Crafting an Individualized Plan to Optimize Patient Outcomes: Safe, Effective, and Personalized Treatment

CMEO Podcast Transcript

Richard Bogan:

Hello and welcome. I am Dr. Richard Bogan, and on behalf of CME Outfitters, I would like to thank you for joining us for this three-part CMEO BriefCase Series titled, *Best Practices for Applying Recent Clinical Trial Data and Individualized Treatment to Fight EDS and OSA*, a three-part BriefCase Series. Today's BriefCase is titled, *Crafting an Individualized Plan to Optimize Patient Outcomes: Safe, Effective, and Personalized Treatment*.

Today's program is supported by an educational grant from Jazz Pharmaceuticals. I am the president of Bogan Sleep Consultants, as well as an associate clinical professor at both the University of South Carolina School of Medicine in Columbia, South Carolina, and also the Medical University of South Carolina in Charleston, South Carolina. I'm very pleased to be joined today by Dr. Paula Schweitzer. She is Director of Research at the Sleep Medicine and Research Center at St. Luke's Hospital in Chesterfield, Missouri. Welcome, Paula.

Paula K. Schweitzer:

Thank you.

Richard Bogan:

So to frame the discussion today, let me review our learning objective. Our goal is that after this CMEO BriefCase, you'll be able to position your treatment strategies for OSA-related excessive daytime sleepiness based on individual patient profiles. So first, let's meet Marty. Marty is a 48-year-old male who is meeting me. Marty has a history of severe obstructive sleep apnea, and as you can see from his sleep study, he had about 38 episodes an hour and a Nadir 02 sat of 78%. And when he presented, he, of course, was sleepy and had an Epworth score of 15, quantifying his degree of sleepiness.

At the time of diagnosis, he noted loud snoring, frequent awakenings, daytime sleepiness. He also had hypertension and elevated BMI, and his excessive sleepiness started around the time that he was snoring and gradually progressively got worse. He had a CPAP validation study performed that showed correction of nocturnal hypoxemia, his AHI, and no snoring at 11 centimeters, and he actually was placed on an auto-titrating device, and he showed 97% adherence with an AHI of 3.2 on the download, average use 7.5 hours. His Epworth score is 13 and his FOSQ is 12. Of course, I'd like for his Epworth to be less than 10 and his FOSQ, I'd like for that to be up above 17 and a half, around 18 or so, so this quality of life measure. CPAP certainly has improved the quality of his sleep and the quality of his daytime fatigue and sleepiness, but he tells me he's still taking naps and he's missed work and he still has daytime sleepiness.

Other pertinent aspects to his history is a history of attention deficit disorder and hypertension, dyslipidemia, and glucose intolerance. He has family history of hypertension and ischemic heart disease, fairly strong family history of myocardial infarction in his father so worried about cardiovascular risk in him. No history of nocturnal motor activity or REM dissociative symptoms, vivid dreams, paralysis, hallucinations, no restless leg

syndrome, no really reported depression or anxiety, but he's been on methylphenidate extended release of preparation, as well as an antihypertensive and Metformin for mild glucose intolerance, and a statin. He doesn't drink alcohol, doesn't smoke, and denies any illicit drug use. So let's meet him and see what's going on.

Marty, good day to you. How've you been doing? What's happening?

Marty:

Hi, Dr. Bogan. It's nice to see you, too. I'm okay.

Richard Bogan:

Yeah. I know you have sleep apnea and you're on CPAP, and you have hypertension and have had some lipid abnormalities, and your body mass index is elevated. So you are above weight. We know obstructive sleep apnea can make people tired and sleepy, but it also can cause some cardiovascular and brain complications. We'll look at your therapy, but tell me how you're feeling.

Marty:

Oh, I don't know what's wrong with me, Doc. I feel like I cannot stay awake. I was sitting here waiting to log in, and my son came in and woke me up. I was waiting, what, 10 minutes. Seems to be my life. If I sit, I sleep.

Richard Bogan:

Hmm. Well that sounds problematic. It sounds like you're more sleepy than you should be.

Marty:

It's debilitating. The only time I'm not tired is when I'm asleep. I just don't know what to do.

Richard Bogan:

Tell me how that sleeping has affected you. I mean, how is it interfering with your life?

Marty:

As long as I'm moving, I'm okay. But as soon as I stop moving, it's like a wave of sleepiness comes over me. I take naps during my lunch breaks. I am so tired, Dr. Bogan.

Richard Bogan:

Right.

Marty:

And I work in a manufacturing plant, so I literally cannot afford to fall asleep on the job. Someone could get hurt. There are times I call in because I'm too tired to go into work and be safe. How long can I keep doing this? I could lose my job, and then what?

Richard Bogan:

Yeah, that's a problem. What about your driving? Do you have trouble driving?

Marty:

Oh, I'll be driving along just fine. I may not even feel that bad, and as soon as I stop. A red light, or if I go into a drive-through, I'm going to get a cheeseburger somewhere, and I'll fall asleep, just sitting there falling asleep with the car running, in gear, my hands on the steering wheel, my foot on the brake. That's scary.

Richard Bogan:

Now when you get home in the evenings, do you have anything left? Are you dozing off?

Marty:

I usually sit in the chair watching television, and I rarely see much of it. I usually fall asleep pretty quickly after I turn the TV on.

Richard Bogan:

Yeah. Usually, I ask what time are you going to bed and get getting up, and make sure you're getting enough sleep. But I have the download from your CPAP, and the CPAP actually has a flow sensor in it that looks at the breathing pattern. In other words, how rapidly does air go in, how deep you breathe, even how fast you breathe. And particularly in the auto mode, it finds that sweet spot to open up the airway, normalize breathing, and we want to correct the oxygen levels and get that abnormal breathing index down below five, and of course, eliminate snoring and decrease work of breathing. I assume on the CPAP you're not snoring any, correct?

Marty:

My wife doesn't hit me anymore during the night. So I guess not.

Richard Bogan:

Okay. Well, it sounds like the CPAP is doing well, and that device actually counts your breaths, and the download looks perfect. I mean, you're getting seven and a half plus hours on it. You're breathing index is fine, and that should be enough to correct the oxygen level and improve the sleep. But while we know there are some individuals who are still sleepy, there are a lot of theories about it. We don't know exactly, but we think that the disrupted sleep, as well as maybe drops in oxygen level may have injured some of the neurons are at least slowed

them down, and so that the speed of processing in the brain is not as good. The brain has trouble staying awake, in other words, and the brain is sleepy despite an adequate quantity of sleep.

So some individuals are still sleepy despite using the CPAP and getting enough sleep. And we think the brain is fine. It's slowed down. We do have some medicines. Now, some of the medicines that are traditionally used, like you've had an ADD drug in the past, those are what we call a Schedule II stimulants, and sometimes they make people nervous or jittery. But we do have wakefulness promoting medications that can speed up these neurons and help you in terms of your daytime alertness, which will help you a lot with your symptoms, both work and family.

Marty:

More medication. I'm on enough pills already, Doc.

Richard Bogan:

Yeah, I know you are. This is a medication that we consider non-addicting. It has low abuse potential and will significantly change quality of life, and I think we certainly should consider trying it for a short period of time.

Marty:

Okay. So what medication are you thinking about?

Richard Bogan:

Well, we have several different choices and we'll discuss that.

Marty:

Okay.

Richard Bogan:

Paula, like a lot of individuals, Marty is very sleepy. I mean, very sleepy in general. What are some of the causes of sleepiness and how does that sleepiness manifest itself?

Paula K. Schweitzer:

There are a number of causes of sleepiness. Obstructive sleep apnea is certainly one of the causes of sleepiness, but sleepiness can be caused by number of other things, including insufficient sleep at night, other sleep disorders, such as narcolepsy, sedating medications, which could be either over-the-counter medications or prescription medications. Alcohol and illicit drug use can also cause sleepiness. Obesity has been associated with sleepiness as well, and in addition, sleepiness can occur with a number of medical, psychiatric, and neurologic disorders. So it's important to evaluate those things when you're looking at a patient with a complaint of sleepiness.

Now, sleepiness is not always manifest with a patient saying, "I'm falling asleep." You can also have mood changes. You can feel depressed. The patient may just say, "I don't feel like doing anything," and the cause could be sleepiness, not necessarily depression. It can have effects on performance, on driving, impaired memory, all kinds of things associated with day-to-day activities.

Richard Bogan:

Yeah, it's interesting. The attention deficit disorder and being on a Schedule II stimulant is kind of interesting, and quite frankly, worrisome, because it does hide some of his symptoms, obviously. And he does have a history of at least cardiovascular risk, so it does make us worry in terms of his particular therapy. Of course, and as you say, one of the most common cause of sleepiness is insufficient sleep, but we do see people with obstructive sleep apnea who are still sleepy. We've done everything we should do. They're getting plenty of sleep. The device is working well, and they still have sleepiness. So what do you think are some of the factors that may impact the excessive sleepiness that we see in these patients?

Paula K. Schweitzer:

In a patient, are you talking about patients that are treated already for sleep apneas?

Richard Bogan:

Yeah. This is somebody with sleep apnea, and they come back to us and they're like, "Doc, I'm better, but I'm still sleepy. What's going on here?"

Paula K. Schweitzer:

Yeah. What's going on? Again, you have to look at how much they're sleeping, and the download from the CPAP device is very useful for that. But you also have to query them to make sure that they're actually sleeping during that time. If they feel like they're only getting three hours and the machine is on for 7.5 hours, that may not be sufficient sleep for them. So number of hours of sleep is still important, and there could potentially be other interruptions in sleep. In Marty's case, we don't think that's the case based on the prior studies that have been done with him, such as periodic limb movements or narcolepsy. He doesn't seem to have the history for those kinds of things, and his overall health status is important, too. What else is going on with him? And are the issues that he has being treated appropriately?

Richard Bogan:

Yeah. Yeah, I think it's important, obviously, duration of sleep and the circadian timing of the sleep and all of those things are very important. And obviously, we consider those when we talk to him. We look for narcolepsy with the REM dissociative symptoms and total hours of sleep. It should have been adequate to help him, and I'm impressed when we look at excessive sleepiness that occurs in individuals, and there are studies. It depends on the cohort that you look at, as you well know, but Terri Weaver and others have done that. But despite adequate treatment with CPAP, many of these individuals still have residual sleepiness. Would you comment on the prevalence?

Paula K. Schweitzer:

Yes. The prevalence in epidemiologic studies varies from about six percent to 18%, depending upon, again, the comorbid factors that you mentioned. But in addition to that, we sometimes don't always recognize sleepiness because we can measure it in many different ways. We can measure the sleepiness with a subjective report, like the Epworth, or we can measure it with objective tests, like the multiple sleep latency tests or the maintenance of wakefulness tests. And those might give us different results in terms of who is sleepy or who is able to maintain wakefulness.

Richard Bogan:

Yeah. That's interesting because, again, it depends on the cohorts you're studying, the definition, et cetera. But when you look at the number of individuals, even the individuals using their CPAP in excess of six hours, I mean, the prevalence of measurable sleepiness with the multiple sleep latency test and the quality of life measures that are still impaired and the subjective sleepiness, I mean, that's really pretty impressive data that shows that, at least, observationally, they're still sleeping. We may not know exactly why they are, and there's some evidence of organicity based on imaging studies and some other things, as well as preclinical animal studies that show animals exposed to intermittent hypoxemia or sleep fragmentation are still sleepy. So what about sleep apnea and cardiovascular health?

Paula K. Schweitzer:

Before we get to that, you were mentioning the animal studies associated with sleepiness. And in those studies, we have seen that there are brain cells. There are changes in the brain cells that affect wakefulness. And there's also changes in white matter that we've seen in humans. And we don't know everything we need to know about this, but there is good data to indicate that there may be some persistent abnormality in cells in the brain.

Richard Bogan:

Yeah. It certainly indicates some organicity there. And of course, clinically, we see this, and we're scratching our head trying to figure out, "Why are these people still sleepy? I'm doing everything I can, and they're using CPAP and they're still sleepy. So now what do I do in terms of medications?" But because these individuals do have some increase in cardiovascular risk, we have to take that into account when we decide on what medications. Can you tell me what we know about the impact of obstructive sleep apnea on heart health?

Paula K. Schweitzer:

Well, we know that sleep apnea increases the risk of a number of things related to heart health. The risk of atrial fibrillation in people with sleep apnea is two to four times higher, and 30 to 40% of people with hypertension also have OSA. Stroke risk is increased as well. So there's a number of things that we need to be concerned about in patients with sleep apnea. And certainly, Marty has that history of ischemic heart disease, myocardial infarction in his father, I believe, at a young age, and he has elevated blood pressure himself.

Richard Bogan:

Yeah. I think the fragmented sleep ... I mean, sleep, obviously, is a homeostatic process, and so the fragmented sleep can clearly increase sympathetic tone, and we see the non-dipping, and it's interesting. The STOP-BANG questionnaire has hypertension listed in there as, obviously, sleep apnea in an obese individual has who is hypertensive and snores, we worry about whether they have sleep apnea or not, and certainly that is something to take into account.

But what do you think about the impact of obstructive sleep apnea related to health-related quality of life? I might make an initial comment, but certainly we know sleepiness has an effect on executive function. So these individuals tell us they have brain fog. I mean, the brain slows down, speed of processing, reaction time, divided tasks, all those are impacted. And obviously, if you're working in a facility that requires dexterity, I mean, those individuals are affected.

They say they're tired. I mean, everyone who's sleepy is tired, and not everybody who's tired is sleepy, but they complain of the fatigue and the brain fog, motivation, even self-esteem, mood changes, driving performance, social interaction. All of those are potentially impacted when someone's sleepy. And sometimes that's actually how they present. They come in and they say, "Doc, I think I'm depressed, or I have dementia, or I'm tired." They don't always describe their sleepiness. I think that's why it's so important, clinically, for us to ask them about the sleepiness. Do you have any comments on that?

Paula K. Schweitzer:

Well, I just want to comment that Marty shows all of these symptoms. His health[-related] quality of life is very poor. He's following asleep at work. He's unable to go to work some days. It scares me that he's driving based on his descriptions of falling asleep at a stop sign or while driving through the drive-through. And so you can imagine he probably has relationship difficulties as well, since he's spending so much time trying to work and sleep and stay awake.

Richard Bogan:

Yeah. When I see a patient in follow-up, obviously, they come to us for two reasons. They want to be well, reduce morbidity and mortality, but they also want to feel better. And so it's important for us to qualify, "Are they sleepy?" and quantify how sleepy they are. And the Epworth score can certainly help us with that. My Epworth score is six. I'm proud that I'm not that sleepy. But when it gets above 10, we begin to worry about how the sleepiness is affecting them. So I ask them, "Do you take naps? Do you feel the need to nap? Does sleepiness interfere with your function? If it does, how does it interfere with it? What's the most prominent symptom that you have? I mean, how does it interfere with you the most?"

And if you listen to Marty, he focused a lot on his work and his social situation. So we can use that as a biological marker in a way to see about the success of therapy, not only the Epworth and the FOSQ, but how are you doing with your workplace performance and how are you doing when you get home? Do you have anything left for the family? So we can use those as markers as we follow the patients to, obviously, optimize our therapy. What do you think?

Paula K. Schweitzer:

I think that's key. And I think it's important that those goals are individualized to each specific patient because patients have different needs, different hierarchies of what's going on. I think Marty is more of a classic case where everything is involved, but in some cases, you want to focus on the primary complaint.

Richard Bogan:

Agree. But when we consider the treatment options, and I mentioned that to Marty, we don't typically use Schedule II drugs. Now his Schedule II drug was primarily for his ADD. Now we know sleepy people have attention problems. And so is it really, truly ADD or not? But we worry about those because of the sympathetic effect, heart rate, blood pressure, and tremor and anxiety, and some other things of that nature. But we do have some FDA-approved drugs. The first one, obviously, was modafinil and it's basically probably a dopamine reuptake inhibitor. And you talked about those neurons that are sensitive to oxidative stress and sleep fragmentation. It just so happens dopamine and norepinephrine, those mono-adrenergic amines, or neurons, that help control wakefulness seem to be sensitive to that. Modafinil does work through dopamine reuptake, and of course we have armodafinil.

Armodafinil is the long-acting isomer in modafinil. Both of those are approved by the FDA, but now we have solriamfetol. That's a new one, and this recent publication is looking at solriamfetol, and solriamfetol is a dual norepinephrine and dopamine reuptake inhibitor, and we have really some good clinical data looking at the effect size on the Epworth score and the MWT and the Patient Global Impression of Scores. And I would really encourage the readers to look at that data for a couple of reasons. One, the baseline data is descriptive. I mean, these people who were in the trial, those are the people you see in your clinic. How sleepy were they? What do they look like?

And then when you see the response, the solriamfetol is interesting because it is renally excreted, and because it's renally excreted, it doesn't induce enzymes, liver enzymes. So that's particularly important when we have a female who's on birth control, because the modafinil and the armodafinil does induce enzymes in the liver that reduce birth control effectiveness. And because they are promoting wakefulness, they could have some increase in sympathetic tone, much less than the Schedule II drugs. So we do want to make sure the blood pressure is stable and monitor their response, and obviously check their heart rate and blood pressure as well. But those are the ones that are approved by the FDA. Do you have any other comments about those?

Paula K. Schweitzer:

Well, I'm impressed with the effect size of solriamfetol. However, there have been no studies that have directly compared these drugs to one another. So it's difficult to state that one is better than the other at this point in time. And so I think, again, the patient needs to be treated individually. Insurance coverage may vary for the different drugs, too. So that has to be taken into account. And the other things that you mentioned are important in terms of monitoring blood pressure and the sympathetic activity issues.

Richard Bogan:

Spot on. I completely agree. Obviously, when we see our patients back, we want to focus on the symptoms and not just the download, because I know a lot of patients come to me and they're like, "I was seen by a physician. They checked my download. My download was great, and they said, 'I'll see you later,' and of course, check your blood pressure and heart, lungs, et cetera." But I think it is important for us to ask our patients about the sleepiness. And I mentioned that earlier in terms of, "Are you napping? Do you feel the need to nap? Is the sleepiness interfering with executive function and mood and productivity and driving?" So we need to identify that.

We can use patient reported outcome measures, as I said, the Epworth and the FOSQ. Obviously, if we're suspicious for narcolepsy, we could go ahead and do a sleep study and follow that by an MSLT on the CPAP so we've eliminated the abnormal breathing, and do a download prior to that study to make sure they're using it and getting adequate hours, and obviously rule out narcolepsy or other things. We don't do a multiple sleep latency tests on all sleepy, obstructive apnea patients. But we do know there's an increase in prevalence of obstructive sleep apnea in individuals with narcolepsy.

And so as our narcolepsy patients age, we have to ask them about snoring and be suspicious, because it can sneak up on you. But after we do those types of things, make sure we have circadian line under adequate treatment and check for other disorders and make sure that there are no street drugs involved, et cetera, and mood is okay, then I think, certainly, we begin to consider treatment. What do you think?

Paula K. Schweitzer:

I think that's excellent. I think sometimes you may consider treatment, and the patient comes back and is still complaining on the subjective scales. May not have sufficient improvement. And in those cases, when would you want to change a medication or change dosage, or would you then go to try to get some objective information on how physiologically sleepy they are with a PSG and an MSLT?

Richard Bogan:

Exactly. I think if they come in and they say, "When I was 15, 16, 17-years-old, I was sleepy when I was in high school, and I had vivid dreams and paralysis and hallucinations, and I may still do that." Then I'm suspicious about narcolepsy. And of course, now we have patients with idiopathic hypersomnia, but typically the sleepiness predates the obstructive sleep apnea. So they were sleepy and now they snore or gasp and choke, and we've the diagnosis of sleep apnea, and they get better, but they still have sleepiness, so that index of suspicion of some other underlying problem.

And of course, we ask them about mood and what drugs are they taking? Are they taking any sedating medications? And all of those help feed into our choices in terms of, "Do we intervene with therapy? Do we do other diagnostics? And what therapy do we choose?" In his case, for example, he was on a Schedule II drug that has some problems with sympathetic tone and perhaps some risk from a cardiovascular perspective. So we certainly take that into account.

So let's summarize our discussion with our SMART goals, which are Specific, Measurable, Attainable, Relevant, and Timely. That is what we hope that you will take from this discussion to apply to your practice, identify CPAP compliant patients who are eligible to receive treatment for persistent EDS, develop individualized successful strategies to reduce EDS and improve quality of life and functioning in patients with OSA, consider patient comorbidities, including obesity, cardiovascular disease risks, such as hypertension, and depression, obesity, and cardiovascular disease risks when making treatment selections. Identify best practices to transition patients from stimulant to non-stimulant therapy.

Today's CMEO BriefCase is part two of a three-part series of case-based activities that can be found on the Sleep Disorders Hub. I hope you'll check out the other two activities and the series that address the far-reaching impact of OSA-related EDS and strategies to apply clinical trial updates to optimize treatment decision making. The Sleep Disorders Hub has these activities and many others on OSA, EDS, in general, narcolepsy, idiopathic hypersomnia, and more.

I would like to encourage our audience to visit the Sleep Disorders Hub for additional information, clinical guidelines, resources, and patient education about sleep disorders. To receive CME or CE credit for this activity, participants must complete the post-test and evaluation online. Participants will be able to download and print their certificate immediately upon completion. Paula, I would certainly like to thank you today for joining me. I don't know if you had any final comments.

Paula K. Schweitzer:

I appreciate your invitation. I enjoyed the conversation, and I'd like to follow Marty along and see what happens to him.

Richard Bogan:

Thank you. And I would like to thank you, our audience, for joining us. Be safe and take care of yourselves so you can provide the best care for your patients.