

So when I first initiate levodopa in any formulation, I'm usually pretty particular about taking it because I want them to develop certain good habits. So let's talk about certain good habits. One is making sure they're taking the dose on time consistently at either the times we allot or within the range of times we allot. Making sure that they're taking it apart from food. Making sure they're taking it with a full glass of water to allow the medication to go in but also to manage some of the orthostasis issues that might be an issue.

I want them to take it apart from food because food may interfere with it. And that may not affect everybody, but for the small amount of folks that it may experience will never find out that it does. And some individuals are more food-sensitive than others, but over the course of time with more frequent dosing, individuals in general tend to become more food-sensitive and there may be interference between food and medication.

So, putting that aside, I actually have utilized Dhivy, which is the fractionated carbidopa/levodopa immediate-release formulation, in individuals exactly like the ones I mentioned-- individuals that have difficulty tolerating the immediate-release formation of levodopa even though they're able to cut it in half, individuals who are not able to cut the dosing in half reliably and struggle with how much they're getting and they say, I'll take one half, and it works well. And I'll take another half, and it doesn't work as well. And I know it's not cut evenly, and they suspect that they're not able to do that.

I've even had individuals try to take 25-100 immediate-release and cut into even smaller portions of it. And you can see in their pillbox the pills are very jagged. Some of the pills are nothing more than a small crumb. And some pills are basically a larger chunk. And I point out to them that while they're doing their best to take the dosage of levodopa that they feel is better-- so they'll take one tablet and a crumb, one tablet and a small chunk of levodopa-- one of the reasons they're fluctuating, or the main reason that they're fluctuating, is because they're not getting a consistent dosing.

And that makes it difficult for me to find out if there are other causes of fluctuations as well or is this the only cause of it because there may be, as we mentioned, multiple reasons why patients experience off. Well, one of them may be they're not getting a reliable consistent dosing and cutting it into small jagged edges is certainly not reliable.

So I've used Dhivy in those individuals-- in three types of individuals-- those that are having difficulty tolerating even levodopa at one tablet, or even half-a-tablet dosage. Two, individuals that need one and plus-something-else of levodopa but do not have the ability to have a consistent cut because there's no way to make that consistent cut. And three, individuals that have a variable need of levodopa-- and some of them are-- and we see this most commonly in our patients in the hospital.

When a Parkinson's patient who is doing well is hospitalized for some other reason, many times when they're under a regular dosage of levodopa they become disconnected on it. The reason being, they have a certain level of activity that they're expecting to have in their day and that is expected. When they're hospitalized and bedbound, the same amount of medication will produce a dyskinesia and that actually needs to be lowered, which tells me that their levodopa needs in some ways will be paralleled based on their level of activity.

We see this in reverse as well. Individuals who are dosed and managed on their current regimen and they're living a fairly sedentary life suddenly go into the hospital and then have to go to rehab where they have to become more active will suddenly need more levodopa because, as they will say, I "burn through" my levodopa, in quotation marks, I burn through my levodopa faster so I need a higher dosage or I need to take it more consistently to maintain that.

Well, in that sense, a fractionable formulation can help adjust their levodopa or reduce their levodopa based on the need that might occur, whether reducing it for when they become less active or increasing it for when they do become more active. And it tells us that the need of patients for levodopa may not be the same throughout the day-- generally being higher first thing in the morning because they haven't had much overnight.

So while sleep has its restorative benefits, as soon as they start their day they need the levodopa to be able to help the brain produce dopamine thereby promoting more movement. So a higher dose in the earlier part of the day, maybe the first dose, maybe the first and second dose, and then maybe having a moderate dosing in the middle of the day and a lower dosing of the evening.

Or some individuals, based on their activity, may start with an average dose in the morning, may need a higher dosage because they may have social activities, exercise classes, physical therapy or they may have an active day in the middle of their day and then tapering down to a lower dosage in the evening. So that variability allows me to customize in many ways.