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Treating Agitation in Alzheimer's Dementia

Announcer:
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Dr. Vega:
Hello, and welcome to this webcast entitled, Treating Agitation in Alzheimer's Dementia. My name is Chuck Vega, I'm a health sciences clinical professor of family medicine at the University of California at Irvine. I am delighted to be joined today by Dr. George Grossberg. Dr. Grossberg, would you mind introducing yourself?

Dr. Grossberg:
I'm happy to so I'm a geriatric psychiatrist, card carrying, and I'm Director of the Division of Geriatric Psychiatry at St. Louis University School of Medicine.

Dr. Vega:
Well, so and today, we're going to be talking about how we can come together as a care team and provide the best care for a challenging issue in clinical care, which is agitation in Alzheimer's-associated dementia. So we're going to be looking at treatment strategies with this particular discussion. And we'll be talking about some emerging pharmacotherapies that are showing promise for this for this condition.

So before we get started, let's go ahead and review our objectives for this CME activity. So at the conclusion, you should be able to identify the role of nonpharmacologic strategies, and when pharmacologic therapy is necessary for the treatment of agitation in dementia. You should also be able to evaluate evidence of current and emerging pharmacologic agents for the management of agitation in patients with Alzheimer's dementia, and demonstrate appropriate prescribing and monitoring of antipsychotics for the treatment of agitation associated with Alzheimer's dementia. So let's get started.

I really liked the fact during your presentations that you talked about how challenging these visits are, because I think it can be not only time consuming, but it's also emotionally draining for, you know, for patients and their care supporters who are engaged in the visit as well. Do you have any pearls as to how to, you know, express empathy and do the right thing, but also do so efficiently so you can move on to that next case, because you know, the patient's waiting there?

Dr. Grossberg:
Yeah, no, I think those are important points. I'm not sure that I have pearls, but I can just share with you things that we recommend. And I think you use the word empathy. And hopefully, all of us as clinicians on the front lines with these patients and their care partners do show empathy and recognize how difficult it is for the care partner to deal with these behaviors.

As far as the practicalities of the busy practice setting, one of the things that we found to be very useful is, number 1, to make sure that whenever we're seeing an Alzheimer's patient, let's say, who comes with the care partner, that very early in the visit, we're asking about behaviors. Because yes, sometimes the care partners are reluctant to mention that, you know, the patient has maybe at times

screaming or they're agitated, or they have a short fuse, and they can explode at times, they feel embarrassed about it. They're also reluctant to talk about it in front of the patient. So we give them an opportunity to have a sidebar with us, before we go into the visit with the patient, while the patient's getting their vitals, that we usually have a little sidebar with the care partner. And often those concerns come out. So I think the important thing is to address it at every visit, and address it right up front so that we know that's going to be a target. If we don't do that, then often we focus on other aspects of the disease. Yes, we pay attention to the care partner. But because of time crunch and other issues, we may not be able to deal with it as effectively.

Dr. Vega:
I think the elephant in the room in these visits is the possibility of going to long-term care. And the reason there's such reticence and people will hide, you know, both on the care partner and certainly the patient side, is that they are worried that this is going to be the thing that puts them in a long-term care facility. And so the other thing I tried to get out early is that's not necessarily what we're going to be reaching for as our first option. And the outcome that gets - it's an automatic thing. We - usually they an interest doing much in the way of behavioral opportunities to try to modify the behavior. Let's start there. We can think about pharmacotherapy. We're a long way from long-term –

Dr. Grossberg:
I like that sense of optimism.

Dr. Vega:
Yeah.

Dr. Grossberg:
And knowing what the care partners' kind of hidden concerns and fears are, which is the notion that they may not be able to take care of this person much longer. They may have to institutionalize them, which is not a desirable outcome. You give them hope. You can come out and say, 'Hey, there are interventions. We can try to figure this out. We can give you some tools that will help you.' I think that's great.

Dr. Vega:
Yeah, and I think if you're not optimistic, and this goes pretty broadly for all therapeutics, if you're not optimistic about how much they might improve patient's condition, then the patient and their care sport is not going to be interested in it either.

And so let's move on to behavioral techniques. I really liked what you said about the fact that you want to keep an agenda for patients, you want to keep it simple, but regular,. But you don't want to let individuals get bored. Because boredom can make agitation worse, it can be a breeding ground for agitation. At the same time, we don't want to overstimulate a patient, we don't want them, you know, take them to the EBM rave down the street. That could, you know, not really go well. So do you find that sometimes people will push a little too far at home and, you know, while they're trying to work out some of these things, and they need to be brought back in a little bit? Because certainly every patient and family is quite different.

Dr. Grossberg:
Yeah, I do. And I think that's an important point to make. I talk about frustration on the part of the patient. So I tell the care partners or the family member that yes, we want to introduce new activities, new kinds of interventions that might decrease behavioral issues like agitation. But if you're introducing a new activity, and you find that it's not working, or it's getting the patient more and more frustrated, because they can't - let's say you want them to do a complicated puzzle that they cannot do, like a jigsaw puzzle that's got too many pieces, and they're getting really frustrated. Take them away from that activity. So we want to design things that the patient can do well, without frustration, that they can feel good about doing. It may be something very basic and repetitive, like you've done the laundry now let, you know, the patient help you fold the towels.

Dr. Vega:
Right? Oh, that's great.

Dr. Grossberg:
They're okay with folding towels over and over again, as long as they feel that they're helping. So I think the key is to avoid frustration.

Dr. Vega:
Yeah, so many folks have been so useful, worked so hard their whole lives, you can't just let that go. And you know, it has to be a bit of a process there. And I really liked the term frustration. And you know, when one way the frustration you run is the care partners frustrated with the patient, because, 'Oh, now they're getting so much worse. And now they never want to get out of bed. And they're-' And so just reiterating talking to the patient is something I'll do in front of the care partner and say, 'Yeah, it's really hard even when you're so tired.' And they'll generally because we have rapport, they'll say, 'Yes. Yes, it is.' And that just kind of level-sets like and lets

that partner see in real time, just how much the individual patient's life is being affected, and puts them in a more empathetic state of mind so they can go home and do good work again. Sometime just a reset is really nice.

Dr. Grossberg:
Yeah. And of course, the care partner knows the patient best. So they know what their likes and dislikes are. So we talk about, for example, the benefits of music therapy, which can be quite substantial. A number of studies have shown that, but I'm reminded of an agitated Alzheimer's patient we admitted to our inpatient unit for difficult-to-control agitation, and he came to our afternoon music therapy session on our inpatient unit. And that afternoon, we were doing Frank Sinatra.

Dr. Vega:
Okay, right.

Dr. Grossberg:
And all the patients over there were enjoying Frank Sinatra. And he was getting more and more agitated. We found out later from his wife that he likes music, but he hated his whole life, Frank Sinatra. So even though he was quite cognitively impaired, it got him more agitated. So again, using the knowledge that the family has can be very, very helpful.

Dr. Vega:
I thought the punchline was going to be it was Tony Bennett. And then you realized he hates Tony Bennett.

Dr. Grossberg:
Whoever.

Dr. Vega:
It could be. So any other things you can share in terms of nonpharmacologic therapy when you know it's not working? Obviously, they're gearing the same level of agitation or worse, even if they're steady, but it's disturbing the family. I want to try to address it. It's time to think about pharmacotherapy. Any other things elaborate on, on that point?

Dr. Grossberg:
I think it's important, as we've pointed out in the other segments, to make sure we've done a thorough kind of evaluation for potential triggers of agitated behavior. One of the things that I often talk about is the importance of pain, where you have a patient who's cognitively impaired, they may be having significant pain, it could be joints or whatever, but they can't tell you that they're in pain. So when I hear from a care partner, for example, that their loved one is usually pretty, you know, mildly behaves, or is kind of calm generally. But then when you try to get them baits into the shower, or try to get them into their PJs at night, that hands-on care, all of a sudden they become very agitated. It could be that that movement is triggering pain or discomfort, so let's get them on scheduled analgesia.

And I think as far as knowing when things are not working, I take my clues from the care partner. And if they're, you know, contacting me saying, 'Well, gee, doctor, we tried all these different things, and, you know, my husband is still very agitated. In fact, he gets to a point where sometimes I'm worried, God forbid, he might even strike out. He's never hit me before. But I'm actually worried,' then we know that we need to go to another level of intervention, and that maybe pharmacotherapy is indicated.

Dr. Vega:
Is there a set amount of time where you might allow that nonpharmacologic approach to work, and then after several weeks, you want to go ahead and -

Dr. Grossberg:
Yeah, I mean, you want to give it time. But, you know, again, a lot of times if the situation becomes rapidly urgent –

Dr. Vega:
Sure, that changes everything.

Dr. Grossberg:

-to accelerate things.

Dr. Vega:
Okay, that makes sense. So speaking of that, let's talk about a case. We have an 81-year-old woman, she has a history of Alzheimer's dementia for 6 years, she's had a gradual decline in cognitive function while on treatment with donepezil and memantine. Her family says that she's becoming increasingly frustrated, angry over the past month, she's swearing at them while they perform routine caring tasks. She throws food around her room at least 5 times per week. And interestingly, 3 months ago, the patient was more withdrawn,

was crying more frequently. So you went ahead and put her on an SSRI, undifferentiated was started this time. And initially that helped her symptoms. And to continue this scenario, we do our homework, so we want to look at were there are other medications that have been introduced or something else that could be bothering her in terms of medication side effects? It's one of the easier things we can tackle, but that review is negative. A laboratory workup was performed, TSH, comprehensive metabolic panel, a CDC, all negative. For me, I want to know what was that SSRI? Because maybe it wasn't the best choice of an SSRI. You mentioned that having relaxing SSRIs was a better choice versus an activating SSRI. So not all SSRIs are created equal. And certainly with agitation in dementia, you know, there's different ones have been studied. And the results have been different as well. So I think that's one thing I want to look at. You know, what do you think of as next steps for her?

Dr. Grossberg:
Yeah, yeah, no, I agree with that as 100%. So we want to make sure that the right kind of agent with the right kind of calming profile was chosen. Let's assume for argument's purposes, that it was the right kind of profile. But then we also want to make sure that we get to the therapeutic dose. You know, as we often say, you know, this is at times of frail, cachectic, older adult-vulnerable population. And a lot of times all of us as clinicians are reluctant to really push the dose gradually to where it needs to be, and then to give it time to work. So I want to make sure that we have the right agent at the right dose for the right amount of time. That'd be very important.

And then, of course, we're always thinking, was there something else that could have been a trigger that I didn't think about? You know, we didn't mention checking a urine, but are they going more frequently to the bathroom than they used to. I had a patient just this past week in clinic, an older gentleman that was on an anticholinergic drug, that was having difficulty voiding. In fact, he was drinking a lot of liquids, but he was only voiding, according to his wife, like once or twice a day. And I said, wow, you know, having the urine kind of pool in the bladder, and the discomfort that is being caused, maybe was the trigger for his agitation. So getting them off of a drug that may have contributed, and then we added, you know, another drug to improve urinary flow, eliminated the agitation problem. So we're always thinking about other options.

Dr. Vega:
Yeah, I think it's very good. And it's good to think about other psychiatric issues that could be going on. We talked about some of the physical issues -

Dr. Grossberg:
You mentioned depression. That's a great point too. Could it be an agitated depression?

Dr. Vega:
Right. Right. So yeah, so - but say, we don't find that, you know, now we're thinking about another agent. So she's still on donepezil and memantine, and it sounds like that's actually done pretty well by her. She's not having side effects. I don't think I necessarily want to, you know, look to alter those to make a difference, you know, here. I will look at the SSRI more critically, but you know, when the behavioral intervention is not working, what would be your next choice? Where would you go next?

Dr. Grossberg:
I think, especially in the urgent situation, when the behavioral interventions are not working, you know, maybe we have an SSRI on board, but we don't have the luxury of time for that to kick in. Or even if we've used it for a while, it wasn't quite doing the trick, then we begin to think about alternatives to the medication that patient's on. Whether it's an antipsychotic medication, there's some utility for the anticonvulsants. The data is relatively sparse, as we mentioned. The one that's been most looked at is divalproex, as well as oxcarbazepine. But we might be thinking about a calming antipsychotic. As we mentioned earlier, the first generation drugs, you know, have just too many liabilities. Those are not the drugs that I want for this patient population. So I'm thinking about the second generation, the atypicals or one of the newer third-generation drugs.

Dr. Vega:
Okay. Right.

Dr. Greenberg:
And like you mentioned with the antidepressants, how do we pick the antipsychotic? Well, I'm not going to pick an antipsychotic that I think is going to activate the patient or I would want something that's more calming. I don't want to knock them out or sedate them too much. But I do want something that's more calming.

So there are a number of things that people try. We could talk about quetiapine. Again, the data is not great with good typing. But often people will go to that people will use olanzapine, another kind of calming drug. They may use something like aripiprazole, all of the, even the second-generation drugs, have a lot of liabilities. And there's a reason why it's the third-generation drugs that are actually now in development for agitation in Alzheimer's dementia.

Dr. Vega:
Yeah, that makes sense to me. But, you know, we're still worried, particularly with a black-box warning regarding earlier mortality associated with the use of antipsychotic drugs in this population. So I've seen it said, 'Well, you want to use a low dose and increase very slowly, if at all on that,' that makes sense to me. You also want to use it for a limited time. But we - you know, from - there's some research, which isn't, I think, a great body of research, which suggests that if they're going to be coming in with more severe agitation, discontinuing the antipsychotic is associated with a fairly high rate of recurrence. So how do you approach it, you know, in terms of talking to families about what's the chronicity of this drug? Is it just kind of a bridge that you want to, you know, maybe, you know, see if they can get over a difficult period? Or is this - do you really push this as 'Well, this is going to be something you're going to want to use over time?'

Dr. Grossberg:
Yeah, that's a really important question. And I don't think we have all the data to answer that question. So I've had people ask me, 'What's the natural history of agitation in Alzheimer's dementia?' And what I tell them is, is that we don't have sufficient controlled long-term studies over years to fully answer that question. But the limited data we do have is, as you pointed out, is that it tends to be a chronic problem. And when you eliminate or even try to cut back on the pharmacotherapeutic intervention, patients become agitated and some of the problems return. So what I tell the family is, is that this may be a long-term treatment, sure, but we're going to try episodically or periodically to see if we can lower the dose or maybe get rid of the intervention, just to see if we can achieve a period of stability without the behavior, without the drug. But often when you do that the behavior returns and you have to get back on what they're on. The good news is that newer agents, particularly the third-generation drugs, are generally better tolerated, even with longer-term use, and have less side effects, just overall better tolerability.

Dr. Vega:
There's a lot of good questions here. And I agree, it can be a major impact. Even as you mentioned, a small change in agitation can lead to an outsized impact in terms of care partners, and the way they feel is they are more likely to re-engage. I think it helps them stick to that behavioral schedule, because that's the foundation right? We can't stray away from that just because pharmacotherapy has been initiated. So I think that's a really good point is, you know, if you get a 5 to 10% reduction, people notice it.

Dr. Grossberg:
Yeah. And as small change for, let's say, you and me, might be a huge change for the care partner.

Dr. Vega:
Right. Absolutely.

Dr. Grossberg:
I'm just reminded of an anecdote, there have been concerns about the cholinesterase inhibitors and memantine that they're also not dramatic drugs. And the changes might be small, maybe compartmental 18:39, maybe over time, that – you know, I had a patient who, before these drugs were introduced, was getting frustrated every day because he couldn't figure out the remote control on his TV.

Dr. Vega:
Sure. I'm – go ahead.

Dr. Grossberg:
After treatment with these - with the combination therapy, he was able to figure out the remote control. Now that may seem like a small thing to me, but to his wife, that was huge.

Dr. Vega:
Oh, right. Right.

Dr. Grossberg:
Because it eliminated that frustration every day.

Dr. Vega:
Right. Yeah. So it's really kind of treating the patient where they're at, and the care partner using those reports to provide good care.

You know, this – it's still a little bit complicated. It's, you know, we don't have - these aren't FDA recommended therapies, you know, you are kind of moving in space. I would recommend getting though a couple agents in this - in that second-generation class, a couple agents in the third-generation class, and then trying to put your – although the third generation does seem to have some advantages in terms of tolerability, which is critical when you're talking about long-term therapy in folks who generally have a decline in function. But should we be, in primary care, be partnering with geropsychiatry, which, you know, which - and many of us don't have a friendly

neighborhood geropsychiatrist as yourself George, or psychiatry in geriatrics. What do you think?

Dr. Grossberg:
No, no, I mean, I think you're on the front line, Chuck. And I think, you know, primary care providers, healthcare providers, whether people in family medicine, general internal medicine, advanced practice nurses and PA's and so on, a lot of them, like you said, wish they had a consultant available. I'm doing virtual consults to a nursing home in rural northwest Missouri. They don't have a psychiatrist within 100 miles. That's why we're doing the virtual.

Dr. Vega:
Wow. Right, right. No.

Dr. Grossberg:
So I think it's important for the primary healthcare providers, like you said, to, you know, you don't have to know every drug, but to be comfortable with a couple of different drugs, maybe the second generation as well as the third generation. And then of course, we're all hoping that we'll have an FDA approved drug, which will give us more guidelines and maybe increase our comfort level with knowing what to do pharmacologically.

Dr. Vega:
And the side effect profiles for these drugs is, it's not insignificant. Do you find that you're able to use a low dose and get efficacy? Because I don't have the wealth of experience you have. But I've generally found that maybe more so than antidepressants in treating depression, that once you initiate a lower dose or a moderate dose, I usually get patients to goal in terms of reducing agitation, care partner status. So what's been your experience?

Dr. Grossberg:
You know, I agree, I agree. Of course, again, a lot will depend on the choice of agent. So we talk about in the antipsychotic world, we also talk about low-potency medications versus the high potency. So low potency, all that means is that you have to give a lot of milligrams, but the lot of milligrams really refers to psychosis, not to agitation. So I'm thinking of a drug, let's say, like quetiapine, which is a low-dose, kind of a second-generation drug, you may need to give higher doses if the patient's psychotic, but even the low doses might have a calming effect. Similarly, with olanzapine and a number of other drugs.

Dr. Vega:
Yeah, but I like what you said earlier. It's start low, go slow, not just start low. Yeah. And they just do that and then just peg it, and expect – yeah, expect miracles. Sometimes you - we need to, you know, continue to be actively monitoring these patients.

So George, thank you for this wonderful discussion. Do you have any final thoughts, things that really might help our audience with their clinic patients every day?

Dr. Grossberg:
Yeah, I have a couple.

Dr. Vega:
Sure, go for it.

Dr. Grossberg:
I think, first of all, it's a very important area. I mean, we want to keep in mind that we want to keep these patients at home as long as possible, as independent with their family as long as possible. We'd like to prevent, you know, premature, especially long-term care placement. And then after falls, severe behaviors, particularly agitation, in the context of Alzheimer's dementia, are now the leading reason for institutionalization. They're also the leading reason for that conscientious, loving care partner who's trying to do everything possible, hopefully with our help, finally throwing the towel in and saying, 'I just can't do it anymore.'

Dr. Vega:
Right. Okay.

Dr. Grossberg:
So whatever we can do, however we can evaluate and assess and intervene in these scenarios, has a huge payoff for both the patient as well as the care partner. And I can't emphasize that enough.

And then the importance of just asking about behaviors. Every patient that we see, who has cognitive impairment, comes with the family to make sure that we don't miss behaviors like agitation.

Dr. Vega:

Yeah, I can't put in a better. And I think that agitation also opens the door for partners to either neglect or abuse folks with dementia. And that is obviously one of the worst possible outcomes you can imagine. And I think you did a great job of elucidating this care ladder, starting with those very important nonpharmacologic approaches. Actually, starting with just a full assessment of the patient to look at reversible factors that can make a big difference. And then using those nonpharmacologic measures, followed by good pharmacotherapy. And I think that with a lot of those cases, when you follow that ladder, and you're taking care of and really paying attention to patients, you take that difficult clinical condition, and you solve it. You improve it, and that's incredibly satisfactory for all involved.

Dr. Grossberg:
Absolutely. And the other good news is, is that, you know, there are new treatments in the pipeline that are looking very promising. Hopefully, we'll get ever better tolerated and ever more efficacious treatments down the road for agitation in Alzheimer's dementia.

Dr. Vega:
Alright. Well, let's hope so. Thank you all very much for attending this series of discussions on agitation in dementia. Hopefully you found it helpful to your practice and very pragmatic. We know everybody's very busy, so it's very appreciated. Thank you again and be well.

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