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

Optimizing Delivery with LAMAs: A Look at Key Considerations & Clinical Data

Announcer:
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Your host is Dr. Muhammad Adrish, Associate Professor of Pulmonary Critical Care at Baylor College of Medicine.

Dr. Adrish:
Inhalers are one of the most common methods of delivery for treatment of COPD. But for some patients, they may not be the most optimal delivery method. Nebulized long-acting muscarinic agents, or in short, LAMAs, may work better for specific patient populations, and on today's program, we'll dive into this delivery option and look at what you need to know.

Welcome to *Deep Breaths: Update from CHEST* on ReachMD. I am Dr. Muhammad Adrish and joining me to discuss research and considerations for LAMA use among specific patient population is Dr. Navitha Ramesh. Dr. Ramesh is assistant professor at Drexel University College of Medicine, and Pulmonary and Critical Care physician and ICU Medical Director at UPMC Central PA, in Harrisburg, Pennsylvania.

Dr. Ramesh, welcome to the program.

Dr. Ramesh:
Hello, Dr. Adrish. Thank you so much for having me here.

Dr. Adrish:
Well, let's begin with some background on two primary LAMAs, glycopyrrolate and revefenacin. Dr. Ramesh, can you share some of the emerging clinical data on these nebulized solutions, and what do we need to know about their safety and efficacy? Let's start with glycopyrrolate.

Dr. Ramesh:
Sure, Dr. Adrish. As you mentioned before, these nebulized LAMAs are recommended for patients with moderate to severe COPD, and there are two types of nebulized LAMAs that are currently available. And we'll start with glycopyrrolate. So glycopyrrolate is a twice daily administered, nebulized LAMA. It's administered via a mesh nebulizer machine, and it was approved by USFDA in 2017 for the maintenance treatment of COPD. So, these background studies that led to the approval of this medication are called the GOLDEN studies, which basically are Glycopyrrolate for Obstructive Lung Disease via Electronic Nebulizer. The GOLDEN-3 and the GOLDEN-4 studies are 12-week, phase 3 trials, which showed that glycopyrrolate significantly improved FEV1 when compared with placebo, and the incidence of the adverse events was lowest among patients who were treated with glycopyrrolate, 25 micrograms twice daily, in both these phase 3 trials.

And the adverse events with the use of glycopyrrolate was not higher than that of placebo. Following these 12-week trials, a longer, 48-week safety study, which is the GOLDEN-5 study, was conducted, to look at the incidence of overall serious adverse events while using glycopyrrolate when compared with tiotropium, which was used as the control medication, and it was noted that the adverse events with glycopyrrolate were not any higher than the controller medication as well.

Dr. Adrish:
Thanks for sharing those points. And what can you share with us regarding revefenacin?

Dr. Ramesh:
So revefenacin again is a nebulized LAMA. The difference is revefenacin is a once daily use, inhalational solution, and it is administered via a standard jet nebulizer machine. This was approved by US FDA, for the maintenance treatment of COPD, in 2018. And similar to the glycopyrrolate studies, there were two phase 2 – phase 3 clinical trials, which were 12-week trials, which showed that revefenacin significantly improved the FEV1, when compared to a placebo. And this study again looked at the adverse events, and there was not a significant increase in adverse events related to revefenacin use, and this was, again, followed by a longer study for 52 weeks which showed that revefenacin was well-tolerated, and it had a safety profile that supported its long-term use in patients with COPD. And it was also not associated with any adverse cardiac events, more than the controller medication, which, again, was tiotropium in this study.

Dr. Adrish:
Thank you, Dr. Ramesh. That was a great summary of the current evidence on the use of nebulized glycopyrrolate and revefenacin. With that background in mind, let's dive into nebulized LAMA usage.

Dr. Ramesh, in your experience, which patient populations are the ideal candidates for this method of delivery?

Dr. Ramesh:
When you look at COPD, Dr. Adrish, as you well know, that inhaled medications are first-line or standard of therapy for patients with COPD. And these inhaled medications can be given via nebulizers or via handheld inhalers. When you look at the handheld inhalers, there are various types, such as a dry powder inhaler, pressurized metered-dose inhalers, or even soft mist inhalers. So, there are certain patient population who are unable to use these handheld inhalers. They include patients who have some cognitive or neuromuscular defects or ventilatory impairments, and also those who have a suboptimal peak inspiratory flow, in order to get the maximal benefits from the handheld inhalers. Such patients, who don't have the hand-breath coordination, such as those with arthritis, musculoskeletal conditions or neurological conditions, who don't have the grip strength or the dexterity to use the handheld inhalers, they are the ones that are best-suited to use the nebulized LAMAs. And the cool thing now is that the nebulizer machines are much quieter, and we have more portable nebulizer machines available, that makes the usage of these nebulized LAMAs a little bit more exciting for our patients.

Dr. Adrish:
So when you determine that your patient is going to be started on one of these nebulized therapies, how do you approach that transition? How do you get them from an inhaler to the nebulizer?

Dr. Ramesh:
Great question, Dr. Adrish. Based on the current evidence, it suggests that the efficacy of treatment, whether you administer these medications via nebulizers or via metered-dose inhalers or dry powder with the proper technique, the efficacy is the same between the two. But the key here is the proper technique. Before you transition a patient from an inhaler to a nebulizer medication, the first point is this the accurate patient population who will benefit from nebulized medication. The second point will be, is this nebulized medication covered by their insurance plan. And then, given the intricacies of the usage of these nebulized medications, it's very important to educate our patients on how to use them.

Dr. Adrish:
Educate and follow up. Very nicely said, Dr. Ramesh. For those just tuning in, you are listening to ReachMD. I'm Dr. Muhammad Adrish, and today I'm speaking with Dr. Navitha Ramesh about nebulized LAMA for patients with COPD.

Now that we have some background on nebulized LAMAs, and which patients might benefit from these medications, let's explore some of the safety considerations. So Dr. Ramesh, once one of your patients begins nebulized LAMA therapy, what do they need to be aware of?

Dr. Ramesh:
Sure, Dr. Adrish. When we say "nebulized LAMA," again going back to there are two types of nebulized LAMA medications – the nebulized glycopyrrolate and the nebulized revefenacin. For the nebulized glycopyrrolate, there are some specifics for this medication. So it has to be administered via a specific nebulizer machine. So once you prescribe this medication to your patients, they get a starter pack with the nebulizer supplies, as well as the medication, as well as an instructional video and instructional pamphlets for these patients. The setting up of this nebulizer machine is very important, and it's well-explained in the starter kit. The thing with glycopyrrolate, again, is we are not supposed to be combining any medications with glycopyrrolate, so this nebulizer uses only glycopyrrolate, and no other medication. And the nebulizer machine needs to be cleaned after every use, so the patients need to be educated on all this. I just want to mention that when we are using nebulized revefenacin there's a little bit of difference because revefenacin can be used with a standard jet nebulizer. It does not need a specific nebulizer machine like glycopyrrolate, so any jet nebulizer can be used while using revefenacin. And there are recent studies coming out with the combination of LAMA-LABA, where

they have looked at using revefenacin along with formoterol as a LAMA-LABA combination, or one after the other in some patients with COPD. So more to come in the future in that space, so it's good to keep that in mind – the difference between the nebulizer usage with glycopyrrolate and revefenacin.

Dr. Adrish:
These are really great points. So the patients need to know how these devices work, and that they cannot combine their other nebulizer medications with this device, and these devices need to be cleaned regularly. What are some of the strategies that we can use to counsel and consult patients regarding the side effects of these medications?

Dr. Ramesh:
Every medication comes with side effects, so it's always important to educate our patients. The first one that I always tell my patients is, sometimes these nebulized LAMAs can cause paradoxical bronchospasm. We don't expect them to cause bronchospasm, but that's why it's called paradoxical. If a patient experiences bronchospasm while using a nebulized LAMA, they should stop using the medication immediately. They should use a short-acting beta agonist, such as albuterol, and reach out to their physician as soon as possible.

The next side effect is, these medications can theoretically precipitate narrow-angled glaucoma. So while using these medications, if they have some blurriness of vision, some pain in the eyes, it's good to keep an eye out for that, and reach out to their provider as soon as possible. And also, in some patients who have bladder outlet obstruction, or they have prostatic hyperplasia – so they need to be aware that the nebulized LAMAs can cause urinary retention. Other than these three adverse events the other one is hypersensitivity reaction, so if a patient develops any kind of hypersensitivity reaction while using these nebulized LAMAs, they should again stop using it and reach out to their physician right away.

Dr. Adrish:
Prior to starting these LAMAs on any of our patients we really need to take good history and ask about any eye problems or any urinary bladder problems prior to starting these medications. Before we close, Dr. Ramesh, do you have any final takeaways you would like to share with our audience?

Dr. Ramesh:
Sure, Dr. Adrish. Inhaled LAMA medications are relatively safe especially in the specific patient population with moderate to severe COPD. So it's very important to identify the patient population, and also to educate the patients based on the inhaled LAMAs the usage, and what kind of nebulizer machines we use, how do we clean those machines. It's very important to educate our patients with that. And also, it's very exciting that this space is just going to grow in the future, considering that COPD is a significant cause of chronic morbidity and mortality, and it's actually predicted to become the third leading cause of death worldwide by 2030. Better disease control is of utmost importance for all our patients.

Dr. Adrish:
You have some great points, Dr. Ramesh. I'm sure our listeners will find this information very useful. And with those considerations in mind, I want to thank my guest, Dr. Navitha Ramesh, for helping us better understand these nebulized LAMAs and sharing key considerations for their use among patients with COPD, and also sharing her personal experience with this medication.

Dr. Ramesh, it was a great pleasure speaking to you today.

Dr. Ramesh:
Thank you very much, Dr. Adrish. Pleasure talking to you, too.

Dr. Adrish:
I'm Dr. Muhammad Adrish and thank you for listening.

Announcer:
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