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Novel and Emerging Treatment Strategies for Narcolepsy

Announcer:
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Dr. Thorpy:
This is CME on ReachMD, and I'm Dr. Michael Thorpy. Here with me today is Dr. Clete Kushida. We're discussing novel and emerging treatment strategies for narcolepsy.

Now, there are a lot of different medications in narcolepsy that are used, and they have different mechanisms of action. We're all aware of caffeine causing an increase in alertness. However, most patients with narcolepsy tend not to use caffeine, although early days, before they get diagnosed, they often use caffeine as a way to try to help them keep alert. But there are other medications. There's the traditional stimulants, methylphenidate and amphetamines. These are sympathomimetic, affecting a lot of alerting neurotransmitters in the brain. Then we have the modafinils, regular modafinil and armodafinil. These are dopamine reuptake inhibitors, and they primarily treat the daytime sleepiness. They don't have any effect on cataplexy at all, but they are effective for sleepiness. They can also affect oral contraceptive agents, which is something one needs to be concerned about in the female population.

Then there's oxybate. And this works through a $GABA_B$ agonist activity and has turned out to be one of the major drugs in the management of narcolepsy these days. There's solriamfetol, which is a dopamine norepinephrine reuptake inhibitor, which is used for treating daytime sleepiness. Again, like the modafinils, does not have any effect on cataplexy but is very effective for treating daytime sleepiness.

There's a medication called pitolisant, which is a histamine H_3 antagonist inverse agonist, increases histamine in the brain, which is a very powerful alerting neurotransmitter. So that's quite a novel action for improving alertness. And then finally we have new agents such as the orexin agonists, and I'll discuss those a little bit more later.

But perhaps, Clete, you could tell us a little bit more about oxybates, as these are some of the major drugs that are being used for the first-line treatment of many patients with narcolepsy.

Dr. Kushida:
Thank you, Michael. You know, we're indeed fortunate, as physicians and also patients, to have 3 different preparations of oxybate. So many of you might be familiar with sodium oxybate; that's been available since 2002. And it contains 1.6 g of sodium at the highest dose of 9 g. And as you can see by this slide, it's taken at bedtime and then a second dose is needed about 2.5 to 4 hours later in the night. Now there's also a low-sodium mixed salt oxybate, which has much less sodium. And that's also the same as the regular sodium oxybate. It's taken at bedtime, 2.5 to 4 hours later in the night. But this should definitely be considered for patients who have hypertension, cardiovascular disease, and heart failure or renal or kidney disease.

Lastly, there's a once-nightly oxybate. It contains 1.6 g of sodium at the highest dose of 9 g, and the benefit of this preparation is that

you would take it at night at bedtime and then you don't need to have a second dose at about 2.5 to 4 hours later. And it's ideally suited for those who awaking in the night would disturb their sleep.

Dr. Thorpy:
Thank you, Clete. Well, in addition to medications I've mentioned, there are a number of medications that are under investigation at the moment, and hopefully we'll be hearing about their approvals in the coming years. There's an antidepressant called reboxetine, which is a medication that can treat both sleepiness and cataplexy. And then we're most excited about the orexin agonists, and there are a number of these that are in production at the present time. One of the main ones is a medication called TAK-861, which replaces orexin in the brain. Initial studies have shown the orexin agonist to be extremely effective at improving alertness. In fact, in some cases even causes hypervigilance where people are over alert. So in the studies they're sorting out what the appropriate dosing is going to be in the future when these become available.

Well, this was brief, but I'm glad that we had the opportunity to share this information about treatment strategies for narcolepsy. Thank you very much for listening.

Announcer:
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