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Vagus nerve stimulation in Parkinson's disease

Submission date
03/05/2020

Recruitment status
No longer recruiting

Registration date
11/05/2020

Overall study status
Completed

Last Edited
22/02/2024

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Parkinson's disease is a condition in which parts of the brain become progressively damaged over many years.
Disorders of gait and falls are common in patients with Parkinson’s disease (PD), particularly as the disease progresses and the patients become frail. PD gait disorders are generally refractory to standard medical therapy.
Research efforts have therefore focused on neurostimulation. Vagus nerve stimulation (VNS) is an established neurostimulation technique used in the treatment of migraine and epilepsy. Evidence from animal experiments has shown that VNS might treat some of the motor and non-motor features of PD. In our open-label pilot study, we found an encouraging result in the treatment of freezing of gait in PD patients. In this randomized, double-blind sham-controlled trial we will explore the role of noninvasive VNS (nVNS) in the treatment of gait and motor symptoms in PD patients.

Who can participate?
Patients with Parkinson’s disease and FOG of both sexes, ranging from 30-80 years old, who can walk independently at a stretch for at least 30 meters without support.

What does the study involve?
Patients will be allocated randomly on one of the two intervention arms, - active nVNS or sham VNS, such that both patient and experimenter will be blinded to the intervention. After the baseline assessments (motor and non-motor symptoms) patients and carers will be trained in the use of the sham/active VNS device and asked to deliver the intervention in their home for one month using a standard dose (total 12 minutes of stimulation per day). At the end of one month, they will be re-assessed. After a washout period of one month, the same patients will be then allocated to the alternate treatment arm and the same process will be followed. No changes will be made to the patients’ other medications (including L-dopa dose) throughout the study.

What are the possible benefits and risks of participating?
Possible benefits of participating: Vagus nerve stimulation is FDA approved for epilepsy and migraine but in Parkinson’s disease till date. The results of this trial may help us to find a better treatment for patients with Parkinson’s disease with vagus nerve stimulation. That way patients will have an opportunity to contribute towards a medical research study. As part of the trial, we

will perform trial-related testing and thorough medical checkup entirely free of cost. If the study protocol works, you will be benefited from the treatment. If proven unequivocally, this may help in evolution of future treatment and understanding the disease better.
Risks of participating: VNS is not associated with the side effects of traditional medications. Patient will feel a mild tingling sensation over the skin of neck while applying stimulation. Side effects may include hoarseness, shortness of breath, change in voice, & skin irritation. These side effects are extremely rare and self-limiting. This stimulation protocol had been tested on patients with Parkinson's disease with favorable results and no major or devastating side effect was observed in earlier studies. In case of any adverse effect related to the intervention, they will be given appropriate treatment, which may also include withdrawal from the study.

Where is the study run from?
Institute of Neurosciences Kolkata (India)

When is the study starting and how long is it expected to run for?
February 2016 to January 2020

Who is funding the study?
Institute of Neurosciences Kolkata (India)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
INK/ MDR/ VNS-FOG/2016

Study information

Scientific Title
Effect of vagus nerve stimulation in freezing of gait and cognition in Parkinson's disease patients: an open-label pilot study

Study objectives
Daily domiciliary application of nVNS for one month could improve gait and freezing of gait (FOG) in patients with Parkinson's disease (PD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/04/2016, Institute of Neurosciences Kolkata Ethics Committee (185/1 AJC Bose Road, Kolkata 700017, India; +91 33 40309999; drgourdas@gmail.com), ref: I-NK/EthicsComm/44/2016

Study design
Randomized double-blind sham-controlled crossover clinical trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Idiopathic Parkinson's disease

Interventions
Patients will be allocated randomly to one of two intervention arms, - active nVNS or sham nVNS, such that both patient and experimenter will be blinded to the intervention. After the baseline assessments (motor and non-motor symptoms) patients and carers will be trained in the use of for using the sham/active VNS device on the left side of the neck. They will be and asked to deliver the intervention in their at home for one month using a standard dose as per (total 12 minutes of stimulation voltage and current per day). At the end of one month the patients will be re-assessed. After a washout period of one month the same patients will be then allocated to the alternate treatment arm and the same process is followed.

The nVNS device produces a proprietary electrical signal that delivers a low voltage (peak, 24 V) and a maximum output current of 60 mA. Users adjust the stimulation amplitude within a preset range. Two stainless steel contact surfaces coated with a conductive gel enable delivery of stimulation to the neck in the vicinity of the vagus nerve (figure e-1 on the Neurology® Web site at Neurology.org). The sham device is identical in appearance, weight, visual and audible feedback, and user application and control but does not deliver identical electrical stimulation. Each treatment consists of two 2-minute self-administered stimulation delivered 5–10 minutes apart to the left side of the neck at 3 pre-specified times every day: (1) within 1 hour of awakening; (2) 6–8 hours after the first treatment; and (3) 6–8 hours after the second treatment.

The devices were dispensed in a randomised and blinded manner. Simple randomisation was performed using a computer-generated list of random numbers to assign either nVNS or sham device in addition to standard treatment in 1:1 ratio.with Random Allocation version 2.0 ratio. Devices were pre-labelled as per the randomization schedule. Till the end of the study the investigators, site coordinators and participants were blinded to the allocation of device. The patients were trained to use the device before dispensing.

Intervention Type
Device

Phase
Phase III

Drug/device/biological/vaccine name(s)
nVNS device

Primary outcome measure
Measured at baseline and 1 month
1. Two dimensional spatio-temporal gait parameters derived from GAITRite walkway
2. Motor function using UPDRS III scrore
3. Extent of freezing of gait estimated from post hoc video analysis and FOGQ score

Secondary outcome measures
Measured at baseline and 1 month
1. Cognitive parameters assessed by MMSE, Mattis DRS scores
2. Severity of REM sleep behavior disorder from REM sleep behavior disorder screening questionnaire RBDSQ
3. Fear of fall by Fall Efficacy Scale
4. Peripheral biomarkers from serum sample (TNF- Alpha, IL-6, IL 10, reduced glutathione, superoxide dismutase)

Overall study start date
01/02/2016

Completion date
30/01/2020

Eligibility

Key inclusion criteria
1. Patients with PD and FOG
2. Age ranging from 30-80 years
3. Can walk independently at a stretch for at least 30 meters without support
4. PD patients were diagnosed as per UKPDS (full form) Brain Bank Criteria

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
33

Total final enrolment
33

Key exclusion criteria
1. Significant visual impairment
2. Coexisting local or systemic diseases (e.g. osteoarthritis, other neurological conditions) which is likely to affect walking
3. History of Deep Brain Stimulation surgery or cardiac pacemakers were also excluded to ensure safe use of nVNS
4. Metallic implant/ metal cervical spine hardware near the stimulation site
5. Known or suspected cardiovascular disease, uncontrolled hypertension, recent myocardial infarction

Date of first enrolment
01/11/2016

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
India

Study participating centre
Institute of Neurosciences Kolkata
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/02d8efy02

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Institute of Neurosciences Kolkata

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
07/06/2020

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/05/2021	10/02/2022	Yes	No
Results article		07/02/2024	22/02/2024	Yes	No