

Perceiving Parkinson's

Dopaminergic Infusions (Day 77)

When a person with Parkinson's commences dopaminergic oral medications, there is a **honeymoon phase** during which they have excellent symptom control. The honeymoon phase usually lasts for several years, but when it ends most people will go on to develop motor complications, namely motor fluctuations and dyskinesias.

Motor fluctuations are alternations between “on” periods (when a person has a good response to medication) and “off” periods (when the medication benefits have worn off and motor symptoms re-emerge). As the Parkinson's progresses, dopaminergic oral medications produce shorter and shorter “on” periods, resulting in more and more “off” periods and a re-emergence of motor and non-motor symptoms throughout the day. This can be a source of considerable distress.

Dyskinesias are involuntary, random writhing movements that may occur if dopamine levels are too high. Five years after commencing levodopa, approximately 50% of people will develop dyskinesias. Most people don't mind having mild or moderate dyskinesias, but severe dyskinesias can impose a considerable burden.

To some extent, motor complications can be managed with dopaminergic oral medications - motor fluctuations can be reduced with selegiline, rasagiline, entacapone, and tolcapone, and dyskinesias can be reduced with amantadine. Yet as time passes, these strategies may not be enough. Luckily, there are further options in the form of **dopaminergic infusions**, namely subcutaneous apomorphine and duodenal levodopa.

Subcutaneous Apomorphine

Used in people with Parkinson's since 1951, **apomorphine** is the oldest of the dopamine agonists; despite its name, it does not actually contain morphine. Apomorphine is the only medication equal in power to levodopa. However, there are two important differences between apomorphine and levodopa. First, apomorphine relieves symptoms in Parkinson's **quickly**, within several minutes rather than 30-60 minutes. Second, apomorphine must be delivered **subcutaneously** through an injection given under the skin, not orally.

Subcutaneous apomorphine can be delivered intermittently or continuously:

(1) **Intermittent** subcutaneous apomorphine is given as a “rescue” medication for people who suffer from disabling **motor fluctuations** resulting in sudden, unexpected “off” periods. It is only delivered when needed, either by the patient or by someone else, using an **injection pen**. Multiple studies have

shown that intermittent subcutaneous apomorphine reduces daily “off” time for both motor and nonmotor symptoms, such as pain, by **up to 50%**.



Intermittent subcutaneous apomorphine is delivered using an injection pen.

(2) **Continuous** subcutaneous apomorphine is very helpful for people with **motor fluctuations**, and it can also be helpful for people who suffer from severe **dyskinesias**. It is delivered on a constant basis, either throughout the waking hours alone, or during both day and night, using a **portable infusion pump** that is worn under the clothes. Multiple studies have shown that continuous subcutaneous apomorphine reduces daily “off” time and troublesome dyskinesias by **up to 80%**.



Continuous subcutaneous apomorphine is delivered using a portable infusion pump.

Potential **side-effects** of subcutaneous apomorphine include mild **skin reactions**, **nausea**, **postural hypotension** (when a person’s blood pressure falls upon standing), and **sleepiness**. In some people, **hallucinations** (sensing things that are not there) or **delusions** (believing things that are not true) may occur. The possibility of developing one of these side-effects must be weighed against the potential benefits of apomorphine.

Duodenal Levodopa

It may be surprising to know that **levodopa** does not have to be administered as an oral tablet - it can also be administered as a **gel** via a portable infusion pump attached to a small tube that goes straight into the **duodenum**, which is the first segment of the small intestine. By administering levodopa straight into the duodenum, stomach emptying is bypassed which means that delivery, and hence blood levodopa levels, remain constant and smooth, day and night.

Duodenal levodopa is very effective for people who suffer from disabling **motor fluctuations** as well as **dyskinesias**. Excellent studies have shown that **over 90%** of people with Parkinson's experience a degree of improvement in motor fluctuations and dyskinesias with duodenal levodopa. Moreover, some of the studies showed improvements in most non-motor symptoms too. Unlike subcutaneous apomorphine, duodenal levodopa can be used by older patients with mild or moderate dementia.



Duodenal levodopa is delivered straight into the duodenum of the small intestine.

Generally, the potential **side-effects** of duodenal levodopa are either technical or related to the tube insertion procedure. The most common side-effect, occurring in 20-70% of people, is a **technical problem** with the infusion delivery system, such as pump failure, tube disconnection, or tube obstruction; such technical problems are rarely life-threatening. Some people may acquire a **tube insertion problem**, such as acute or chronic infection. In addition to these side-effects, nausea, postural hypotension, and peripheral neuropathy may occur.

To wrap up, the honeymoon phase with dopaminergic oral medications ends after several years, and motor fluctuations and dyskinesias can become a major problem in people with Parkinson's - yet there are still options in the form of dopaminergic infusions:

(1) Subcutaneous apomorphine is indicated for people **under 70 years of age**, with **normal cognition**, who have **disabling motor fluctuations**. Subcutaneous apomorphine is available in Hamilton - speak to Parkinson's nurse Linda Gilbertson if you are interested.

(2) Duodenal levodopa is indicated for people of **any age**, with **normal cognition** or **mild or moderate cognitive difficulties**, who have **disabling motor fluctuations** and/or **dyskinesias**. Duodenal levodopa is not yet available in New Zealand, but with some luck that will change in the next several years.

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References

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- (3) Abbruzzese et al. 2012. Continuous intestinal infusion of levodopa/carbidopa in advanced Parkinson's disease: efficacy, safety and patient selection. *Functional Neurology* 27(3), 147-154.