patients are not controlled with step 3, the next step is step 4, patients treated with medium-dose ICS-LABA with the additional option of a long-acting muscarinic antagonist, a LAMA, or also a leukotriene receptor antagonist, and then step 5, which are patients treated with high-dose ICS-LABA. And if those patients are not well-controlled with that regimen, the next choices include adding a LAMA or a biologic agent that targets T2 inflammation.

Dr. Corbridge:
Thank you for that review, Matt. I really like how you started with reminding us to do our due diligence in clinic to understand where patients truly are because I think when you do that, we all realize that patients may not be as good as we think they are and that we have work to do to achieve asthma control, so thank you.

I wanted to talk a little bit more about the parasympathetic nervous system. It's often overlooked, and we know that the parasympathetic nervous system plays an important role in asthma[3], and you've mentioned a long-acting muscarinic receptor antagonist, or LAMA. Can you tell us a little bit more about those, particularly their mechanism of action, how they work?

Dr. Hegewald:
Yes, so the airways are innervated by postganglionic, parasympathetic, cholinergic nerves that release acetylcholine that regulates airway smooth muscle tone and bronchoconstriction in conjunction with the sympathetic nervous system.[3] The parasympathetic nervous system dysfunction is well-established in asthma and is manifested as improved lung function with administration of anticholinergic medications, and the parasympathetic nervous system also contributes significantly to the increased diurnal variability in lung function that occurs with everyone but is more pronounced in patients with asthma and increased airway hyperresponsiveness after viral respiratory infections and allergen exposures.[3,4,5] The bronchoconstriction associated with parasympathetic innervation of the airway is mainly mediated by the effects of acetylcholine binding to M3 receptor on the airway smooth muscle.[3] The available inhaled anticholinergic medications have high affinity and long receptor binding kinetics on the M3 receptor on airway smooth muscle resulting in smooth muscle relaxation through competitive inhibition of the M3 receptor.[3,6]

Dr. Corbridge:
Great. Well, thank you for that review. If I bring it back to the Global Initiative for Asthma or GINA strategy that you mentioned, they have positioned LAMA therapy for adolescents and adults with asthma.[2] And just remind us again where that recommendation fits in the current treatment paradigm.

Dr. Hegewald:
Yes, so to review again, the goal of asthma therapy is two-fold.[2] One is symptom control, and two is the risk reduction including exacerbations, lung function, side effects and medication side effects. So the GINA 2020 strategy recommends the stepwise approach to asthma management. And where does LAMA fit in? Well, as part of step 4, LAMA is an option for add-on therapy to medium-dose ICS-LABA, and step 5, LAMA is an option as an add-on therapy to high-dose ICS-LABA combination.

Dr. Corbridge:
For those just joining us, this is Deep Breaths on ReachMD. I'm Dr. Tom Corbridge, and I'm speaking with Dr. Matt Hegewald about new and emerging treatments for uncontrolled asthma.

So, Matt, let's continue our discussion of LAMA in the management of asthma, and the next question that I'd like to ask you is, do we actually have data about the benefit of adding LAMA to patients receiving medium dose in step 4 versus high-dose ICS-LABAs?

Dr. Hegewald:
Yes, so we have multiple phase 3 studies that have shown significant improvement in FEV1 when adding a LAMA to both medium-dose ICS-LABA and high-dose ICS-LABA.[2] Also, there are generally positive effects on asthma symptoms and exacerbations with adding LAMA to both of these groups of patients treated with medium-dose ICS-LABA and high-dose ICS-LABA.[2,7]

Dr. Corbridge:
It's good to see. And then kind of switching gears to a topic that certainly is of current interest is what do we know about LAMA in patients with type 2 versus non-type 2 asthma? That is type 2 high versus type 2 low asthma. Is LAMA therapy effective, certainly when added to ICS-LABAs, for both of these phenotypes?

Dr. Hegewald:

Yes, that's an excellent question. First of all, T2-low asthma is often not considered when we are talking about the asthma treatment approaches. So, T2-low asthma phenotype is characterized by being less responsive to inhaled corticosteroids, often times associated with neutrophilic inflammation—these patients are often older, obese, and have smoking history—whereas T2-high asthma phenotype is characterized by atopic features, responsiveness to inhaled corticosteroids, eosinophilic inflammation, high blood eosinophils and high FE(NO)—that's exhaled nitric oxide—and younger age.[8,9] We have good evidence that LAMA added to an ICS-LABA combination reduces the risk of exacerbations requiring systemic steroids and asthma worsening and improves lung function and asthma symptoms independent of IgE levels, blood eosinophil level and clinical judgment of allergic asthma, so we know that adding a LAMA to ICS-LABA is effective for both T2-high and T2-low asthma phenotypes, which I think is an important point for clinicians to remember.[10]

Dr. Corbridge:
Right, so it's nice to have LAMA add-on to ICS-LABA as an option, both in the T2-low asthma phenotype but even in the T2-high asthma patients who remain symptomatic as a viable option. So, before we wrap up, Matt, do you have any other kind of thoughts or take-home points that you'd like to leave with the audience before we part?

Dr. Hegewald:
Yes, I think the key points are that a personalized asthma management approach is best, so we shouldn't use a "cookie cutter" approach and treat every patient the same. Second, we want to make sure we assess control based on those 2 domains of symptoms and risk.[2] And then third, adjust medication treatment with the goal of achieving control. We've discussed the place of LAMA in the management of asthma. This treatment is underappreciated by both specialists and primary care providers. And then, finally, we need to review the response to therapy, to review responses to changes in therapy and then make further changes accordingly.

Dr. Corbridge:
Great. Well, that is a great way to round out our discussion today, and I really want to thank my guest, Dr. Matt Hegewald, for joining me to discuss recommended treatments for patients with uncontrolled asthma.

Matt, it was absolutely great having you on the program today. Thank you.

Dr. Hegewald:
Thanks for including me.

Announcer:
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