Therapeutic effects of an inhaled levodopa dry powder formulation on the recovery from off periods in patients with Parkinson's disease

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The primary objective is to determine the time until maximum effect is reached of inhaled levodopa on motor function of Parkinson's disease patients during an off period. The secondary objectives are to determine the clinical improvement of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON55857

Source
ToetsingOnline

Brief title
Effectiveness of inhaled levodopa in Parkinson's disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
parkinsonism, Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Martini Ziekenhuis

Source(s) of monetary or material Support: Ministerie van OC&W,Parkinson Vereniging

Intervention

Keyword: Dry powder inhalation, Levodopa, Off period, Parkinson's disease

Outcome measures

Primary outcome

The primary outcome is the time until maximum effect on motor function.

Secondary outcome

The secondary outcome is the maximum change in MDS-UPDRS III score as pseudo-quantitative measure for the clinical improvement in motor function. Additionally, a secondary study outcome is the levodopa blood profile after inhalation of 90 mg levodopa in comparison to 100/25 mg orally administered levodopa/benserazide. Pharmacokinetic parameters that will be derived from the concentration vs. time curve are tmax, Cmax and AUC0-180.

Study description

Background summary

Very limited treatment options are available with a rapid onset to counter off periods in Parkinson*s disease patients. Therefore, the development of rapid onset levodopa formulations is warranted, for which an inhalable formulation of levodopa is being investigated. In a former study, we assessed the ability of Parkinson's disease patients to perform a correct inhalation manoeuvre during an off period. Based on their inspiratory capacities, a levodopa inhaler with levodopa powder for inhalation combination has been developed. This levodopa inhaler has subsequently been tested in mild Parkinson's disease patients to assess the pharmacokinetics of levodopa after inhalation in comparison to oral administration.

Study objective

The primary objective is to determine the time until maximum effect is reached

of inhaled levodopa on motor function of Parkinson's disease patients during an off period. The secondary objectives are to determine the clinical improvement of motor function of Parkinson's disease patients after inhalation of levodopa in comparison to oral levodopa and to determine the pharmacokinetic profile of a dose of 90 mg inhaled levodopa in comparison to 100 mg levodopa orodispersible tablet .

Study design

. The study is an open-label randomized two-way one-period crossover trial. Participants will stay in the clinic for three days and receive one dose of inhaled levodopa (90 mg) and one dose (100 mg) of levodopa orodispersible tablet on two consecutive days in randomised order. A timed tapping test and Timed Up & Go test will be performed pre-dose and on set time points up to 90 min post-dose as measure for motor function. The MDS-UPDRS III score will be assessed pre-dose and on set time points up to 60 min post-dose as pseudo-quantitative measure for the clinical improvement of motor function. Levodopa blood profile after inhalation of 90 mg levodopa in comparison to 100/25 mg orally administered levodopa/benserazide will be determined by blood sampling pre-dose and on set time points up to 180 min post-dose.

Intervention

Participants will receive one dose of inhaled levodopa (90 mg) and one dose (100 mg) of levodopa orodispersible tablet on two consecutive days in randomised order.

Study burden and risks

To minimise the burden of the study on the patient, they will be admitted to the Punt voor Parkinson clinic for the entire duration of the study (three days). Standard, oral levodopa treatment will be withheld during each night for two nights and each following morning. Once the patient has become off, interventional medication will be administered. 180 minutes post-administration the patient*s standard, oral levodopa treatment will be resumed and they can spend the rest of the day as they wish, although they have to stay in the clinic for supervision. The burden of the intervention and measurements on the patient is considered to be mild. Pharmacokinetics and safety of inhaled levodopa have been investigated previously at lower doses and so far inhaled levodopa is found to be well-tolerated and safe to use. Although no effects of levodopa inhalation on lung function have been found, lung function will be checked upon admission and discharge as a safety control. Since this study aims to determine the effectiveness of inhaled levodopa, it has to be performed in advanced PD patients who experience regular, predictable off periods. Their participation is essential for further clinical development of this new

administration method of a well-known drug.

Contacts

Public
Martini Ziekenhuis

Van Swietenplein 1
Groningen 9728 NT
NL
Scientific
Martini Ziekenhuis

Van Swietenplein 1
Groningen 9728 NT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Diagnosed with Parkinson*s disease;
- At least 18 years of age;
- Predictable off periods totalling *2 h per waking day despite PD medications, including oral levodopa taken at least four times daily;
- Recognisable off periods for themselves and others;
- Sufficiently large (measurable) difference between on and off state
- At least 2 years of levodopa use;
- At least 4 weeks on a stable medication scheme prior to inclusion;

- Able to perform spirometry; - Signed informed consent.

Exclusion criteria

- Cognitive dysfunction, which precludes good understanding of instructions and/or informed consent;
- Current treatment with apomorphine or duodopa by pump;
- Severe off periods during the night;
- Current or past experience with depression/depressed mood;
- Known symptomatic orthostatic hypotension;
- Active pulmonary disease;
- Prolonged QT-interval;
- Pregnancy or breast-feeding.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-05-2019
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Levodopa Cyclops

Generic name:	Levodopa powder for inhalation
Product type:	Medicine
Brand name:	Madopar 125 mg, orodispersible tablet
Generic name:	Levodopa/benserazide 100/25 mg orodispersible tablet
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-11-2017
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	07-06-2018
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	28-05-2019
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	06-09-2021
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-004006-18-NL
CCMO	NL63553.099.17

Study results

Date completed: 27-01-2022

Actual enrolment: 9