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Sodium Oxybate in the Management of Narcolepsy: One Molecule, Three Formulations – and the Critical Role of Shared Decision-Making in Its Use

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Welcome to CME on ReachMD. This activity, titled "Sodium Oxybate in the Management of Narcolepsy: One Molecule, Three Formulations – and the Critical Role of Shared Decision-Making in Its Use" is provided by Prova Education.

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Dr. Kushida:
This is CME on ReachMD, and I'm Dr. Clete Kushida. Today, Dr. Michael Thorpy and I will be discussing the management of narcolepsy with and without cataplexy, and how best to optimize patient outcomes across different sodium oxybate formulations. Welcome, Michael.

Dr. Thorpy:
Thank you, Clete. Pleasure to be with you.

Dr. Kushida:
Michael, there are currently three FDA-approved sodium oxybate formulations available for the treatment of narcolepsy with or without cataplexy. Could you discuss their formulation and dosing differences?

Dr. Thorpy:
Certainly, Clete. There are three different formulations that are available. They all have the same active moiety, that is oxybate. So in general, and in terms of the data on efficacy, they're all just as efficacious. So, that is one thing about oxybate is that it's very effective for treating the three main features of narcolepsy: that is the excessive daytime sleepiness, the abnormal REM sleep phenomena of which of course cataplexy is one of the main ones, and also disturbed nocturnal sleep. So, these three agents will effectively treat all those symptoms of narcolepsy.

Now, the first one that was approved was Xyrem, which is sodium oxybate. That was approved in 2002, so we've had a lot of experience with Xyrem over the years. The company that produces it decided that they would produce a formulation that had much less sodium. So, they produced in 2020 a formulation called Xywav, and Xywav has calcium, magnesium, potassium, and 92% less sodium than the original.

And both of these medications are generally given twice at night. They're given before bedtime and 2.5 to 4 hours after bedtime. And usually they're given in equal doses, although in some cases it may be asymmetrical dosing. But because they're given twice at night it means that the individual has to awaken in order to take the second dose.

Now, sometimes people have difficulty in doing this, either they just sleep through an alarm clock or they forget to set the alarm clock and just sleep through and not able to take the next dose.

Because the second dose has to be taken about 4 hours before awakening in the morning, sometimes people may be too late to take that second dose.

There's a third form of oxybate called Lumryz, and this is a once-nightly formulation. Now, it's still sodium oxybate, it has the same amount of sodium as the original Xyrem does, but it's taken as a single-dose before bedtime. It can be taken in up to the same maximum doses of both Xyrem and Xywav, which is 9 grams in one particular night. So, we have these three options that are now available to us.

Dr. Kushida:
Thank you, Michael. That was a terrific summary of the three different preparations.

Dr. Thorpy:
So Clete, perhaps you can tell us from your point of view and clinical practice, how do you use these three different agents? What sort of dosing do you use, and how tolerable are these, and how would you adjust the medications according to comorbidities?

Dr. Kushida:
Thank you, Michael. So, one of the things to consider is how tolerable the patient might be to waking up in 2.5 to 4 hours after dosing. We know that sometimes, especially the younger individuals that have a lot of preexisting sleep debt, sometimes that is a struggle. And we do know that twice nightly dosing, if they tend to forget the dose or if they take the dose too late, it can have problems with effectively treating their condition and/or it can cause some residual daytime sleepiness. Also, another thing is the salt content as you mention. So, individuals that might be particularly at risk are those with conditions like renal failure or congestive heart failure. So, those patients you would move away from ones that might have higher salt.

Another thing to consider would be if the individual has uncontrolled hypertension.

Dr Thorpy:
So, Clete, it seems as though sodium is a very important consideration with these medications. But in terms of efficacy, they are equally efficacious, and so a lot of it really depends upon our discussion with the patient and partly patient preference as well. So, shared decision-making is really an important factor in prescribing these medications.

Dr. Kushida:
Thank you, Michael.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Clete Kushida, and here with me today is Dr. Michael Thorpy. Our focus today is how to best optimize patient outcomes for narcolepsy with and without cataplexy across the different sodium oxybate formulations.

Shared decision-making, or SDM, is critical in optimizing patient outcomes and ensuring long-term adherence to therapy for narcolepsy with or without cataplexy. Before we get into our SDM discussion, could you please first discuss the quality-of-life issues that we must keep in mind when managing these patients?

Dr. Thorpy:
Well, yes, Clete. The thing about narcolepsy is that it really is a very burdensome illness for the patient. They are bothered by the symptoms of narcolepsy on a daily basis. So it's absolutely important that when they're on medication, that their medication use is continuous and that they don't miss days. Of course, the main symptom is excessive daytime sleepiness, and this can affect the patient in every aspect of their daily life. And can affect their driving, of course, and make them at risk of motor vehicle accidents. So, it's important that we effectively treat the daytime sleepiness not only for the patient's comfort and benefit of being without the sleepiness, but also from a safety point of view and other peoples' safety.

There are also abnormal REM sleep phenomena that occur. We mentioned cataplexy, which is a weakness that can occur, and in the untreated patient who has cataplexy this can be very disabling. The patient may laugh or just hear a joke – somebody telling a joke, and they can fall to the ground. So, it can result in injuries to some patients.

There are other symptoms of abnormal REM sleep, like sleep-related hallucinations. Patients will start to dream as they're waking up or as they're falling asleep at night and these symptoms can be very bothersome for the patient. The patient may have nightmares and weird and very distressing dreams at night, and they can persist into periods when they're awake. And often coupled with that, can be sleep paralysis where they can't move – a very frightening sensation. And so, it may be interfering with their schoolwork, or with their education. And, of course, it can interfere with any of their work activities.

So, there are really major effects of the symptoms of narcolepsy and it's important to consider all of these different issues when it comes

to prescribing medication to patients. And patients may also have some concerns about the medications being used as to whether it's going to be habit-forming or what about the side effects. There are many aspects to the treatment in patients with narcolepsy.

Dr. Kushida:
I couldn't agree more Michael.

Dr. Thorpy:
Clete, you mentioned shared decision-making and that's so important for patients that the physician and the patient need to be able to discuss issues related to their treatment. So, perhaps, Clete, you could tell us a little bit about this shared decision-making in patients with narcolepsy.

Dr. Kushida:
Yeah, so, a complex disorder like narcolepsy warrants a very frank discussion with the patient starting with even the initial evaluation of the patient that has narcolepsy. And part of the reason why there's such an emphasis on shared decision-making, instead of more like a quote, paternalistic approach towards the patient, shared decision-making really includes the ability to discuss with the patient their lifestyle and how important different facets of their life are to the prescribed treatment. And we do know that when there is that shared decision-making, there is improved adherence to treatment and medications, and also less anxiety or fear about the proposed treatment.

So, some of the factors that are important for the treatment of narcolepsy are their lifestyle preferences, their sleep schedule, when they go to bed and when they wake up, and how varied their daytime activities are. And we can't ignore their diet and exercise factors, too.

Also what's important is to consider their sleep habits. So, if they do tend to sleep throughout the night and have difficulty waking up during the night, then we might consider having once-nightly dosing. So, there's all these factors that influence the ultimate decision which medication best fits their lifestyle.

Dr. Thorpy:
Well, everything that you said Clete, is so important when making a decision about treating the patient, and in addition, we also have to remember that the patient isn't alone. They're usually in a family unit and there's family issues that need to be addressed, too, particularly with younger patients where the parent may be actively involved in the child's treatment and may in fact in some cases have to wake the child to give the medication. So, shared decision-making is not only just between the patient and the doctor, but also maybe involve the whole family unit.

Dr. Kushida:
Absolutely. Well, this has certainly been a fascinating conversation, but, Michael, before we wrap up, can you briefly share one take-home message with our audience?

Dr. Thorpy:
Yes, well, I think that it's an important thing for any patient who has narcolepsy to make sure that they see someone who's familiar with the new medications that are available for the treatment of narcolepsy.

Dr. Kushida:
One point that I just wanted to bring up that we discussed previously, as a take-home message, is that because of the complex and debilitating nature of narcolepsy, it really is important to not be afraid to express all your concerns to your provider and tell the provider what factors in your daily lifestyle are most important to you, and then come to a mutual decision about what would be the best treatment course moving forward with their condition.

That's all the time we have today, so I want to thank our audience for listening in and especially, thank you, Dr. Michael Thorpy, for joining me and for sharing all of your valuable insights. It was great speaking with you today.

Dr. Thorpy:
I very much enjoyed it, Clete. Thank you, and good-bye.

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