A randomized phase 1b/2a trial of the effectiveness of intermittent hypoxia interventions in Parkinson*s disease

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To explore the safety, feasibility and net symptomatic effects of multiple intermittent hypoxia intervention sessions in individuals with PD. Secondary outcomes include exploring induction of relevant neuroprotective pathways as measured in serum.

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

Summary

ID

NL-OMON53977

Source
ToetsingOnline

Brief title
TALISMAN-2

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Michael J. Fox Foundation

Intervention

Keyword: Hypoxia, Parkinson's disease, Preconditioning

Outcome measures

Primary outcome

- Number and nature of adverse events

- Movement Disorder Society-Unified Parkinson*s Disease Rating Scale

(MDS-UPDRS) part II and part III score (Activities of Daily Living and Motor

score).

- Feasibility questionnaire

Secondary outcome

- Purdue pegboard test (PPT)

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

- MDS Non-Motor Scale (NMSS)

- Parkinson*s disease questionnaire-39 (PDQ-39)

- Accelerometry data on tremor and pronation-supination as part of the

MDS-UPDRS III (using the Movisens® Move 4 activity sensor)

- Hypoxic ventilatory response (ventilation, breathing frequency, tidal volume)

- Hematocrit, neurofilament light chain (NfL), clusterin, GFAP, UCH-L1, BDNF,

platelet-derived growth factor receptor beta (PDGFRβ).

Study description

Background summary

Intermittent hypoxia interventions are a well-established intervention used by athletes and individuals with cardiovascular disease, amongst others. The

safety and feasibility of (intermittent) hypoxia intervention and its short-term effects on Parkinson*s disease (PD) symptoms were assessed in a previous exploratory phase I trial. However, the net effects of multiple hypoxia intervention sessions on PD symptoms are unknown. The results of the previous phase I trial informed the study design of the newly proposed phase 1b-2a safety and efficacy trial.

Study objective

To explore the safety, feasibility and net symptomatic effects of multiple intermittent hypoxia intervention sessions in individuals with PD. Secondary outcomes include exploring induction of relevant neuroprotective pathways as measured in serum.

Study design

The study concerns a two-armed double-blinded randomized controlled trial.

Intervention

45 minutes of normobaric intermittent hypoxia (FiO2 0.163 for 5 minutes interspersed with 5 minutes normoxia) will be delivered via a hypoxicator (a device that titrates decreased fractional oxygen from room air) through an oxygen mask at participants* homes. Interventions will be conducted 3 times a week, for 4 weeks in total. An instructor will be present for instructions during the first session, and will remain present until necessary for safe and comfortable hypoxia administration. This is followed by remote expert assistance during the first week of interventions, followed by weekly videocalls to ascertain adequacy of administration, safety and compliance. During a pilot phase of the first four participants, participants visit the hospital in the second week to closely monitor bodily responses to repeated administration.

Study burden and risks

The mechanism of action of hypoxia interventions on the cardiovascular and cardiorespiratory system in humans is relatively well-known in healthy individuals and fragile individuals with a wide variety of conditions. Extensive literature exists on hypoxia interventions, including more intense or longer hypoxia trials than the current. Previous studies inducing intermittent hypoxia in human individuals have shown significant positive cardiovascular effects. Importantly, outside PD, IHT is a widely adopted intervention proven safe in a variety of disciplines, including longer-term and more frequent interventions in fragile populations such as elderly, individuals with chronic obstructive pulmonary disease (COPD), and cardiac morbidity. Many studies have used hypoxicators, including the models like the one that is used in this

protocol.
Cardiorespiratory complications intrinsic to PD have not led to adverse events in intense aerobic exercise trials and participants are thorougly screened before study initiation. In PD, our TALISMAN-1 trial seems to indicate hypoxia administration is safe and feasible after having performed a structured screening procedure. There is no indication of significant symptom worsening in TALISMAN-1. Although there are no foreseeable adverse events in this population, we take extensive safety measures that minimalize the risk of any adverse events, albeit reversible or irreversible. In addition, the proposed method of hypoxia administration is the most widely used. Studying this intervention is warranted by the combination of preclinical evidence, and our previous study results. There is potential discomfort due to breathing through a mask or (unexpected and unprecedented) reversible worsening of symptoms. Primarily, this will lead to physical discomfort. Moments of worsening of symptoms might also cause psychological discomfort. We anticipate no social, societal, privacy-related, financial or stigma-related adversity for our participants.

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

- Informed consent
- Clinical diagnosis of Parkinson*s disease by a movement disorder specialized neurologist.
- Hoehn and Yahr staging 1 to and including 3 (indicating mild to moderate PD).
- Availability of an observant (partner, family member, friend, other relative) during at-home hypoxic interventions.

Exclusion criteria

- Individuals with diseases leading to restrictive and obstructive pulmonary diseases, apnea and cardiac output deficits, such as pulmonary fibrosis, COPD, sleep apnea or excessive alcoholic intake, and congestive heart failure respectively, and individuals with coronary artery disease NYHA classes III and IV
- Arterial blood gas abnormalities at screening procedure (as per normal limits in chapter 8.1.1)
- Individuals with shortness of breath or other airway or breathing-related inconvenience related to lack of dopaminergic medication
- Inability for in-clinic measurements in OFF phase
- Individuals with active deep brain stimulation

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-07-2023
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Hypoxicator
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	21-06-2023
Application type:	First submission
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	NL83301.091.23