An N-of-1 double-blind randomized phase 1 trial of the safety and feasibility of (intermittent) hypoxia therapy in Parkinson*s disease

Published: 26-01-2022
Last updated: 05-04-2024

To explore the safety and feasibility of continuous and intermittent hypoxia therapy in PD and the differences of symptom modification of different hypoxia protocols. Secondary outcomes include exploring the responsiveness of subjective and...

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

Summary

ID

NL-OMON54087

Source
ToetsingOnline

Brief title
TALISMAN-1

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease; Parkinson's

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Michael J. Fox Foundation (MJFF)

Intervention

Keyword: High altitude, Intermittent hypoxia, Parkinson's disease, Symptoms

Outcome measures

Primary outcome

As this is an exploratory study, primary outcomes are multidimensional and assess safety as well as feasibility of this study:

- Nature and total number of adverse events (including vital parameters abnormalities)

- Feasibility questionnaire (including feasibility questionnaire sum score)

- Sensitivity (change) of secondary outcome measures pre- and postintervention

Secondary outcome

Secondary

- Self-reported overall symptom impression and one important or altitude-responsive symptom chosen by participant on Likert scale 1-10 (allowing half points), as well as urge to take dopaminergic medication on usual moments of intake, on 10-point scale ranging from *substantially less* to *substantially more* (allowing half points).

- Bradykinesia quantified using a Modified Perdue pegboard test)

- Mobility (Timed Up & Go Test, steps and time)

- Balance (MiniBES test, totaal- en subscore)

- Movement Disorder Society-Unified Parkinson*s Disease Rating Scale (MDS-UPDRS) part III (sum score and individual elements)

- Finger tapping test (amount of taps and errors)

- Accelerometry registration of hand tremor (with Movisens Move 4 accelerometer)
- Non-motor symptoms (stress, mood, anxiety, pain, fatigue) on Likert scale 1-10 (allowing half points).
- Heartrate variability (using Polar smartwatch)

Lab outcomes:

- Serum platelet-derived growth factor receptor β (PDGFRβ) from baseline ABG and last ABG during intervention (fifth ABG including baseline)
- Serum cortisol before and after baseline clinical assessment, and three ABGs (between directly post-intervention and +-40 minutes post-intervention).
- Serum erythropoietin before baseline and last blood gas (+- 40 minutes post-intervention).
- Venous blood gas at baseline and blood draw at the end of the intervention

Other characteristics and effect modifiers:

- Baseline characteristics (age, gender, PD severity (Hoehn and Yahr), disease duration, quality of life (Parkinson*s Disease Questionnaire 39-PDQ39), pulmonary function testing, diffusion capacity (DLCO), p0.1, MIP, other medication (e.g. beta-antagonists)
- Potential effect modifiers (measured before every intervention): levodopa equivalent daily dose, sleep (item 9 of PSQI), physical activity (IPAQ-SF)

Study description

Background summary

Anecdotal evidence suggests that visiting high-altitude areas improves motor symptoms of Parkinson's disease (PD). It is hypothesized that the positive effect of altitude on the symptoms of PD results from decreased oxygen pressure at high altitudes that leads to adaptive mechanisms that influence PD symptoms. This will be assessed in an exploratory phase I trial, which will additionally address the potential of strong inter-individual differences of modification of symptoms by altitude simulation, and for the identification of the optimal protocol to simulate high-altitude.

Study objective

To explore the safety and feasibility of continuous and intermittent hypoxia therapy in PD and the differences of symptom modification of different hypoxia protocols. Secondary outcomes include exploring the responsiveness of subjective and objective motor outcome measures to assess the acute effects of this intervention on PD symptoms, as well as elucidating mechanisms of administering hypoxia relevant to PD.

Study design

Multiple randomized double-blinded N-of-1 trials (single patient cross-over trial).

Intervention

Normobaric hypoxia will be delivered provided via an oxygen mask: one of the following in OFF-condition: continuous hypoxia comparable to 2000m altitude (16.3% O2) for 45 minutes, continuous hypoxia comparable to 4000m altitude (12.7% O2) for 45 minutes, intermittent hypoxia for 45 minutes at 2000m, intermittent hypoxia for 45 minutes at 4000m, continuous sea level conditions (20.9% O2) for 45 minutes. 8 age-matched controls undergo the screening intervention once.

Study burden and risks

Participants will visit our hospital 10 times across 10 consecutive weeks. Each visit will commence in the morning with an estimated duration of 2.5 hours per intervention day. Every participant will be screened for cardiorespiratory comorbidities and if present, will be excluded. Induction of normobaric hypoxia results in reduced oxygen availability for individuals living at sea level, which typically does not lead to any physiological discomfort when applied at

the levels proposed in this study. Two senior physiologists on this project have ample experience with both comparable and significantly more intense hypoxia experiments.
However, it should be noted that experience in applying these techniques specifically in Parkinson patients is limited. Therefore, during experiments, vital parameters will be monitored continuously to monitor safety of the intervention, and the use of clear cut-off values to terminate studies if necessary.
Participants' benefit include adding to new insights into effect modifiers of PD symptoms that might additionally provide insight into disease mechanisms. For PD patients, these factors are important motivators for trial participation.

Contacts

Public
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6525GC
NL
Scientific
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6525GC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Able to provide informed consent
- Age >18 years
- Clinical diagnosis of Parkinson*s disease by a movement disorder specialized neurologist with Hoehn and Yahr staging 1.5 to 3.
- (for age-matched controls: all of the above, except for PD)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Individuals with diseases leading to restrictive and obstructive pulmonary diseases, pulmonary diffusion deficits, apnea and cardiac output deficits, such as pulmonary fibrosis, chronic obstructive pulmonary disease (COPD), sleep apnea or excessive alcoholic intake, and congestive heart failure respectively.
- Arterial blood gas abnormalities at screening
- Individuals with shortness of breath or other airway or breathing-related inconvenience related to lack of dopaminergic medication will be excluded.
- Inability to comply to intervention in off-medication condition (for example due to extreme discomfort, distress or severe head tremor due to being OFF, i.e. without dopaminergic medication).
- Individuals with unstable dopaminergic medication dose (changes in the last month)
- Individuals likely to start dopaminergic treatment in the next month, also judged by their treating neurologist
- Individuals with active deep brain stimulation
- Individuals unable to provide informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-02-2022
Enrollment:	28
Type:	Actual

Medical products/devices used

Generic name:	Hypoxicator (B-chat Hypoxicator)
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	26-01-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-04-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL77891.091.22

Study results

Date completed: 17-11-2023

Actual enrolment: 20

Summary results
Trial is onging in other countries