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Parkinson's Disease Psychosis: Watchful Waiting vs Proactive Treatment

Announcer:
Welcome to CME on ReachMD. This activity, entitled "Parkinson's Disease Psychosis: Watchful Waiting vs Proactive Treatment" is provided by MedEdicus LLC and is supported through an educational grant from ACADIA Pharmaceuticals Inc.

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Dr. Caudle:
A 65-year-old woman with Parkinson's disease comes in for a follow-up visit. Her tremors are well controlled at this time. Her husband states that she leaves the dryer on continually in the house. The patient notes that everything she touches in the house feels wet. So she keeps throwing items in the dryer all the time. What's going on? And is it important?

I'm your host, Dr. Jennifer Caudle, and I'd like to welcome Dr. Kevin Black, professor of psychiatry, neurology, radiology, and neuroscience at Washington University School of Medicine in St. Louis, Missouri. Dr. Black is joining me to share his insights on the importance of early identification and evidence-based management of psychotic symptoms in our patients who have Parkinson's disease. Dr. Black, welcome to the program.

Dr. Black:
Thank you. I'm glad to be here to share some of my thoughts about one of the challenging non-motor aspects of Parkinson's disease.

Dr. Caudle:
Yeah, this is actually a very important topic, and 'm really glad that you're here. So let's just dive right in. Dr. Black, why is a diagnosis of Parkinson's disease psychosis such a big concern?

Dr. Black:
So psychosis is a very serious complication of Parkinson's disease for a number of reasons. First of all caregivers are already stressed out, of course, but they tend to rate psychotic symptoms as among the most difficult and stressful for them to deal with, much more than say difficulty walking even.

Second, occasionally psychotic symptoms can lead to very serious consequences, including violence. For instance, if someone has a delusion that they're being attacked they might attack back.

Next psychotic symptoms are identified as the reason for almost a quarter of all hospital admissions for people with Parkinson's. And as similarly, Parkinson's patients who also have hallucinations, are two and a half times more likely than other PD patients to be admitted to a nursing home.

And finally the three-year mortality rate for Parkinson's patients who also have psychosis is about 40%. So not trivial at all.

Dr. Caudle:
And how can a clinician identify Parkinson's disease psychosis in the early stages?

Dr. Black:
Right. So you have detecting symptoms, and then you have making a diagnosis.

So as far as detecting symptoms the problem that we face is that patients often underreport symptoms of hallucinations or delusions for several reasons. This could include because, you know, it's embarrassing. It could be because sometimes patients have cognitive impairment or lack insight into the abnormal nature of the symptoms. Or in some cases, I've seen patients who knew it was a problem, but had no idea that it was related to their Parkinson's or his treatment. And the way to address that problem is by proactively asking patients about this symptom during the appointment, just like you would ask about orthostatic hypotension or just like you would ask about dyskinesias. One way that I like to ask the question is, does your mind ever play tricks on you? Because it doesn't sound negative or critical or pathological even. And, of course, you get into specifics like do you ever see or hear or feel things that aren't there that other people don't see?

As far as making the diagnosis the first step is really to rule out infections or side effects of drugs that could be causing delirium with hallucinations and delusions.

I guess the other factor would be to have your hackles raised, so to speak, you know, to be more on the lookout for psychotic symptoms in patients with longer duration of PD greater severity of Parkinson's, and on more anti-Parkinsonian medications, especially anticholinergics and dopamine agonists.

Dr. Caudle:
Thank you for that. And what does the psychosis spectrum in Parkinson's disease consist of?

Dr. Black:
So early symptoms are not necessarily pathological. And they can include transient very brief hallucinations. They could also include what are called presence hallucinations, which is kind of that creepy feeling that there's somebody standing behind or that somebody just walked by or illusions. And the classic example of an illusion is like you wake up and you're scared because there's somebody in your doorway and then you turn on the light, you realize it was just your rope hanging there. So an illusion is a real percept that you misinterpret.

And then on average, as the disease progresses the next most common symptom would be visual hallucinations. You know, typical like I'm seeing somebody sitting there at the dinner table that's not there. Initially, this can be, you know, not a disconcerting experience. For example, I remember one patient that was laughing when she came to the office and she said, 'I turned around and looked in the backseat, and there was Mr. Clean, that guy from the commercials.' And she knew it wasn't real, she laughed about it. But as the disease progresses often people lose insight, and they believe that their experiences are real. And this can of course, lead to delusions, where you have a fixed false belief that is idiosyncratic to yourself. Of course, individual patients are going to be different in how they experience these different symptoms over time.

Dr. Caudle:
Very helpful.

And for those of you who are just joining us, this is ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to talk about the management of psychotic symptoms in patients with Parkinson's disease is Dr. Kevin Black.

So now that we've talked about diagnosis and detection, let's take a look at treatment. So, Dr. Black, how do you decide when to initiate Parkinson's disease psychosis treatment?

Dr. Black:
Right. Well, that's a key question, isn't it? And we can be guided to some extent by the evidence that we have, and by the typical considerations that you make in everyday medical practice of weighing benefits and risks. So for what are sometimes called minor psychotic symptoms, such as illusions, or the passage or presence hallucinations there's much less evidence as to whether treatment makes a difference. And so often I'll hold off on active treatment in those cases. But there is substantial evidence for efficacy for treating typical visual hallucinations or delusions.

One of the reasons for early treatment, which is what I tend to prefer is that symptoms are often quite bothersome to patients or caregivers. As one example, if you are a patient who believes that someone's trying to harm you, that's a scary sensation, it's very uncomfortable and it kind of ruins your life at the moment. But imagine the caregiver who has to deal with addressing, you know this in conversation or, let's say dealing with it if the patient calls 911.

Additionally, it would be too late to wait for severe problems to develop to start treatment. We want to try to prevent the bad complications of psychotic symptoms, not wait for them to happen first.

And finally, we do have some evidence for starting treatment earlier. In a careful, longitudinal observational study of a large Parkinson's center they tracked patients after the very first time in the chart that it was noted that they had hallucinations, even with insight. So relatively mild symptoms. And those patients who were started on an anti-psychotic after that point had a much better outcome. Specifically, it took much longer for them to develop severe hallucinations with loss of insight or to develop delusions. This suggests that earlier treatment beginning even when symptoms appear relatively benign probably leads to better clinical outcomes.

Dr. Caudle:
It's helpful. And what can we do to optimize the treatment then of Parkinson's disease psychosis?

Dr. Black:
The first step is to make sure that there's not delirium due to another illness or due to a non-Parkinson's medication. And often it helps to simplify or remove other medications that affect the brain such as opioids or benzodiazepines.

But the next step is to simplify the anti-Parkinsonian medication regimen. Generally, this involves removing anticholinergics in a stepwise fashion, then amantadine, and then dopamine agonists. And since this will probably result in worsening of the motor signs you'll generally have to balance that by increasing the dose of carbidopa levodopa. And trying to cut back on levodopa would be the last step.

At this point, many patients however, are going to have enough clinical worsening that in terms of their Parkinsonian signs, that they need something different. And at this point is when you generally add an anti-psychotic.

Now there are three anti-psychotics that have been judged clinically useful for PD psychosis according to the Movement Disorder Society published guidelines. They are pimavanserin, clozapine, and quetiapine. So to take them one at a time.

Pimavanserin is the only FDA approved agent. It's a serotoninergic drug and it is not a dopamine agonist which is probably why it is better tolerated in that there are no motor side effects of using it, as opposed to all the dopamine antagonists anti-psychotics.

Clozapine it would be an off-label use to treat for Parkinson's psychosis. But there's very substantial evidence showing that it's clinically effective. The main downside is a practical one that it's use requires initially weekly blood draws that eventually space out somewhat in time. And this is somewhat of a hassle, both for patients and for clinicians and pharmacies.

Finally quetiapine may be the most commonly used anti-psychotic in Parkinson's disease psychosis. But again, it's an off-label use and there's really no evidence for efficacy. In other words, there have been four or five randomized control trials, and in no case did the prespecified outcome improve more with quetiapine than with placebo.

Now, once we talk about anti-psychotics in Parkinson's, it's worth noting that all of them have a blackbox warning that says that there's increased mortality in elderly patients with dementia-related psychosis when they're treated with anti-psychotics. The label of course for pimavanserin is altered to say it's not approved for treating patients with dementia-related psychosis unrelated to its actual indication unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis.

Dr. Caudle:
Okay, and Dr. Black, before we close, are there any key take-home messages that you'd like to share with our audience?

Dr. Black:
Yeah, thanks. The way I'd summarize it is this. Psychosis is actually fairly common in Parkinson's disease as it progresses over time. One estimate is that maybe half of patients will experience it at some point in their illness. But you may have to look for it to know that it's there, because patients don't always tell you. Untreated, it can cause serious problems, including difficulties with care for caregivers hospitalization, or even death. But fortunately, it is treatable.

Dr. Caudle:
And that's a great way to round out our quick overview discussion on Parkinson's disease psychosis. I'd like to thank our expert, Dr. Kevin Black, for helping us better identify PDP early and initiate effective treatment. Dr. Black, it was great speaking with you today.

Dr. Black:
My pleasure. Thanks.

Announcer:
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