

Episode 94: Understanding Neurogenic Orthostatic Hypotension

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Dan Keller: Welcome to this episode of *Substantial Matters, Life, and Science of Parkinson's*. I'm your host, Dan Keller. At the Parkinson's Foundation, we want all people with Parkinson's and their families to get the care and support they need. Better care starts with better research and leads to better lives. In this podcast series, we highlight the fruits of that research, the treatments, and techniques that can help you live a better life now, as well as research that can bring a better tomorrow. A potentially troublesome non-motor symptom occurring with Parkinson's disease is neurogenic orthostatic hypotension, abbreviated nOH, and also called postural hypotension.

It's a sharp drop in blood pressure when standing up from a chair or getting out of bed, and is estimated to affect almost 60% of people with PD. It often occurs in the mid to late stages of the disease but may be present much earlier with or without symptoms. In general, it's associated with older age and longer duration of the disease. The arrival of new treatments to address orthostatic hypotension in PD makes it even more important for clinicians to detect the condition to be able to offer treatments to people who need them.

I spoke with neurologist, Dr. Katie Longardner of the University of California, San Diego, who discussed some of the symptoms, therapeutic strategies, and outcomes of orthostatic hypotension. This podcast is sponsored by Theravance Pharmaceuticals. All content is the responsibility of the Parkinson's Foundation. I first asked Dr. Longardner, if she would break down the terminology of neurogenic orthostatic hypotension for us.

Dr. Katie Longardner: I'll start with orthostatic hypotension, that is a drop in blood pressure when standing up. It's defined by a drop in systolic blood pressure, that's the top number when you measure your blood pressure of at least 20 millimeters of mercury or 20 points or a drop in diastolic blood pressure, that's the bottom number of at least 10 points after changing position from either sitting or lying down flat for at least five minutes. When you go from that position to standing up within three minutes.

If your blood pressure drops by 20 on the top number or 10 on the bottom number within three minutes of standing up, that is what we call orthostatic hypotension. The neurogenic part means that the drop in blood pressure is due to a problem with the nervous system, specifically what we call the autonomic nervous system that controls your blood pressure, meaning it's due to a problem with the nerves, not medication or dehydration or some other cause.

Dan: Do you find in Parkinson's disease that it's particularly prevalent? What percentage of people might experience it over the course of their disease?

Katie: Great question. The studies have shown that somewhere between about a third and about half of people with Parkinson's disease can have orthostatic hypotension. It is very prevalent. It's something I'm interested in because I think it's relatively under-recognized.

Dan: Now you said not related to medication. I take it is a cause inherent in the disease but also can medication also add to it, medication for Parkinson's?

Katie: Yes, and yes. The disease itself can cause this problem. In Parkinson's disease, the main cause of orthostatic hypotension is a lack of the chemical norepinephrine, that is a chemical that works on the blood vessels to constrict the blood vessels. When that chemical is lacking, the blood vessels don't constrict properly when people stand up, leading to low blood pressure. It is a problem from the disease itself. However, the medications that we use to treat Parkinson's disease including levodopa, that is the mainstay of treatment can also lower the blood pressure, but it's from the disease itself.

Dan: You said that it's diagnosed by a drop in blood pressure within three minutes of standing up. How long does it last?

Katie: Good question. It could last only a few seconds, or it could last for minutes or it could happen after three minutes, and that's what we call delayed orthostatic hypotension, meaning that it doesn't happen right away within a few minutes. Sometimes people might have this problem after standing for five or 10 minutes or even longer.

Dan: Is it mainly diagnosed by patients' reported symptoms, or do you do specific tests in the clinic, measure blood pressure, different positioning to really nail it down?

Katie: That's a great question. The way that we diagnose it is, as you said, measure the blood pressure in different positions. That could be done in a clinic, or in a special laboratory setting with a tilt table. That is exactly what it sounds like I said, sort of Gurney-like bed or table that the person lies on, secured with straps, and it can be raised and lowered at different angles to simulate standing up. We measure the blood pressure in different positions to make the diagnosis.

However, when we do either of those tests, it just represents a snapshot of the person's day. Just because they don't have orthostatic hypotension when we do those measurements, doesn't mean they don't have it at all, so we might miss it, doing those tests. With regard to your question about symptoms. A lot of people who have this, orthostatic hypotension, are asymptomatic, meaning that they don't have the classic symptoms that we think of associated with low blood pressure, such as feeling light-headed, or dizzy, or foggy, or faint, or having vision changes. Those are just a few of the most common symptoms. People can have very low blood pressures without having symptoms.

If they don't report symptoms, a lot of times people don't check for it. We don't know yet the clinical relevance or what is the importance of having low blood pressure without symptoms.

Dan: Right. What are some of the effects of orthostatic hypotension? What happens to the patient? Are there risks?

Katie: The risks are the symptoms, as I mentioned, a feeling light-headed or dizzy, sometimes can cause people to fall and hurt themselves from the fall or even faint or pass out.

Dan: When in the course of disease does it occur? Is it from the start or anytime or only late?

Katie: Great question. We used to think that it's a later manifestation. A lot of research has come out recently showing that it can be even the first sign of Parkinson's disease occurring many years before the other symptoms. It could happen at any point in the disease and in some cases, might be the first symptom that happens years or rarely, decades before the other symptoms become apparent.

Dan: When should a person see a doctor for this? Should they come in with some record or idea of what causes it or what they were doing or when it happens?

Katie: Yes, I think any time someone with Parkinson's disease or anyone that's having some symptoms that are worse when they're standing up or symptoms when they stand up should see a doctor about this to be evaluated. I think it's important to address early on since there are treatments and measures that one can take to improve it. I've seen before that [unintelligible 00:09:00] such as dehydration or sometimes over-the-counter medications can worsen orthostatic hypotension. That can lead to problems such as falls or fainting, which can really be a big problem. That's what we're trying to avoid.

I think that anytime anyone has any symptoms when standing up, or if they notice when they're measuring their blood pressure routinely, that it's low, they should talk to their doctor about it. In terms of things to bring, it's helpful for people to measure their blood pressure and the physicians as we would do in clinic and that would be either sitting or lying down quietly at rest for at least five minutes and then standing up and measuring the blood pressure again at three minutes. Each doctor might have a slightly different way of instructing the patient to measure the blood pressure but that is sufficient to measure the change from lying or sitting to standing.

That's helpful information to have, especially since when we see of someone in clinic, it's just a snapshot of their day. The more data points we have, the more likely we are to make the diagnosis if it's present.

Dan: There are so many things that can cause orthostatic hypotension, endocrine problems, thyroid, anemia, all sorts of things. If someone comes in with it, who has Parkinson's disease, do you run a full metabolic panel or do you assume first off Parkinson's is the cause?

Katie: Yes, I think that's a great question. I think sometimes when a person has Parkinson's disease, we tend to blame a lot of the symptoms on Parkinson's disease. It's important to remember that they might have more than one thing. I do recommend getting blood work and checking for other causes if that hasn't been done recently.

Dan: What are some of the possible treatments - ones you can provide or ones that people can do for themselves?

Katie: There's two main categories of treatments. One is non pharmaceutical or non-medication and the second kindest medication, whenever anyone sees me with orthostatic hypotension, the first step is to look at their current list of medications and

supplements and see if they're on anything that could be lowering their blood pressure and to first eliminate anything that might be lowering the blood pressure, of course with the collaboration of their primary care doctor or cardiologist, whoever's prescribing the medication. Oftentimes people are on anti-hypertensives or might be on other medications such as antidepressants or medications for prostate enlargement that could lower the blood pressure.

First to eliminate anything that could be worsening the situation. The next thing after eliminating medications is to do non-pharmacologic measures, that includes drinking plenty of fluid, at least 64 ounces or two liters of water a day, adding extra salt to the diet, at least 1 to 2 teaspoons of extra salt. There are devices such as abdominal binders that is a cinch that goes around the waste and compresses the veins to increase blood flow back to the heart that can improve the problem or compression stockings that come up to the waist. Also, lower body strengthening exercises can help by strengthening the leg muscles that also squeezes blood from the legs back up to the heart to improve the circulation.

Those are all some things that people can do to improve the problem without medications.

Dan: What about elevating the head of the bed since they would then start in a little bit more upright position when they get up?

Katie: Yes, that is another important thing to do. We usually tell people to buy a furniture wedge that you can put underneath the mattress, that elevates the head of the bed. Other things that people can do include eating smaller and more frequent meals because sometimes a large meal can divert blood to the organs of digestion away from the circulation again, and that can improve the problem and to avoid alcohol, which can also drop the blood pressure more. The simple thing to do is to be slow when changing positions from sitting or lying to standing and not jumping up.

Dan: What outcomes do you see both good and bad in the long term?

Katie: Yes, it's a hard problem to treat because it's always fluctuating - blood pressure is so dynamic and changes minute by minute in response to position and internal and external factors. I think the worst outcomes are what we're trying to avoid. That is the fainting or the falling resulting in fractures or injuries or hospitalizations. In terms of the good outcomes, I have seen people that are treated appropriately and their symptoms are much better and their daily function is much better. I think it's important to realize that this is a treatable problem. It's not an easy problem to treat but we do have treatments. I'll just mention briefly the agents that we have available to treat orthostatic hypotension.

One is Fludrocortisone, that is a steroid type of medication, Midodrine, and Droxidopa are two others that are FDA-approved for orthostatic hypotension, and Pyridostigmine is another one that we sometimes use, but certainly, we need more options to treat this problem. All of these medications work by increasing the blood pressure and they should be taken in the first half of the day, because one thing I didn't mention yet but it's the flip side of orthostatic hypotension is that oftentimes people with orthostatic hypotension, that is low blood pressure when standing, will have too high of blood pressure when laying down.

That's what we call supine hypertension and so the problem is a dysregulation of blood pressure that it's too low when they stand up and too high when they lie down and so for that reason, it's an especially hard problem to treat since we're aiming for somewhere in between and medications that raise the blood pressure when people stand up also would then raise it when laying down. That complicates the treatment.

Dan: Are there trials in this area and can they benefit people by joining them?

Katie: Yes, there are trials. We are looking at different agents that can help to treat the symptoms. There's a few trials ongoing investigating new therapies.

Dan: I looked at a couple of your-- An abstract and a paper. You have this paper on cognitive decline after orthostatic hypotension. Is it more of a marker or a causative process possibly through decreased cerebral perfusion, probably in short bursts might account for that, I would guess or is it a marker of neuronal dysfunction, something else of which may be leading to the cognitive decline?

Katie: That's the golden question and that is what I'm interested in setting, we don't know. It could be both, it could be that orthostatic hypotension over time contributes in some way to cognitive dysfunction by damaging the brain from, as you said, repeated hypoperfusion, or it could be that people with orthostatic hypotension have a more severe form of a disease and it's a marker. That's what we have not figured out yet, but my hypothesis and what I'm interested in studying is if we modify orthostatic hypotension by treating the low blood pressure, could we prevent some of these outcomes of worse falls and worse cognition and more hospitalizations.

Dan: That's a moderately long study. I would take it.

Katie: Yes, it's going to be in parts but many people are studying the same disease process and so hopefully with collaboration we can answer some of these important questions because I think anything that we can do to prevent cognitive decline is a huge improvement for people with Parkinson's disease.

Dan: Have we missed anything important or anything interesting to add?

Katie: Yes, I would just add, as I said and emphasize that just because people don't have symptoms doesn't mean that they shouldn't be screened for this problem. My research interest is, and others are studying this too, is that there may be similar problems from orthostatic hypotension in terms of falls, hospitalizations, and function, regardless of whether people exhibit the classical symptoms of lightheadedness and dizziness. I think it's important for anyone with Parkinson's disease to be screened for this using the positional blood pressure measurements as we discussed.

Dan: Very good. I appreciate it. Thank you.

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Dan: More information on neurogenic orthostatic hypotension is available in our series of expert briefings at parkinson.org/EB. One, by Dr. Ronald Pfeiffer from January 2019 called, Non-motor symptoms: What's new? says the condition occurs in almost 6 in 10 people with PD, many of them without symptoms. The expert

briefing describes the problem, the goals of treatment and some nonpharmacologic and pharmacologic approaches. You can also find fact sheets and publications addressing nOH by visiting parkinson.org/library. Medline plus at Medlineplus.gov has extensive information about orthostatic hypotension, including information on some of the drugs used to treat it.

If you're interested in reading about clinical trials or even possibly participating in one, take a look at clinicaltrials.gov and search the site for orthostatic hypotension and Parkinson's disease. The site lists several trials being conducted in the US and internationally, as well as the results of some completed trials either on the site, or via links to publish papers from the studies. As always, our PD information specialists can answer questions and provide information in English or Spanish about today's topics or anything else having to do with Parkinson's. They can also help you find a neurologist in your area specializing in movement disorders. You can reach them at 1-800-4PD-INFO.

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