

## WHAT IS DELAYED ON?

Patients may also experience delayed ON, which is characterized by a prolonged latency of the onset of effect of levodopa after the ingestion.

## WHAT IS LEVADOPA DOSE FAILURE?

Levodopa dose failure is complete lack of effect of a certain dose of levodopa, seen in advanced Parkinson's disease. This problem may be due to many factors including poor absorption of drug in the intestine.

## HOW IS LEVADOPA DOSE FAILURE TREATED?

The following are strategies used to treat levodopa dose failure:

- Dissolving the tablet formulation in carbonated beverage, orange juice, avoiding ingestion with meals and treating constipation may improve the response to levodopa.
- Protein-rich meals may also decrease absorption of levodopa, thus patients who like to be more active in the afternoon may prefer to take their main meal in the evening whereas those who like to be more active in the evening may take their main meal in the afternoon.
- In addition to adjusting the dose and frequency of Levodopa, your neurologist may also suggest COMT inhibitors or MAO-B inhibitors, which reduce the severity of OFF periods and can enhance the duration of ON periods, and may allow the lowering of the individual doses of levodopa.



## DID YOU KNOW?

Millions of Parkinson's patients are suffering from poverty around the world. The number of Parkinson's patients will double by 2040.

- Cannot afford to buy their medications
- Cannot afford to purchase a cane, walker, or a wheelchair
- Cannot obtain educational literature about Parkinson's in their language
- Are not able to afford consulting a neurologist and remain undiagnosed and untreated

## OUR SERVICES

We provide unique services for Parkinson's patients including:

- Parkinson's medications to those patients who can't afford to buy them
- Canes, walkers & wheelchairs to prevent falls
- Parkinson's educational brochures in many languages
- Free electronic educational newsletter
- Chapters of the World Parkinson's Program in various parts of the world

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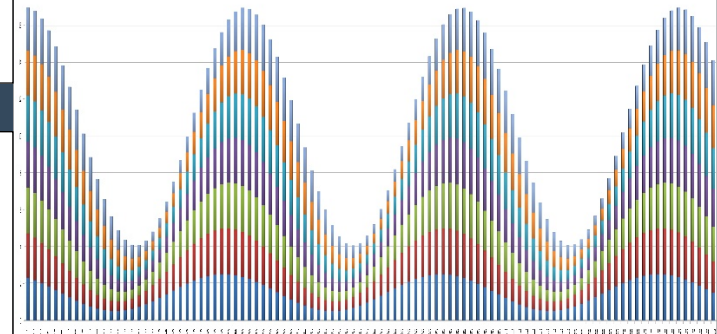
This information is not a substitute for medical advice. Consult your Physician before applying this information.

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Frequently asked questions about...

## MOTOR FLUCTUATIONS IN PARKINSON'S DISEASE



ENGLISH - 18



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*"Those who fight Parkinson's with knowledge always find solutions"- Dr. Rana*

Parkinson's disease is a progressive neurodegenerative condition characterized by tremors, slowness of movements, stiffness, and balance problems. In addition, Parkinson's has many non-motor symptoms such as memory or cognitive issues, speech and swallowing problems, depression, and sleep difficulties. It affects almost 10 million individuals around the world.

### WHAT IS DYSKINESIA?

Dyskinesia is a term used for abnormal involuntary movements usually seen in advanced cases of PD. Most patients describe them as rocking movements. Dyskinesia can be classified into peak-dose dyskinesia, diphasic dyskinesia, and OFF period dystonia. Peak dose dyskinesia starts usually after an hour of taking levocarb, and they may decrease as dose of levodopa wears off. One way to treat peak-dose dyskinesia to take levodopa along with a meal. Diphasic dyskinesia occurs towards the end of the dose and before the beginning the effects of levocarb. These can be difficult to treat, so adjusting the dosage of levodopa can help. OFF period dyskinesia occur before levocarb is taken in the early hours of the day. To deal with OFF period dystonia, using an additional dose of levodopa one to two hours before waking up in the morning can help.

### WHAT DOES "WEARING OFF" MEAN?

The term wearing off is usually used for the return of Parkinsonian symptoms in less than 4 hours after a dose of levodopa which are the most common initial predictable motor fluctuations. Subtle on and off phenomenon may be present during the initial treatment phase with levodopa, but the oscillations between the ON and OFF states become more prominent as the disease advances.

Levodopa is the gold standard medication for Parkinson's disease and almost every patient requires Levodopa during the disease. Initiation of levodopa in early Parkinson's disease is followed by a good response which is maintained for a few years in most patients (Honeymoon period). Early in the course of Parkinson's disease, the response to an individual levodopa dose weans only slowly, but as the disease progresses, the duration of effect gradually becomes shorter. This is manifested by the return of symptoms of Parkinson's disease before the next scheduled dose of levodopa. Intermittent return of symptoms of Parkinsonism during the daytime is commonly known as wearing off.

### WHAT ARE THE SYMPTOMS OF WEARING OFF?

During the OFF state, patients get exacerbation of Parkinson's like numbness, pain, tingling, stiffness, tremor, balance problems, drooling, falls, freezing, and speech problems.

### WHAT ARE THE RISK FACTORS OF WEARING OFF?

The following are the factors influencing the development of motor fluctuation:

**Age of the patient:** Patients younger than 40 years of age develop motor fluctuations more frequently and earlier than the older patients, if exposed to levodopa.

**The severity of the motor deficit:** Severity of the motor deficit increases the risk of developing the motor fluctuations.

**Dose, Frequency, and Duration of Levodopa:** The higher the dose, frequency and duration of levodopa, the greater the risk of earlier development of motor fluctuations and dyskinesia. Patients feel disabled during off periods and treatment should be modified.

### HOW IS WEARING OFF TREATED?

Levels of levodopa in your blood can be increased by adjusting the dose of levodopa by your neurologist, increasing its frequency and decreasing the intervals between the dosages, taking the early morning dose of regular levodopa to treat early morning OFF period.

Adjunctive therapy with COMT inhibitors or MAO-B inhibitors may reduce the severity of OFF periods. Selective MAOB inhibitors include Rasagiline and Selegiline. Rasagiline is a more potent MAO-B inhibitor and used once daily and does not have the side effect of insomnia like Selegiline. Selegiline is used twice daily.

Apomorphine is a short-acting, injectable dopamine agonist with a very fast onset of action. It has the ability to reverse OFF periods in patients with motor fluctuations. This drug may be administered by intermittent subcutaneous injection or by constant subcutaneous infusion. Apomorphine infusion can reduce dyskinesia by more than 50% and improve the motor fluctuations as well.

Duodopa gel, given through stomach tube can also reduce the wearing off phenomenon as it maintains a constant blood level of levodopa.

Deep Brain Stimulation surgery is also helpful in refractory cases. It is the most common surgery for treating advanced Parkinson's. DBS surgery involves placing thin metal electrodes into brain targets and attaching it to a computerized pulse generator, which is implanted under the skin in the chest (much like a heart pacemaker).