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Recognizing Methamphetamine-Associated PAH: Strategies for Complex Care

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This program is produced in partnership with the American College of Chest Physicians and is sponsored by Actelion Pharmaceuticals US, Inc. And now, here's your host, Dr. Rodolfo Estrada.

Dr. Estrada:
This is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Rodolfo Estrada, and I'm an Associate Professor of Internal Medicine in the Division of Pulmonary and Critical Care and the Director of the Pulmonary Hypertension Program at the University of Texas in San Antonio.

Today, we're taking a closer look at diagnostic challenges and evidence-based treatment strategies for methamphetamine-associated pulmonary arterial hypertension, or PAH for short. Joining me in this discussion are Drs. Steven Hollenberg and Dana Kay.

Dr. Hollenberg is a Professor of Medicine at the Emory University School of Medicine and the Director of Cardiac Intensive Care at the Emory Heart and Vascular Institute in Atlanta.

Dr. Hollenberg, welcome to the program.

Dr. Hollenberg:
Thank you. It's a pleasure to be here.

Dr. Estrada:
And Dr. Kay is an Assistant Professor of Clinical Medicine in the Division of Pulmonary and Critical Care at the University of Cincinnati.

Dr. Kay, it's great to have you with us as well.

Dr. Kay:
I'm glad to be here and looking forward to our discussion.

Dr. Estrada:
Well, to begin our discussion, I'd like to share a patient case. This patient we'll call Felix. Felix is 42 years old. He's a male patient with a history of polysubstance abuse, including methamphetamines, alcohol, and tobacco, who presented with one week of dyspnea on exertion and bendopnea. He also has chest tightness and lower extremity edema, and he has had these symptoms for the last year but has gotten worse over the last six weeks.

In his review of systems, there's no cough or fevers. There's no joint pain or allergies. He does have a history of hypertension and asthma. He is treated with amlodipine 10 milligrams daily and albuterol as needed. In his social history, he has no insurance, has two small kids, works in construction, and uses meth via inhalation.

When we saw him in the hospital, on physical exam, he was afebrile with a blood pressure of 117 over 78, heart rate of 102, saturating 93 percent on room air. He was dyspneic when bending over but not in acute distress. His lung exam was unremarkable. His cardiac exam had a loud P2 and a JVD to the clavicle at 90 degrees. Regular rate and rhythm. He does have 2+ pitting edema but no cyanosis or clubbing.

Important studies on admission include a BNP of 529 picograms per milliliter and a chemistry with normal electrolytes, a bicarbonate of 24, and a creatinine slightly elevated at 1.33. He did have an AST of 27, ALT of 22, and a total bili of 1.8. His CBC was unremarkable, except the hemoglobin was slightly higher at 17.1. His connective tissue disease panel, hepatitis panel, and HIV were all negative.

The patient had a CTPA as part of his evaluation, which showed a dilated PA at 3.2 centimeters, and he also showed an enlarged cardiac silhouette on the chest x-ray. On his echocardiogram, his left atrium was called normal. The left ventricle was also normal in function and size with an EF of 57 percent. But his right ventricle had severe dilation with reduced function and a PASP—a pulmonary artery systolic pressure—of 60 millimeters of mercury. The right atrium appeared dilated, estimated at 15 millimeters of mercury pressure, and no pericardial effusion. Of note, when seen on the image, the left atrium was smaller than anticipated.

We got a right heart catheterization in this patient with a right atrial pressure of 16 millimeters of mercury, a right ventricular pressure of 54 over 9, with an EDP—end-diastolic pressure—of 24 millimeters of mercury, a PA pressure—pulmonary artery pressure—of 70 over 26 with a mean pressure of 41, a pulmonary artery wedge pressure of 23 millimeters of mercury with a thermodilution cardiac output of 2.9 liters per minute, a cardiac index of 1.43, and a PVR of 6.14 Wood units. His PA saturation was 53, and his aortic saturation was 92. Other testing included a VQ scan that showed no perfusion defects and unremarkable pulmonary function tests, including the DLCO.

With that case in mind, I'd like to turn to my guests. Now, we'll hear from Dr. Kay later on, but first, let's discuss these diagnostic considerations with Dr. Hollenberg.

What are the key clinical signs and risk factors we should look out for when we're evaluating these patients with methamphetamine-associated pulmonary arterial hypertension?

Dr. Hollenberg:
Well, the first thing you have to do is identify methamphetamine use. And it's not very useful to think that you can know the type of patient who might be using methamphetamine. You have to ask as part of a nonjudgmental universal protocol. You have to say something like, “We ask all these questions, we just want to help, we don't want to judge people.” And so you want to identify methamphetamine use, and you're starting a relationship, so you want to be honest with them, and you want them to be honest with you.

And there are some signs that might make you think about methamphetamine. People may be fidgety, they may have jaw clenching, and they may tell you that they're not sleeping or they're losing weight without trying. And so there are some things that you might think about that clue you into the diagnosis.

The symptoms can be challenging. It can be hard to diagnose pulmonary arterial hypertension. People are dizzy, fatigued, and short of breath. And so I think you have to have a high index of suspicion. There are some things that might make you think about methamphetamine, including other co-infections, such as hepatitis B. But I really think a high index of suspicion is important if you're going to make the diagnosis.

Dr. Estrada:
We have seen regional variability within the United States. How do you think regional variability impacts both clinician awareness and the diagnostic approaches we use?

Dr. Hollenberg:
Well, it's very important. So, as you know, there's a predominance of methamphetamine use in western states, and that's largely historical based on distribution factors and production and all that of this illegal substance. But just because it's predominantly in the west doesn't mean that it's not prevalent in other states and in fact increasing, not only in the west, but in other states. So I think that clinician awareness—you won't make the diagnosis if you don't think about it—is important.

And also local factors—you can look at things on a statewide level, but within states, and even within cities within states, there are places where there may be more local use than others. So I think all clinicians need to have a higher index of suspicion, but also when you start seeing it, you need to begin to think about it and begin to screen patients for it.

Dr. Estrada:
Thank you, Dr. Hollenberg. You brought up very important points about how the condition is often underrecognized in patients, and how regional variabilities affect those diagnoses. So keeping those concepts in mind, what best practices would you recommend to cardiologists and pulmonologists who are working together to ensure timely diagnosis?

Dr. Hollenberg:
Well, it's important for them to work together. I will point out that both of them have a chance to make the diagnosis. So somebody might get referred to cardiologists for shortness of breath, and they might have the opportunity to diagnose pulmonary hypertension. The pulmonologist might get that and might be able to diagnose pulmonary hypertension. For both, echocardiography is a good screening study, but for particularly severe pulmonary hypertension, invasive hemodynamic assessment is important, and the pulmonologist and the cardiologist have to work together to make the diagnosis.

And after the diagnosis is made, particularly in patients with the possibility of both left and right heart involvement, it's important to take a multidisciplinary approach, and that extends not only to cardiologists and pulmonologists, but to other specialties like psychiatrists and behavioral specialists and social workers and all that. It's really a team sport.

Dr. Estrada:
I like that. A team sport is the best way to call the approach we have to have for these patients.

For those just tuning in, you're listening to *Deep Breaths: Updates from CHEST* on ReachMD, I'm Dr. Rodolfo Estrada, and I'm speaking with Drs. Steven Hollenberg and Dana Kay about how clinicians can better recognize and manage methamphetamine-associated pulmonary arterial hypertension.

So Dr. Kay, I'd like to bring you into the conversation to discuss some treatment strategies. What can you tell us about our evidence-based options?

Dr. Kay:
The regimen for treatment of meth-PAH mirrors that of idiopathic PAH, so we want to use combination therapy with a PDE5 inhibitor and an endothelin receptor antagonist as first-line therapy. And based on risk stratification with our current tools, such as the REVEAL score, the timing of initiation of prostacyclins or activin signaling inhibitors such as sotatercept can be individualized.

It's important to utilize risk-stratification tools at the time of diagnosis and during follow-ups to help determine the intensity of PAH therapy needed to optimize patient care. However, what we know based on studies that have compared patients with meth-PAH to those with idiopathic PAH is that patients with meth-PAH often have more severe symptoms, worse hemodynamics, and increased risk of complications and mortality, yet they are less likely to be initiated on triple therapy and more likely to be hospitalized, telling us that there are unique challenges in treating those patients with meth-PAH, possibly related to issues with nonadherence, comorbidities, and psychosocial barriers.

So our treatment goals should not only include improved functional status, slowed disease progression, and improved quality of life with treatment of their PAH, but additionally, attention needs to be paid to supporting patients in cessation of amphetamine use, supporting them with psychosocial barriers, and also being mindful of possible left-sided heart disease that is more prevalent in those with a history of methamphetamine use.

Dr. Estrada:
Thank you. Sounds like the treatment for these patients is quite challenging. How can regional differences in clinical practice and access to care affect treatment outcomes in this specific population?

Dr. Kay:
So we know that there is variability in the prevalence of methamphetamine use and methamphetamine-associated PAH across our country. But in those who get diagnosed with meth-PAH, it is surprising that 31 percent do not get initiated on treatment. Some of the northeastern and southeastern states, such as New Jersey, Florida, and West Virginia, just to name a few, have some of the lowest number of meth-PAH treatment rates in those carrying a diagnosis of pulmonary hypertension.

Such nationwide discrepancies in the percentage of patients treated are likely multifactorial. We know that it takes a multidisciplinary approach to treat meth-PAH because not only does the PAH need to be treated, but these patients also require the support of addiction specialists, psychiatrists, social workers, cardiologists, pharmacists, et cetera. And so in areas that meth-PAH is not as prevalent, or in more rural areas, having a multidisciplinary approach may not be as readily available and may lead to delays in care.

Additionally, access to social services is really important in supporting patients with psychosocial hardships, such as those that need support with housing stability, medical insurance, and transportation, just to name a few. And there are differences in accessibility to social services in different regions that can further lead to the discrepancies we note nationwide in treatment of patients with meth-PAH.

Dr. Estrada:
Finally, Dr. Kay, what strategies have you found most effective when you engage these patients in their care?

Dr. Kay:
It is important to individualize patient care because each patient faces unique challenges. We need to be mindful to simplify their medication regimens when possible, work on educating patients on their disease processes and how the medications help, put efforts towards frequent communication in order to help anticipate problems and avoid delays, and also be mindful that a diagnosis of PAH is a pretty significant lifestyle change, and it does take a bit of time for the patient to successfully adopt all the required changes. And if a patient experiences occasional slip-ups, we need to be understanding of the significant lifestyle change they are dealing with, and that it

doesn't necessarily mean that they are purposely being non-compliant.

Again, it takes a multidisciplinary approach to successfully treat a patient with meth-PAH, so engaging all possible resources to help support the patient is very important.

Dr. Estrada:
We have now heard about great diagnostic and therapeutic approaches to treating these patients. We'll go back to our case with Felix and how we ended up managing the next steps for him. He was deemed to be high risk and started on triple therapy, including IV prostacyclins. Unfortunately, on day two, he left against medical advice on monotherapy. He was then readmitted twice to other health systems, where he also left against medical advice and eventually came back to our system six months later with syncope and a blood pressure of 100 over 60.

At this time, he was amenable to therapy, and he was started on triple therapy with IV prostacyclin for three weeks, eventually being discharged on sildenafil and macitentan, and through shared decision-making, added selexipag. He was then seen in clinic at two and four weeks later, with a BNP of 120, a functional class two, and able to go roller skating with his daughter—unfortunately, still using meth. He now has been working with the addiction medicine team and the social worker, as well as having insurance and a stable job.

So a key point from Felix's case is lower socioeconomic status has been associated with increased prevalence of meth-associated PAH as well as unemployment. Unfortunately, there's increased healthcare utilization—about 2.3 higher emergency room visits and 1.4 higher hospitalizations in this population—and it's very underrecognized. About 70 percent of patients are on PAH therapy only.

What is enough exposure is sometimes part of the question. Some reports say that greater than three episodes per week for more than three months is what would be reported as enough. So it's important to remember that this population is also undertreated when it comes to parenteral therapy. Registries show that, compared to idiopathic pulmonary hypertension, 15 percent of meth-associated PAH and 28 percent of idiopathic PAH are treated with parenteral prostacyclins. But in expert centers, this number can go up to 45 percent. And really what we're trying to do is a multidisciplinary approach.

So some summary recommendations with increasing meth use in the United States—we have been seeing this with regional variability. There's worse presentation in meth-PAH cases with a higher recurrent hospitalization, as we discussed in our case. There is universal screening that is recommended, whether that's with a questionnaire or with a test, and it can involve the left heart disease via direct toxicity.

So, in conclusion, we want to create management that is non-judgmental, that encourages the abstinence of use, and that addresses the extrapulmonary components, and then we add the PAH-specific medications. And in the end, we want to focus on teamwork.

With those key takeaways in mind, I want to thank my guests, Drs. Steven Hollenberg and Dana Kay, for joining me to discuss how we can better care for patients with methamphetamine-associated pulmonary arterial hypertension. Dr. Hollenberg, Dr. Kay, it was great having you both on the program. Thank you.

Dr. Kay:
Thank you for having me.

Dr. Hollenberg:
It's a pleasure to be here.

Announcer:
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