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Released: 10/15/2024
Valid until: 10/15/2025
Time needed to complete: 1h 13m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Innovative Therapeutics: How Pathophysiology Guides New AAD Treatment Development

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Portsteinsson:
This is CME on ReachMD and I'm Dr. Anton Porteinsson. Joining me today is Dr. Brendon Montano.

Brendon, let's talk about how the pathophysiology of agitation in Alzheimer's disease and Alzheimer's disease guides treatment development. Let me start by pointing out that we now have disease-modifying treatments that target the beta amyloid plaques and can, within a relatively short order, eradicate those amyloid plaques. But it's important to understand that the patients that participated in those studies and where those medications are indicated, are very early in their disease. And those patients had almost no meaningful behavioral burden, so nothing in terms of psychotic symptoms or agitation or aggression. And the best we know for these medications is that maybe they can modify the emergence of neuropsychiatric symptoms, but they certainly don't play much of a role for acute treatment.

The same actually goes for the other Alzheimer's treatments, such as the cholinesterase inhibitor and memantine. In some situations, they may modestly help, in other situations it may harm. So, coming back to the pathophysiology, I think it is more important to understand the impact of the disease on neurotransmitters and that is that, the disease has a major impact on serotonergic pathways, on noradrenergic pathways, on dopaminergic pathways. And this knowledge has informed us in terms of medication that are being developed or designed, as well as medications that maybe are seeking an expanded indication or being repurposed for the treatment of agitation in Alzheimer's disease. And there's certainly is a tremendous need out there for effective treatments.

I want to point out that right now, there's only one drug that is FDA approved for this indication that is agitation in Alzheimer's disease, and that is brexpiprazole. There are multitudes of other medications that are used off-label and we have to be careful about that, as we covered in another episode. And that there's also numerous medications that are currently in development. And most of these medications focus on those neurotransmitters that I mentioned before or some novel aspects such as the cannabinoid receptors and we will hopefully see more medications that become available to us for this purpose. But right now, we still have just one.

But Brendan, what would you like to add?

Dr. Montano:
Well, I agree with everything you said, Anton. The only other thing I can say is that we have been using genetic testing in the sense of the little swabs that you use to send out and see if there are any drug-drug interactions or perhaps genetic changes in the liver pathways that can make you more susceptible to adverse events associated with the use of many drugs. I know that I was once medical director at a nursing home and in that capacity, the average number of drugs that a person was on was somewhere in the 13 every month. Thirteen drugs. So, there’s lots of room for drug interactions, and there's lots of room even in the diet with grapefruit juice and

things for drug interactions.

I think, having as much information as possible is going to make it much less likely that you're going to enter into any unwanted problems. Keeping inflammation down also is something that we like to do. Inflammation even peripherally, I understand, can have adverse effects in the central nervous system with agitation in Alzheimer's, and so anti-inflammatory protocol, looking for anything that's not been treated properly peripherally in the body, other than in the brain, I think is also valuable.

Dr. Porteinsson:
Brendon, thanks for a great discussion and thanks to our audience for tuning in.

Announcer:
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