

Episode 109: Medication Timing

[music]

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 long-standing debate in Parkinson's disease has centered on when to start medication to treat symptoms in the early stage of the disease, and whether doing so will limit its usefulness later.

In this episode, Dr. Indu Subramanian of the West Los Angeles Veterans Affairs Medical Center discusses the current thinking on this question and dispels myths and misconceptions. She also provides some strategies for optimizing beneficial effects of medications and minimizing side effects such as blood pressure drops and gastrointestinal upset. She says the key is to have an ongoing dialogue with your doctor to understand why you're taking a medication, what the effects and side effects are, and to design ways to make the medication most effective and least troubling.

Dr. Subramanian trained in modern Western medicine, but also became interested in and is board certified in integrative medicine; the intersection of Western medicine and traditional healing practices. When we spoke she described why she believes that integrating the different approaches can be especially beneficial for people with Parkinson's. First, I asked her thoughts on when people should consider first starting a medication for their Parkinson's.

Dr. Indu Subramanian: Well, I think that this has been kind of controversial and a bit confusing, and I think the media has confused things. The pendulum has swung a little bit this way and that way over even the last 20 years that I've been a Parkinson's doc. I think there's been some dialogue that's shifted. With my understanding of the current literature, I personally have the sense that patients should start on dopaminergic therapy or anti-Parkinson's therapy, or whatever you want to call it. Basically, a Parkinson's medication that's going to change dopamine.

They should start that medication when they start to have symptoms that get in the way of their daily life activities, or if they have symptoms that are affecting their ability to exercise.

Dan: Are there misconceptions or myths or reservations about starting medications? I think some of it is called levodopa phobia.

Indu: Yes, absolutely. I think patients have really been sold this story that levodopa could be toxic, and we have studies that show that it is not toxic. In fact, it may be beneficial for helping brains to stay happier. Some of those studies are not very clear because people are moving better. They're able to do more, they're more connected with their daily life functioning. They're exercising more. We think that many of these things are beneficial for the brain too, so it's a little tough to control for those

variables. I really do think that there's been the sense that levodopa should be spared, kept in the back pocket until you're absolutely not able to move well.

Really, that there's a very limited timeframe in which levodopa is going to be effective. I think that those are really myths. We have a sense that one should start levodopa when either their other medications are not functioning well enough to keep them exercising and living a full good quality of life and do their activities of daily life well. That would be when you would start levodopa. I really think that this delay, or keeping it in the back pocket until people are absolutely needing it, definitely sets people several years behind, because what ends up happening is people don't exercise. Sometimes they get asymmetry of movement.

I have a background in yoga teaching, and it's not fun to teach a Parkinson's patient when they're really having a lot of difficulty with that asymmetry of movement. Sometimes that asymmetry, because of untreated motor symptoms, can actually put the spine at risk. It can put the lower back at risk. It can put the joints at risk. Some of these patients end up having hip injuries, knee injuries, shoulder injuries. Really, it's from not adequately treating motor symptoms. I personally think that exercise is medicine, and that one should try to treat symptoms to help with symmetry of movement so that people can exercise well and keep moving.

The sense that the timeline of levodopa is very limited is really a myth. I've taken care of many patients now for upwards of 20 to 25 years, and we can always use levodopa. We just have to adjust the dose. Sometimes early on in the disease, we're able to get away with less frequent dosing because buffering and storage of the chemicals that we're giving exogenously. As the disease progresses, the gut uptake can be different. The same amount of medication may not absorb as well. It might not get into the brain as well, so we might have to give more doses. We also can get limited from our doses by extra movements that may get induced, and sometimes even fluctuations of symptoms.

The sense that levodopa has limited lifespan is really erroneous. I actually have a passion also for taking care of patients into the end of life, into palliative care timeframes, and even hospice. I really emphasize for those sorts of providers to continue to give levodopa even into those dying patient hours, and really try to continue to replace dopamine because it is something that the brain depends on throughout the lifetime of the disease.

Dan: It sounds like the dopaminergic medication or the levodopa is not wearing out because you're using it. Medication adjustments are required just because the disease is progressing, or as you said, as people get older their absorption of drugs may be different. Is that a reasonable way to look at it?

Indu: Absolutely. We try to give drug, and levodopa is quite protein sensitive. I like to give it about an hour before meals to keep it away from protein. We try not to limit protein in general in Parkinson's patients but try to take it away from the levodopa. The reason I like to give it before the meal is because swallowing is helped by the levodopa. If you have swallowing issues your swallowing muscles are well treated when you go to eat if you take the medicine an hour before the meals. Additionally, I think it's not just as a person ages, it's as the disease advances. Some people, the gut can actually get affected even in early stages.

Many of our patients present with constipation, they have very slowed gut motility. We're relying on the gut to absorb the drug, and the drug can sometimes be competed with for absorption by protein. Then it has to go into the blood and then get converted in the brain to dopamine. There's a number of steps that can get altered. It's not that the drug is not effective; it's just that we have to give it sometimes more frequently, give it in enhanced forms. Sometimes treat these other issues that may be happening at the gut. Sometimes if you have terrible constipation the drug does not get well absorbed. I think treating these sorts of other issues that are going on can really help.

Adequate water intake, adequate hydration can also definitely help as well, and can even mitigate some of the side effects of the drug. Sometimes people will say, "I feel like I take the Sinemet, or the carbidopa-levodopa, and I feel a little bit woozy." That is better tolerated if you drink a good amount of water because blood pressure can drop a little bit with any dopaminergic medication. Then some people also feel that they get a little bit of nausea with the Sinemet, so taking it with some crackers or some bread can sometimes help settle the stomach. There are some other strategies that can help us get people to tolerate the levodopa as well.

Dan: You mentioned that taking medications may help facilitate exercise, which has been shown to be beneficial. I suppose you can also improve balance, limit falls, fractures, things like that. Are there any downsides to starting a medication?

Indu: Every medication that we have in our mentoring, I think even in medicine in general has some side effects. It's important to weigh the risks and the benefits, to understand why the doctor is considering a medication, and be part of the dialogue of helping to choose the medicine because ultimately you're going to be the one, if you're a patient, to take it, and you want to feel like you're helping your body. I think if there's a sense that you could be harming yourself, I know sometimes patients don't ask these questions but do we need to monitor labs. Is it damaging my liver? Is it going to harm some other organ? Am I going to get addicted to it?

These are all questions that we get all the time when people are honest about why they don't take their medicine. When starting a medicine it's important to understand what it is, what the expectations are that it should help, and then also to understand the side effects. Then with that information you can choose a medicine, customize it to your symptoms, and then feel like you've made a good choice so that you'll be more likely to comply. Many of the times, once we've started levodopa therapy, is we're talking about at least three times a day medication.

Trying to stay compliant, setting pill times on a schedule, and perhaps setting your phone alarm or other alarms, maybe having a pill timer or a box that you carry around will help you stay compliant and to really reap the rewards of the medicines. Sometimes people don't understand why they're taking it, and then they take it at the wrong time. They take it very radically, and then the blood levels don't ever build up to actually a beneficial effect. I think it's always important to get educated so that you can empower yourself and take the pills correctly. That would be my take on why one should take it in general.

The dopamine agonist class, this is a different medicine that we sometimes give to younger people, maybe tremor dominant people who might be younger. This type of

medicine definitely we should be counseling patients on side effects. There is an issue in some people with problems called impulse control disorders. Patients can sometimes pleasure-seek and have issues with gambling or hypersexuality. Issues with spending money, doing certain types of things that are pleasurable: buying, shopping, eating.

I think it's important for you to understand that these are things that are possible side effects, and to have somebody help you monitor if you're a patient these sorts of issues if they come up. There are also other side effects to certain other classes. The dopamine agonists can also sometimes cause sleepiness. They can sometimes cause confusion, sometimes cause hallucinations definitely more often than, for example, levodopa.

Levodopa, we talked about side effects that include low blood pressure and sometimes nausea. Once you start levodopa there seems to be an increase in the incidence of dyskinesia. There's these extra movements that develop with Parkinson's disease therapy. My sense is that the things that cause dyskinesia are really how long a patient has had the disease seems to contribute. It also seems to be important as to how you take the medication. If you have very pulsatile stimulation of the dopamine receptor and you don't take the medications on a very stable blood level, so maybe taking it twice a day or once a day, this can propagate extra movement.

Other things that seem to be more risk factors for extra movements including younger patients, sometimes more low body weight. Women, for example, seem to have a little bit of a pre-disposition to these extra movements. This would not be a reason to not take the medication. I think that we still have an important role for levodopa, but again, this boils down to that education piece. Understanding that we have to take it multiple times a day. We usually start at a dose of three times a day. Some people would even tout, for example, taking half a tablet of Sinemet 25/100 four times a day as a starting dose.

Taking it low doses, evenly spaced, multiple times a day is going to give you more of an even blood level. Then as you have years of disease progression and time from starting the drug, it's going to be a matter of reporting back to your doctor about what's happening in the cycle of the day. If there are gaps in terms of wearing off of the drug where you feel like the symptoms of Parkinson's are reemerging you might have to fill that gap, or if there's extra movements that are happening often at peak doses of drug you might have to alter the medications as well.

My strategy is to teach people, get them complying from the get-go with taking the pills away from protein multiple times a day. Getting them on a compliant schedule where it becomes routine for them to wake up at a certain time, go to bed at a certain time, exercise at certain times, and take their pills at certain times. Set times for eating too, hydrate well so we have a very even lifestyle of taking all these types of things in. I really feel like this type of healthy lifestyle approach where we have a routine every day can really help facilitate compliance and help people with the benefits of their medication.

Then we come in on routine follow-ups, so we report back about motor issues, non-motor issues, things like extra movements. You're constantly in a dialogue with the

doctor or whoever the treating provider is and then they tweak your medicines. There's a constant interplay between sometimes over time taking away certain medicines, sometimes adding certain medicines. We use certain medicines like entacapone, like rasagiline to enhance the Sinemet sometimes. It's a constant interplay with changing the medicines over the lifetime of the disease.

Dan: Besides standard traditional medical training as well as advanced training and movement disorders, you have a background in integrative medicine. Is there any reason for people to try integrative medical strategies and delay dopamine replacement initiation, or conversely can they work well together?

Indu: That's a really good question, and I'm glad you asked that. I went into the study of some of these topics like yoga and mindfulness because I thought there was certain things that we did very well in Parkinson's disease treatment, but then there was this whole area of non-motor issues especially that we didn't have good treatments for. I ended up doing a deeper dive in yoga and mindfulness and learned about integrative medicine, which is really the intersection between Western medical approaches and these other systems of medicine, including traditional Chinese medicine and Ayurveda and all kinds of things.

I ended up learning about this and taking a board exam. I think at the end of the day, my thought of integrative medicine is literally integrating the best parts of Western therapies, which in Parkinson's disease I feel like levodopa is a cornerstone of therapy. I really do feel like it helps people exercise and live a very healthy lifestyle and be able to reap the rewards of many of the wellness approaches that we hope to have them including in their day-to-day functioning. Things like yoga classes or getting out and socializing with friends, going for hikes, being with their grandchildren. Being able to play with their grandchildren fully on the floor, throwing a ball in the backyard.

All of these things really are going to help people with their health and with their holistic kind of approach to health. For me, integrative medicine is really the-- The old title was complementary and alternative medicine. I really don't love that title because it implies that there's an alternate form of practice. I really think that we want to take the best of both and integrate them together.

I've been kind of in a unique situation to really learn about what we do well in Western approaches as a Parkinson's doc who's Western-trained and working in a Western setting for the last 20 years. I also have great respect for some other integrative medicine approaches when it comes to the things that we don't do well in Western medicine for Parkinson's patients.

Dan: Yes, I think in the West we sometimes think these are kind of hocus pocus, but people and cultures aren't going to fool themselves for 4,000 years on stuff that has no use. [chuckles]

Indu: Yes. I think we're realizing now in the pandemic how important many of these strategies are, and I've been quietly cheering behind the scenes when we see the types of things that people are using now. We talk about this cardiac breath or something. These are age-old practices of pranayama, modulating the breath to affect the nervous system and the autonomic nervous system very powerfully. I think

a lot of people are using these strategies in their podcasts or their apps to help with anxiety and calming. Even meditation are things that have been around in many parts of the world since humans existed.

Getting back to basics is very helpful. We have the need to continue to push the envelope to look for new therapeutic strategies, both pharmacologically and surgically, for our patients. I think that's definitely something that people are doing. I'm spending my time learning a little bit more about these other sorts of systems of mind-body approaches that I'm really realizing can be very powerful just in my own life. When I've been worried through this pandemic I really find myself gravitating to some of these things.

If you're not a meditator or if you're not somebody that's going to go to a yoga class, we can still take away some of these things just by getting out in nature. Maybe going to the beach and watching the waves can be a meditation. Going around trees and inhaling the scent of trees. Putting your hand in the earth and gardening a little bit. Connecting with nature can be actually a very powerful mind-body approach. There are very many teachable strategies that one doesn't realize can be very effective in helping the body and helping the mind. Since these are two things that are so connected in a disease like Parkinson's, I think some of these can be very powerful.

Dan: People can find on the Parkinson's Foundation website Mindfulness Mondays so they can participate in or get introduced to some of these things if they wish. Well, I really appreciate it. It's a wide-ranging topic and you've brought in some parts of it that wouldn't normally be associated with when do you start medication, but it all sounds good.

[music]

For lists of Parkinson's medications, when they're used and what to expect from them, you can go to parkinson.org/library and search on Medication. Within the list of extensive resources on the page, you can find a book on medications titled *Medications: A Treatment Guide to Parkinson's Disease*. You can read it in your browser, download it for offline viewing, or transfer it to your Kindle. If you want a free copy in print you can order it at parkinson.org/store, or by speaking with one of our helpline staff.

Coming up in our fall 2021, spring 2022 Expert Briefings series are three briefings on understanding disease progression, what's new in medications, and complementary therapies in PD. You can see the list and dates of the Expert Briefings at parkinson.org/EB. If you're in the early stages of Parkinson's and not ready to start medication, you may want to consider volunteering for a clinical trial that follows progression of the disease to test medications that are in development to slow progression. You can hear about this opportunity in our podcast called *The Golden Year for Testing Disease-Modifying Drugs*.

To learn more about the kinds of integrative medicine approaches that Dr. Subramanian mentioned, search our website for integrative medicine. If you have questions about this topic or anything else having to do with Parkinson's, our information specialists can provide answers in English or Spanish. You can reach

them at 1-800-4PD-INFO. News and updates about future events and resources are available by joining our email list at the bottom of our website's homepage.

If you want to leave feedback on this podcast or any other subject you can do it at parkinson.org/feedback. If you enjoyed this podcast, be sure to subscribe and rate and review the series on Apple Podcasts or wherever you get your podcasts.

At the Parkinson's Foundation, our mission is to help every person diagnosed with Parkinson's live the best possible life today. To that end, we'll be bringing you a new episode in this podcast series every other week. Until then, for more information and resources visit parkinson.org, or call our toll-free Helpline at 1-800-4PD-INFO. That's 1-800-473-4636. Thank you for listening.

[music]

[00:22:11] [END OF AUDIO]