

Treating of Off Time has become a very large algorithm for physicians to try to figure out, and I think that it depends upon habits and what you found successful in your practice over time, what you do. So patients that are just beginning to have wearing off again, classically, we extend their day of treating with carbidopa/levodopa to four times per day to shorten the dosing interval between doses to help keep them on, is the first step that most folks do.

There's many options once you go beyond that to treat patients for wearing off. Again, there's data that selegiline and rasagiline both, as MAO-B inhibitors can reduce wearing off by about an hour per day. You can add a COMT inhibitor, such as entacapone upon with each dose of levodopa, tolcapone or opicapone, which could be helpful for wearing off as COMT inhibitors. And then if a patient is a good candidate, they could even go on a dopamine agonist to reduce wearing off. Dopamine agonists have fallen somewhat out of favor because of impulse control disorders, and other side effects that they have, but they can be useful in certain patients that have wearing off that can tolerate a dopamine agonist.

Other options that patients may benefit from for wearing off, if it's a sudden wearing off apomorphine injection, sublingual apomorphine, can be useful as rescue medications, and so can inhaled levodopa, Inbrija, to hopefully help turn folks back on so they can go about their day. And there's lots of other options that you can treat significant wearing off with, deep brain stimulation actually reduces wearing off by about 6 hours per day, 4 to 6 hours per day, depending on the study you look at, and so can carbidopa/levodopa intestinal gel, called duopa duopa can reduce wearing off by about four hours per day too.

So it depends on the patient and how much off time they have how significant their disease is what you do to treat their wearing off. But it certainly is complex and it just takes time to figure out your own algorithm for treating off in a patient and how severe it is.