Fecal Microbiota Transplantation for Parkinson*s Disease: a pilot study

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Primary objectives: 1. Assess the feasibility of FMT in PD patients.2. Assess the safety of FMT in PD patients. Secondary objectives:1. Explore whether FMT leads to alterations in motor complications (fluctuations or dyskinesias) and PD symptoms in...

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

Summary

ID

NL-OMON52432

Source
ToetsingOnline

Brief title
FMT4PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease; Parkinson disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Parkinson vereniging

Intervention

Keyword: Fecal microbiota transplantation, Gut microbiota transplantation, Parkinson's disease, Safety

Outcome measures

Primary outcome

Main study endpoints:

1. Feasibility of FMT in PD patients: the number of included patients that

cannot undergo FMT due to a patient- or procedure-related reason.

2. Safety of FMT in PD patients: FMT-related serious adverse events (SAEs)

Secondary outcome

1. Alterations in gut microbiota structure (16S rRNA gene amplicon sequencing)

after FMT, with comparison to the donor gut microbiota, and how these associate

with PD symptoms and motor complications.

2. Changes after FMT (as compared to the change observed after one-week

standard-of-care observation) and differences between patient groups based on

the selected donors on the following aspects:

• Severity of motor complications, i.e. number and duration of off periods and

periods with troublesome dyskinesias per day (3 days diary)

• MDS-UPDRS (on medication)

• Required PD medication dose

• Hoehn and Yahr score

• Q10 questionnaire (wearing off)

• Montreal Cognitive Assessment (MOCA)

• Severity of GI symptoms and defecation frequency

• Bristol stool scale

• Other non-motor symptoms (SEverity of Non-dopaminergic Symptoms in

Parkinson*s Disease (SENS-PD) scale)

3. Ease of the study protocol, assessed by the reasons for refrainment of

participation in the

study after receiving full information at V1, and study load for participants,

assessed bij 0-10 scale and open questions.

4. FMT-related AEs in PD patients after FMT, assessed by the registration of

FMT-related AEs.

Study description

Background summary

The available literature suggests a role for the gut microbiota in the pathophysiology of Parkinson*s disease (PD). Changing the gut microbiota by means of fecal microbiota transplantation (FMT) could act on the pathophysiology of the disease and development of Levodopa-mediated motor complications in PD patients. In the proposed pilot study, FMT with feces from healthy donors will be performed for the first time in a study in PD patients. We hypothesize that FMT is feasible and safe in this patient group. In addition, we hypothesize that FMT will lead to a decrease of motor complications and PD symptoms in the short term, and an alteration of the intestinal microbiota composition towards that of the donor.

Study objective

Primary objectives:
1. Assess the feasibility of FMT in PD patients.
2. Assess the safety of FMT in PD patients.

Secondary objectives:
1. Explore whether FMT leads to alterations in motor complications (fluctuations or dyskinesias) and PD symptoms in the long term (up to 12 months post-FMT).
2. Determine alterations in gut microbiota composition and donor-recipient similarity, and their association with PD symptoms and motor complications.
3. Assess the ease of the study protocol.
4. Assess which FMT-related AEs are observed in PD patients after FMT

Study design

Single center prospective self-controlled interventional donor-FMT pilot study.

Intervention

FMT, with vancomycin and bowel lavage as pre-treatment and domperidone prior to FMT.

Study burden and risks

The participants will receive bowel lavage and antibiotics prior to FMT. They are not allowed to eat on the day of FMT prior to FMT. The FMT-procedure requires a gastroscopy to inject the fecal suspension directly into the horizontal duodenum or to insert a nasoduodenal tube with a pediatric gastroscope for later infusion of the fecal suspension, which are both minimally invasive procedures. The patient and the investigator or gastroenterologist can decide together which route is preferred. The nasoduodenal tube will remain in place until approximately 30 minutes after FMT. On the day of FMT, the patient will be in the hospital for approximately 2-4 hours. During this study, the patient has to visit the LUMC six times in total and will have two telephone appointments. Blood will be drawn three times. Physical examination, questionnaires, diary and collection of stool samples are repeated at each visit after screening (except for the FMT-visit).
FMT is a relatively safe procedure, but patients often experience mild self-limiting adverse events (AEs). The percentage of patients experiencing FMT-attributable AEs is 20-45%. In 0-5% of the patients, FMT-attributable SAEs are reported. The type and probability of specific procedure-related problems and (S)AEs in the group of PD patients is unknown. FMT in this pilot study will be performed via the upper GI route. Swallowing problems, delayed gastric emptying or decreased Gl motility may increase the risk of aspiration. However, we will exclude patients that cannot swallow 2 liters of laxatives. Importantly, nasoduodenal tube placement and nasoduodenal feeding are usually carried out without problems in PD patients.
The gut microbiota is considered to have a role in the pathophysiology of PD and in the metabolization of anti-PD medication. Based on animal studies, it is hypothesized that FMT with feces from healthy donors might improve the symptoms

of PD, improve the effect of medication such as levodopa and limit their side effects, and/or slow down the disease progression. No studies have been performed with FMT in PD patients so far to confirm these findings. This study will provide crucial information about the safety and feasibility of this treatment in patients with PD, which, in the near future, could be further explored in larger trials aiming at determining the efficacy of FMT in PD patients. The participating patients will have the chance to experience this novel treatment and may possibly benefit from it.

A preliminary version of this study protocol was discussed with two Parkinson patients (patient-investigators), appointed by the Dutch Parkinson patients association (Parkinson vereniging), to review the study load, the safety and the patient-centered value of the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Clinical diagnosis of idiopathic PD according to UK Brain Bank criteria
- PD disease duration of at least five years.
- Use of levodopa.
- Presence of motor complications (motor fluctuations or dyskinesias), despite adequate PD medication and regardless of severity.
- Written informed consent.

Exclusion criteria

- Hoehn and Yahr scale stage 5 (most severe stage in scale for severity of PD motor symptoms).
- Comorbidity or condition impairing ability to participate in the study according to the investigators.
- Current use of probiotics or in the previous three months.
- Unstable PD with change in type or dose of PD medication in the previous three months.
- Symptoms of a GI infection during the previous three months.
- Current need of antibiotics or use in the previous three months.
- Current GI malignancy or in the previous six months.
- Known obstructions, paralysis or severe motility problems of the gastrointestinal tract, or severe dysphagia with incapability of swallowing 2 liters of macrogol + electrolytes, or inability to receive oral feeding.
- Known diagnosis of Inflammatory Bowel Disease (IBD) or celiac disease.
- Intestinal resection in medical history.
- Recent intraabdominal surgery(< 3 months).
- Platelet count < 70x10^9/L
- Participation in another study within 16 weeks of screening visit.
- Known severe food allergy or allergy to medication that a donor could have used (intake may lead to a life threatening situation).
- Immunocompromised state.
- Current use of immunosuppressants or opiates, or in the previous month.
- For women with child-bearing potential: Pregnancy; current wish to be pregnant or absence of contraception; lactation.
- Impaired ability to understand the study content and to give written informed consent.
- Unwilling or not capable to comply with the study requirements.
- Inability to communicate in Dutch.
- Inability to visit the LUMC.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-12-2021
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO

Date:	29-01-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	15-10-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 25789
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL73701.058.20
OMON	NL-OMON25789