

# Effect of Rectal Levodopa Administration: A Case Report

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## Key Words

Pharmacotherapy · Parkinson's disease · Levodopa

## Abstract

**Objective:** The aim of this report is to discuss whether or not rectal levodopa administration is useful in some situations. **Background:** In situations where oral intake of levodopa formulations is not possible, the treatment options of Parkinson's disease patients are limited. The literature describes no or low rectal absorption of levodopa. **Case Description:** A patient with an ileus was unable to take oral medication. After consulting the neurologist and pharmacist, the surgeon decided to prescribe a rectal formulation of levodopa/carbidopa (100/25 mg) once daily. On day 3 of the therapy, 1 h after administration of the rectal formulation of levodopa/carbidopa, a blood sample was drawn. The patient was unable to take his other Parkinson medication; therefore the dose of the rectal levodopa/carbidopa was increased to 5 times a day. **Results:** Full control of the symptoms was not achieved, but alleviation of the most severe tremor and rigidity was seen, which was confirmed by the neurologist, nurses and patient. The levodopa concentration detected was 17 nmol/l. Compared to levodopa concentrations described in the literature (1,400–12,000 nmol/l), the concentration is very low. There are some possible explanations for the low concentration detected. The presence of a specific amino acid transport system in the rectum is not known, which could lead to no or reduced absorption. The poor rectal absorption of carbidopa leads to a higher conversion of levodopa to dopamine peripherally. **Conclusions:** In situations where patients are unable to take oral medication, rectal administration of levodopa/carbidopa is worth considering.

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## Introduction

Oral levodopa is the cornerstone of the treatment of Parkinson's disease. In some situations, oral administration of levodopa is not possible, for example after bowel surgery or in case of an ileus. The treatment options in these situations are limited. In these circumstances, the hospital pharmacy in the Martini Hospital manufactures a rectal formulation of levodopa/carbidopa 100/25 mg/ml, citric acid, glycerol (85 per centum) and purified water, based on the case report of Cooper et al. [1].

We describe a patient with Parkinson's disease with an improvement of his Parkinson symptoms after rectal administration of levodopa/carbidopa.

## Case Presentation

A 64-year-old male with Parkinson's disease was admitted to the surgical ward for a laparoscopic sigmoid resection because of a volvulus caused by a dolichocolon. In 2007, he was diagnosed with Parkinson's disease. Until surgery, he used amantadine 100 mg b.i.d. and ropinirol controlled release formulation b.i.d., in the morning 10 mg and in the afternoon 8 mg. At night, he used one 100/25 mg levodopa/benserazide controlled release formulation. After surgery, the patient developed a paralytic ileus for which he was on a 'nil per os' regime. This regime led to a deterioration of his Parkinson symptoms.

After consultation of the neurologist and pharmacist, the surgeon decided to start rectal administration of 100/25 mg levodopa/carbidopa once daily, in accordance with his oral levodopa/carbidopa dose. The patient gave informed consent for this treatment.

As he was unable to take his other Parkinson drugs (dopamine agonist, amantadine) too, an increase of the Parkinson symptoms was seen, since he only used 100/25 mg levodopa/carbidopa rectally once daily. For that reason, the dose was increased to rectally administered levodopa/carbidopa 100/25 mg 5 times a day. This led to an improvement of the Parkinson symptoms. Optimal control of his Parkinson symptoms was not pursued, but alleviation of the most severe tremor and rigidity was seen, which was confirmed by the neurologist, nurses and patient.

On day 3, a blood sample was drawn 1 h after administration of the rectal levodopa in order to determine the serum levodopa concentration. We found a levodopa serum concentration of 17 nmol/l (determined with liquid chromatography-mass spectrometry/mass spectrometry).

When levodopa is combined with a decarboxylase inhibitor, the half-life of levodopa is 1.5 h. In this patient, the oral levodopa formulation was stopped 24 h before the rectal formulation was started. The blood sample was drawn 3 days after the rectal formulation was started, which is 96 h after the last oral levodopa gift.

Since the half-life of levodopa (combined with a decarboxylase inhibitor) is 1.5 h, it can be assumed that after 96 h (64 half-life); all levodopa due to the oral administration was washed out. Therefore, the detected levodopa in this patient is not due to the oral medication.

However, it is not sure whether the detected levodopa is endogenous or due to the rectal administration of levodopa, since one study described an endogenous concentration of levodopa of  $38 \pm 32$  nmol/l. Increase of the levodopa concentration after rectal administration of the formulation we used in human are not described in the literature. The serum levels of levodopa described after oral administration are much higher, in the range of 1,400–12,000 nmol/l [2–4].

## Discussion

The available studies on the rectal absorption of levodopa show conflicting information [5]. A couple of case reports describe the successful rectal treatment with levodopa/carbidopa [1, 6]. Theoretically, the advantage of administration via the rectum compared to the small intestine is the lower level of decarboxylase activity in the rectum. This supposedly leads to a lower conversion of levodopa to dopamine in the rectum, and thereby to an increase of the amount of levodopa available for absorption [7]. The study of Leppert et al. [7] showed no effect of rectal carbidopa on the levodopa serum concentration after different routes of administration of levodopa. This makes us assume that carbidopa is not absorbed rectally, which leads to a higher conversion of levodopa to dopamine peripherally.

It is recognized that levodopa is well absorbed in the small intestine by a specific amino acid transport system [8]. Whether this transport mechanism or another mechanism for absorption is present in the rectum is not known [9]. The serum level in this patient is low compared to the serum levels found in the literature (after oral administration).

Despite that the Parkinson symptoms were not officially scored with the use of the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS), the clinical status of the patient improved. Whether this effect is due to the levodopa or is a placebo effect must be revealed in further research. Part of this research should include determination of the endogenous levodopa concentration at baseline, and multiple blood samples should be drawn to study the pharmacokinetics of rectally administered levodopa.

The development of new administration forms of levodopa such as subcutaneous or inhaled levodopa would be an alternative in the treatment of these kinds of patients. At this moment, rectal administration of levodopa/carbidopa is worth considering, if there are no other treatment options.

## Statement of Ethics

The authors have no ethical conflicts to disclose.

## Disclosure Statement

The authors state that they have no conflicts of interest.

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