Transcript Details

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The Impact of Individual Autonomic Domains in Parkinson's Disease

Dr. Lisk:
Up to 70 percent of patients with Parkinson's disease experience impairment of the autonomic nervous system, which may be an indicator of more aggressive disease progression. So what do we need to know about the impact of individual autonomic domains?

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Jerome Lisk. And joining me to discuss a recent five-year observational study that aimed to determine the impact of individual autonomic domains associated with Parkinson's disease is Dr. Katherine Longardner, who is an assistant professor of neurosciences at UC San Diego Health.

Dr. Longardner, welcome to the program.

Dr. Longardner:
Hi. Thanks so much for having me.

Dr. Lisk:
Okay. Well, let's jump right in, Dr. Longardner. What were the objectives of your research?

Dr. Longardner:
So the main goals of this research were to determine the five-year risk of clinical milestones in Parkinson's disease, which we defined as dementia, falls, postural instability, dysarthria, and dysphagia, comparing people with and without autonomic impairment at baseline and to see how the different autonomic symptoms—and when I say autonomic symptoms, I'm talking about lightheadedness on standing from orthostatic hypotension, loss of bladder control, constipation, problems with sweating, for example—and how these symptoms affected the clinical milestones, and also activities of daily living and health-related quality of life.

Dr. Lisk:
Okay. So tell the audience how your study was designed and your inclusion-exclusion criteria.

Dr. Longardner:
Sure. So these patients were recruited from a movement disorders clinic in Torino, Italy by the co-authors, and they were defined as having clinically diagnosed Parkinson's disease for at least two years, aged between 18 and 80 years, but all of them were much older than 18 and having a stable dose of dopaminergic therapy and stable dose of medications that could affect blood pressure for at least four weeks before they were recruited. People were excluded if they had neurological signs that suggested a diagnosis besides Parkinson's disease or if they had diabetes mellitus or other conditions that could cause autonomic impairment.

Dr. Lisk:
Okay. And can you enlighten us on some of the scales that you used for the study?

Dr. Longardner:
So for the autonomic symptoms, we use the SCOPA-AUT. That's a questionnaire that participants answer themselves about autonomic symptoms over the past month, and this includes questions about trouble swallowing, excessive saliva, constipation, urinary function, sexual function, lightheadedness on standing, fainting, excessive sweating, and intolerance to extreme temperatures, for example. The other scales that we used in the study include the MDS-UPDRS. That's a four-part questionnaire that includes non-motor symptoms of Parkinson's disease, as well as an objective assessment of motor performance by the movement disorders doctor and questions about motor symptom fluctuations. We also used the PDQ-8, which is a measure of health-related quality of life in Parkinson's disease.

Dr. Lisk:
Can you tell us about some of your key findings in the study?

Dr. Longardner:
Sure. So we assessed patients at baseline and then a five-year follow-up, and the main findings were that people who had orthostatic hypotension at baseline had a seven times higher risk of developing dementia and a five times higher risk of falls compared to those that did not have orthostatic hypotension symptoms at baseline. Those with orthostatic hypotension symptoms at baseline also developed worse impairment in activities of daily living and health-related quality of life compared to those without. Interestingly, none of the other autonomic symptoms, such as urinary dysfunction, constipation, heat or cold intolerance, for example, had any relevant associations between these clinical outcomes, so orthostatic hypotension alone, among the different autonomic symptoms that we looked at, was associated with worse outcomes.

Dr. Lisk:
And so the five milestones that you looked at in the study to show decline in disease progression, can you tell us what those were? And how did you assess them?

Dr. Longardner:
Yes. So the milestones were dementia. We used the Montreal Cognitive Assessment score. We used a score of less than 21 out of 30 points; falls, that was by self-report of number of falls in the past four weeks; postural instability, that was assessed by the pull test—That's a standardized part of the MDS-UPDRS part 3 item 12—And dysarthria and dysphagia, that was from the MDS-UPDRS non-motor symptom scales.

Dr. Lisk:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Jerome Lisk, and I'm speaking with Dr. Katherine Longardner about the impact of individual autonomic domains in Parkinson's disease.

So with those findings in mind, Dr. Longardner, how were the patients' quality of life impacted, and what were the scales you used for quality of life?

Dr. Longardner:
So the patients with orthostatic hypotension had worse health-related quality of life at the five-year mark. And we used a scale called the PDQ-8. That is specifically for people with Parkinson's disease who self-report their quality of life. We also used the composite score of the MDS-UPDRS parts 1 and 2 that assess the non-motor and motor symptoms in their daily life and used that for the global experience of daily living, and those scores were also worse in people with orthostatic hypotension.

Dr. Lisk:
So, Dr. Longardner, you looked at several different types of autonomic dysfunction, or dysautonomia, in Parkinson's disease. Can you tell me if any of these other ones had an impact on disability or progression to dementia?

Dr. Longardner:
No. So that's the interesting thing. So we looked at both the all-together score of all of the autonomic symptoms and the individual autonomic symptoms in this group, and only the cardiovascular dysautonomia, that is NOH, was associated with worse outcomes.

Dr. Lisk:
That's very interesting. And so, why do you think that neurogenic orthostatic hypotension causes dementia and leads to further cognitive decline and disability?

Dr. Longardner:
Well, I should say we don't know that it's a causative relationship. That's something that needs to be determined by other studies, but that's the debate is whether it is causative or if it's just associated for other reasons. My own hypothesis and I think this is shared by several of the co-authors, is that these repeated episodes of low blood flow to the brain can either accelerate or cause worse neurodegeneration in people with Parkinson's disease, but that hasn't been proven yet, and our study certainly doesn't prove any causation.

Dr. Lisk:
So let's look ahead for just a moment. What additional research may be needed in this area?

Dr. Longardner:
I think you brought up the good point that we don't know whether orthostatic hypotension is causative of these worse outcomes, and so I think the important studies would be to look at this as a modifiable risk factor for these worse outcomes and do large prospective studies seeing whether treating NOH can make a difference on these worse outcomes.

Dr. Lisk:
So let me ask you another question, Dr. Longardner. In clinical trials with NOH with a medication such as droxidopa, they seem to be more effective in patients that have larger drops of more than 30 points. Did you notice any differences in patients that had larger drops, say 30 points or more, versus patients that had drops less than 20 points from laying to standing in blood pressure?

Dr. Longardner:
Well, we didn't look at that in this study. In my clinical experience, I think it's hard to say, to be honest, because people can have dramatic fluctuations in blood pressure and still be asymptomatic even with very large drops and very low blood pressure.We need more larger prospective studies to evaluate those, but based on my clinical experience, often times treating the orthostatic hypotension does make people feel better. There's a lot of symptoms of NOH that often go unrecognized. It's hard in people with Parkinson's disease to identify this sometimes because they're having fluctuating symptoms from many things; from the disease itself, from taking levodopa, from the side effects of levodopa, from wearing off of medicine, so it can be hard for them to isolate the symptoms from NOH, and it could be many things besides lightheadedness, dizziness, or feeling of fainting. It can cause visual changes, cognitive changes, fatigue, generalized weakness, knees buckling, and sometimes it can be asymptomatic, as well, and we don't know the clinical implications of asymptomatic orthostatic hypotension. Some of the co-authors of this research paper that we're discussing have published on the relevance of asymptomatic orthostatic hypotension, and they show that people who have Parkinson's disease with orthostatic hypotension have worse outcomes regardless of symptoms, so even if they don't feel bad, they still have worse outcomes.

Dr. Lisk:
That's very important. And I would like definitely for our audience to know, as Dr. Longardner also can attest to, is that the non-motor symptoms of Parkinson's disease, such as autonomic dysfunction, can be more disabling or as disabling as the motor symptoms, and patients don't need to have lightheadedness or dizziness when standing to have symptoms of neurogenic orthostatic hypotension that

lead to falls. Sometimes just leg weakness is enough, as she mentioned before.

Dr. Longardner:
Absolutely. And I think that NOH is so important for providers and patients to be aware of because we have so many different treatments for it. So it's a treatable problem, but I think it's under-recognized.

Dr. Lisk:
And before we close, Dr. Longardner, were there any additional thoughts you wanted to share with our audience today?

Dr. Longardner:
Yes. I would just make a plug that to diagnose orthostatic hypotension is something that patients can do on their own at home or doctors can do in the office, and it just involves blood pressure measurements. The patients would be sitting down or lying down for five minutes and then measure their blood pressure, and then stand up for one minute, measure their blood pressure again, and stay standing for a total of three minutes and measure it again at three minutes, and that's sufficient to diagnose it.

Dr. Lisk:
So, Dr. Longardner, you are doing very important work, and keep on bringing these things to light. These are certainly important findings as it relates to our patients with Parkinson’s disease. I want to thank my guest, Dr. Katherine Longardner, for a great discussion, and especially all the work that you're doing in Parkinson’s disease. It was a pleasure talking to you today. I'd love to have you back.

Dr. Longardner:
My pleasure. Thanks so much for having me.

Dr. Lisk:
For ReachMD, I'm Dr. Jerome Lisk. To access this and other episodes in our series, visit ReachMD.com/NeuroFrontiers where you can Be Part of the Knowledge. Thank you for listening.