

TITLE 1: “Ask the Doctors”

TITLE 2:

DATE: February 1998

AUTHOR/S: Wayne Hening, MD, PhD

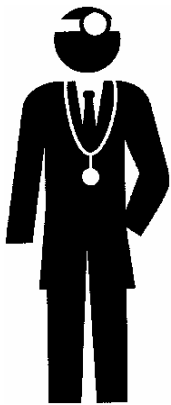
KEYWORDS:

- Pharmaceutical treatment

ABSTRACT OVERVIEW: Dr. Wayne Hening provides a detailed answer to a question about whether or not a reader has become immune to carbidopa/levodopa drugs (Sinemet). Dr. Hening explains why these drugs often stop working and result in augmentation. He also provides helpful suggestions for dealing with the loss of successful treatment for bothersome RLS symptoms.

COPY OF ARTICLE:

Q. *I have been taking carbidopa/ levodopa for several years, and it has helped my symptoms of RLS; however, in the last few months, I have noticed that it is becoming less effective. Have I become immune to the medication? What can I do to regain the original effectiveness of the medications?*



A. Unfortunately, what you have experienced is relatively common for patients treated with carbidopa/levodopa, a medication also referred to by the brand name Sinemet. This medication, when it reaches the brain, effectively becomes dopamine, which is one of the major chemicals that transmits signals between some of the cells in the brain. In very low doses, this medication will often temporarily reverse almost all of the symptoms of RLS. Thus, by providing the extra amount of dopamine, the drug allows some of the cells to work better, but these same cells have at least two other ways they respond to dopamine. Both of these other ways are used to adjust the amount

of dopamine that is produced in the brain. When lots of dopamine is made available, these brain cells effectively adjust their activity to compensate, in part, for this extra dopamine, with the result that the dopamine provided by Sinemet begins to have less benefit. To make matters worse, Sinemet provides increased amounts of dopamine for only a short period of time (about 3 - 5 hours), but the brain appears to make a long-term adjustment. Not only do the brain cells that use dopamine become less responsive to carbidopa/levodopa, but they also have less effective functioning throughout the day. The basic underlying problem of RLS actually becomes more severe. Thus the major adverse effect of using this medication is an augmentation or worsening of the RLS condition. If you find that the Sinemet is not working as well as it had previously, it is also likely that you are finding that your RLS symptoms are now occurring earlier in the evening or afternoon and are more severe. You may also find that the RLS symptoms appear to occur more readily so you simply cannot sit or lie down for as long a period as you could before the augmentation began. In extreme cases of augmentation, the RLS symptoms can start to involve other parts of the body. All of these changes in symptoms are seen with more-severe RLS, but they will also occur for patients treated with larger doses of Sinemet.

The best way to correct this problem is to change to another medicine that also improves the activity of the brain cells that use dopamine but does not directly provide increased amounts of dopamine to the brain. The medication that has now been shown in well-controlled scientific studies to do this is pergolide, also referred to by the brand name Permax. This medication mimics dopamine in the brain and works on some but not all of the dopamine-sensitive parts of

brain cells. It has been found to have far fewer problems with augmenting RLS symptoms than does Sinemet. If you are having problems with Sinemet being less effective, you may want to discuss with your doctor changing to Permax or another medication.

An alternative way to correct the problem is to come off the Sinemet for a few days, but you may need to gradually decrease the dose, depending upon how much you are taking. This is a medication that you should NOT stop abruptly without first checking with your doctor. When you come off Sinemet, you will notice the augmentation of your RLS symptoms but, after experiencing a difficult withdrawal period (usually lasting 5 to 7 days), you will probably find that your symptoms will return to what they were before you started taking Sinemet. If you then resume taking Sinemet, the drug will probably work as well as before, but it will also start causing augmentation as it had before. Your doctor will be able to advise you on what alternate medications you can use to reduce the RLS symptoms during the withdrawal period.

The best way to avoid this problem with Sinemet is to keep the dose very low. One recently published study showed that Sinemet produced RLS augmentation in 85% of the patients when it was used in doses exceeding 2 tablets of Sinemet 25/100 per day. If the dose is increased beyond 3 tablets a day, the augmentation begins to be much worse than the RLS was initially and becomes even worse as the medication is further increased to correct for the augmentation. It is generally advised that the maximum dose should be 3 tablets a day of Sinemet 25/100 and that if benefits are lost, an alternate medication should be considered.

Wayne Hening, MD, PhD