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Nebulized Therapy in COPD: Patient Selection, Regimens, and Adherence

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, and this episode is a non-promotional, non-CME educational program brought to you by CHEST and supported by Viatris. And now, here's your host, Dr. Samridhi Gulati.

Dr. Gulati:
This is *Deep Breaths: Updates from CHEST* on ReachMD. I am Dr. Samridhi Gulati, pulmonologist and critical care medicine specialist at University of Wisconsin Health. Joining me to discuss nebulization in chronic obstructive pulmonary disease, or COPD, care are Dr. Raghav Gupta and Chelsea Bernard.

Dr. Gupta is a pulmonary and critical care physician and COPD Medical Director at Deaconess Hospital in Evansville, Indiana. He also serves as Adjunct Clinical Assistant Professor at Indiana University School of Medicine Evansville. Dr. Gupta, welcome to the program.

Dr. Gupta:
Thanks, Samridhi. Really glad to be here.

Dr. Gulati:
And Chelsea Bernard is a pulmonary and critical care medicine nurse practitioner at University of Wisconsin Health. Chelsea, thanks for being here today.

Chelsea Bernard:
Thank you for having me.

Dr. Gulati:
To start, Dr. Gupta, when we think about nebulization, many of us still associate it primarily with acute exacerbations, but the maintenance treatment landscape has evolved. What does the evidence tell us about nebulizers compared with handheld inhalers when technique is optimal, and what has changed in our therapeutic options?

Dr. Gupta:
GOLD treats the nebulizers as a legitimate delivery choice when the patient cannot use a handheld device effectively due to low inspiratory flow, impaired cognition, poor dexterity, or frailty.

There are two drugs to lead with. First, ensifentrine. This is the biggest news in COPD in two decades. Approved by FDA in June 2024, it is the first inhaled therapy that combines bronchodilator and non-steroidal anti-inflammatory action in a single molecule: a dual PDE3 and PDE4 inhibitor. PDE3 relaxes airway smooth muscle. PDE4 calms the inflammatory cells. It comes nebulized three milligrams twice daily.

The phase 3 ENHANCE-1 and ENHANCE-2 trials met their primary lung function endpoint. The trial did not enrich for frequent exacerbators. They actually excluded patients with recent hospitalizations or steroid-treated exacerbations. And yet the pooled analysis showed a 41 percent reduction in the rate of moderate-to-severe exacerbations, with a number needed to treat of just over six to prevent one exacerbation per year.

There was also a 2025 post-hoc analysis from the CHEST meeting showing that even patients without exacerbations during the trial had meaningful improvements in breathlessness and quality of life.

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So this is not just an exacerbation drug. GOLD now positions ensifentrine as an add-on option for patients who have maximized standard therapy and still carry significant disease burden.

Second, revefenacin. Approved back in 2018, this is the first once-daily nebulized LAMA—175 micrograms via a standard jet nebulizer. It uses a soft drug design, metabolically labile, so it clears rapidly from the systemic circulation after leaving the lung. High lung selectivity means few classic anticholinergic side effects. In the phase 3 program, FEV1 improved by about 145 milliliters over placebo at day 85, and 52-week data showed sustained benefit.

What I find most useful clinically is that in patients with suboptimal peak inspiratory flow rate and severe airflow limitation—the exact patients who cannot use a dry powder inhaler—revefenacin has showed efficacy comparable to or better than tiotropium. Honest caveat, it has never been evaluated for exacerbation reduction, and at roughly 1,000 dollars a month, it often needs prior authorization.

So when I judge these drugs, I look past the lung function numbers to three things: exacerbations, symptoms, quality of life, and whether the patient can actually get and use the drug every day. Nebulizers are not the clunky machines of 2005. Vibrating mesh nebulizers are whisper quiet—under 35 decibels—and finish a dose in five to eight minutes versus 10 to 15 with old jet compressors, with very low residual volume. They're handheld, portable, and battery powered. That changes the patient conversation.

And we are entering the connected era. These are devices that track adherence and treatment delivery, data we never had with a compressor and a plastic cup.

Dr. Gulati:
I'd like to talk about patients and clinical scenarios where I most often find nebulization to be the right fit. For me, honestly, the central question is not simply which inhaler versus nebulizer I should prescribe. It is, can this patient reliably get the medicine into the lungs?

We sometimes label a patient as having refractory symptoms or escalate their therapy without first checking whether the drug is being delivered effectively. There are a few groups where nebulization becomes particularly valuable. The first is patients with severe airflow obstruction, hyperinflation, or reduced inspiratory muscle strength, particularly following an exacerbation. The second group includes patients with physical or cognitive limitations. And the third group I pay particular attention to is patients transitioning out of the hospital.

What I appreciate about nebulization is that it allows medication delivery during tidal breathing without requiring the same degree of coordination or inspiratory effort. Of course, nebulization isn't necessarily superior to handheld inhalers when those inhalers are used correctly. But it can be a much more practical option for selected patients. The key point is that device selection should be individualized and reassessed over time rather than treated as one-time decision.

Chelsea, I'd like to turn to you now, because you see these patients day to day, and you're often the one who works through the device selection with them. So what does your assessment look like when choosing a delivery method for an individual patient? What factors, such as inspiratory capacity, inhaler technique, dexterity, cognition, or patient preference carry the most weight? And how do you bring the patient into that decision?

Chelsea Bernard:
Dr. Gulati, in terms of choosing—or as I do more often, following up on a delivery method—it depends on the individual. I typically start my visit by assessing symptom burden and exacerbation history.

Then I assess if their inhaler provides symptomatic benefit. And always, even if it does provide benefit, their technique is assessed. I also assess their dexterity and their strength. Say, for instance, they are on a dry powder inhaler. Can they take a fast, forceful, deep breath? If they can, I ask them to show me. If not, a metered dose inhaler may be a better option for them. However, with a metered dose inhaler, coordination is crucial. Can they time their deep breath with the actuation? If not, we can discuss a spacer.

For patients that have concerns for increasing dyspnea, exercise limitations, and frequent exacerbations, I will generally transition them to a metered dose inhaler, or we will start talking about nebulized bronchodilators. This can be a sign of low peak inspiratory flow rate. We can assess this by having them do a peak flow rate in the clinic. If they have a peak flow rate that is less than 10 or 20 liters per minute, it is a good indication that they need to be on a nebulizer.

Other things that can cause people to have a low peak inspiratory flow are if they are elderly, have a short stature—particularly women of short stature—if they have a low forced vital capacity, severe airflow limitation, hyperinflation, or neuromuscular disease, or it's directly after an exacerbation or hospitalization.

For patients with cognitive impairment, we can discuss a metered dose inhaler with a mask or a spacer without a mask. For nebulizers, we can discuss if they feel that this is the best option for them in terms of time. Nebulized therapies can be time-consuming and are not

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always the best option for patients if they are still working or if they do not have the insurance to cover some of the nebulized therapies that we would recommend for them.

Dr. Gulati:
For those just tuning in, you're listening to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Samridhi Gulati, and I'm speaking with Dr. Raghav Gupta and Chelsea Bernard about optimizing nebulization in COPD management.

Dr. Gupta, I'll come back to you now. Once you have determined that nebulization is the right choice for a patient, how do you build the overall treatment regimen, keeping potential barriers in mind and setting the patient up for good adherence once they leave hospital or your clinic?

Dr. Gupta:
I think it's very crucial how we build the overall treatment regimen, keeping barriers in mind and setting the patient up for good adherence. Regimen design is pattern matching the drug to the patient and to real life, replacing entirely when the handheld cannot be fixed. If I have coached techniques three times, switched device types, and the patient still cannot generate adequate inspiratory flow or keeps making critical errors, stop negotiating with the device and change the platform.

Use full nebulized maintenance—for example, once-daily revefenacin as the LAMA backbone. Combine when each device covers a different territory. A common hybrid nebulized maintenance at home—where adherence is highest—could be revefenacin or ensifentrine twice daily with a handheld rescue inhaler for travel. Or use the mirror image: keep the handheld triple therapy the patient uses well and add a nebulized agent for the problem it does not solve, like ensifentrine as add-on for symptom burden despite maximum therapy.

And start with the phenotype. If we see frequent exacerbators with eosinophilic signals, these are biologic conversations. We have subQ injections like dupilumab and mepolizumab, and the inhalers we already know, which are steroid inhalers.

And think about the day. Twice-daily nebulization is roughly 10 to 15 minutes of treatment time a day with a mesh device. That's actually less than some patients spend on four separate inhalers with technique rituals. But schedule burden is real for working patients, and so the once-daily option has a simplicity advantage worth discussing with the patient.

How do I judge whether it is working? I use symptoms first, like CAT score, dyspnea scale, and rescue use. Exacerbations would be my second. And third would be the burden of the disease. Is the patient actually doing the treatments? A regimen the patient will not do is not a regimen. Here is something I use in the clinic. After a hospitalization, the patient's inspiratory flow is often at its worst, exactly when we hand them back the same dry powder inhaler that did not work before the admission. The post-exacerbation transition is the single highest yield moment to reconsider the delivery device, not just the drugs.

Dr. Gulati:
That's a really good point, Dr. Gupta. I think you've summed it up really beautifully. We sometimes underestimate the practical burden of COPD treatment. Patients may already be managing oxygen, multiple medications, frequent appointments, and significant functional limitations. Adding nebulization can be beneficial, but we need to make sure we are not simply replacing one barrier with another. Chelsea, do you have something to say?

Chelsea Bernard:
I think treatment time is the one that I hear the most. We have plenty of patients who either still work, care for grandchildren, or do not have the time or patience to sit still for 15 to 45 minutes to do their nebulized treatments. In this scenario, I typically discuss, again, the pressurized metered dose inhaler with a spacer versus the nebulizer schedule. Sometimes creating a written plan that works out for them can make a big difference.

Another barrier, though, of course, is insurance coverage. There are some nebulized treatments we just have a difficult time getting covered. This is dependent on their plan.

In terms of strategies to promote the best outcomes, tailoring management per the individual's needs and schedules takes time and attention. Regimen simplification should always be prioritized. Many of our patients have comorbidities and are already inundated with information. As simple as possible and as clear as possible is always the goal.

Dr. Gulati:
With that being said, I'd love to hear from both of you one more time before we wrap up. Dr. Gupta, what final message would you like to leave with our clinicians managing complex COPD in outpatient and transitional care?

Dr. Gupta:
The number one would be nebulizer is a precision choice. For too long, putting a patient on a nebulizer felt like admitting defeat, as if

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we failed with inhalers, so here is the fallback. The data has flipped that.

The second message I would give is check the device before you blame the patient, and even before you blame the drug. When COPD is not responding, my first move is not to escalate therapy. It is to watch the patient use their inhaler and check their inspiratory flow. Half the time the problem is the delivery, not pharmacology.

Dr. Gulati:
And Chelsea, how about you?

Chelsea Bernard:
My two big takeaways are, again, just focus on making sure that the patient demonstrates their technique in the clinic, and really try to have an individualized approach, looking at what they have going on in their life, their symptom burden, and where they are at in terms of what would be the best thing for them.

Dr. Gulati:
Finally, I think I would like to echo both of your opinions. If there's one message I hope clinicians take away, it's that the right medication delivered through the wrong device may not translate into effective treatment. In COPD, we need to personalize not just what we prescribe, but how we deliver it.

And that brings us to the end of our conversation. I want to thank Dr. Raghav Gupta and Chelsea Bernard for sharing their insights and expertise on nebulization in COPD. Dr. Gupta, Chelsea, it was great speaking with you both today.

Dr. Gupta:
It's a pleasure to be here, and I'm excited to be part of this conversation.

Chelsea Bernard:
Thank you very much for having me.

Announcer:
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