

Patients with early treatment in Parkinson's disease, typically as I mentioned, start on Sinemet or Carbidopa/Levodopa 25, 100, three times per day is a classic dosing regimen. And patients may initially have the honeymoon phase, where they're smooth and don't notice any wearing off, but over time, they start noticing that their symptoms return. And the way to recognize that between doses, is that patients will have resting tremor return before their next dose is due, rigidity and slowness.

But not only do you have motor symptoms as these, you may also have non-motor symptoms, such as anxiety, a feeling of fogginess, and cognition. Different non-motor symptoms can herald the onset of Off as well. And so, you have both motor and non motor symptoms of Off in these patients. And so, it can be quite difficult for patients to verbalize initially what they're going through.

I remember anecdotally in my practice, I had a patient that said you know, I just don't feel good at some parts of the day. And I asked her, I said, well, ma'am, what do you think is going on, and what is the timing of your medication? She didn't correlate the two between off and feeling poorly, but I brought her in, and observed her through a whole cycle of dosing of levodopa. And what I noticed was when I watched her over 4 hours or so, she took her medication initially and had a nice improvement of her tremor and slowness and her bradykinesia was better and her stiffness was better, testing her tone. But I also followed her as she wore off. And what had returned, well, tremor, slowness, all these cardinal features of Parkinson's disease had returned in her, and she didn't correlate that with wearing off.

But a lot of patients and clinicians may not be aware of what off is, or how to detect it. But if you ask your patients about off every time they come in, you'll pick up a lot more because sometimes they won't volunteer it.