ISRCTN64294760 https://doi.org/10.1186/ISRCTN64294760

Can a ketone drink reduce the severity of symptoms of Parkinson's disease?

Submission date
21/12/2018

Recruitment status
No longer recruiting

Registration date
31/12/2018

Overall study status
Completed

Last Edited
10/08/2020

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Parkinson's disease (PD) is the second most common neurodegenerative disease in the world, affecting up to 3 in 100 people aged over 65 years. PD is characterised by the death of neurons (nerve cells) that release the chemical messenger dopamine. The death of these neurons contributes to the classic motor (movement) symptoms of PD, which include slow movement and tremors (shaking). It is also increasingly appreciated that PD causes a wide variety of other types of symptoms, including sleep problems, loss of smell, depression, apathy, and cognitive dysfunctions (problems with memory and thinking).
There is no cure for PD, although there are a number of available treatments. A non-pharmacological (non-drug) therapy that has shown promise is the ketogenic diet. The ketogenic diet tricks the body into thinking it's in a state of starvation so that it produces molecules called ketone bodies. Ketone bodies represent a highly efficient source of fuel for the brain and serve several signaling functions that may counteract the progression and treat the symptoms of PD. Encouragingly, research on PD mice has shown that ketone bodies prevent the death of PD-sensitive dopamine-releasing neurons and also that they reduce the symptoms of PD. Furthermore, human patients who were on a strict ketogenic diet for 28 days experienced substantial improvements in their PD symptoms.
Unfortunately, ketogenic diets come with two major drawbacks. Firstly, they are extremely restrictive and difficult to keep to. Secondly, most of the fuel energy measured in calories comes from fat and may increase cardiovascular (heart and circulation) disease risk. A research team at the University of Oxford has recently invented a ketone body dietary supplement (DeltaG) that may be able to provide the pros of ketones without the cons of ketogenic diets. Results in healthy people has already demonstrated that DeltaG is a tolerable and safe way to increase ketone body levels and favorably alter energy metabolism. The main aim of this study is to investigate whether DeltaG can be used to reduce the symptoms of PD.

Who can participate?
Patients with Hoehn and Yahr stage 1 or 2 Parkinson's disease who are taking L-dopa, who are between the ages of 40 and 80, and who are fluent in English.

What does this study involve?
Participants will be recruited by word of mouth, emails to departmental mailing lists, posters

located in university departments, and an advertisement on the Oxford Parkinson's Disease Centre's webpage. Potential participants will be interviewed to determine eligibility and asked to give informed consent.
Participants accepted to the study will be randomly allocated to one of two groups. One group will receive a ketone ester drink (DeltaG) and the other will receive a placebo control (dummy) drink. Participants will be expected to drink their respective drinks four times every day for 1 month. During the trial, participants will undergo a series of motor, non-motor, and blood tests conducted at the John Radcliffe Hospital and in their own homes.

What are the potential benefits and risks of participating?
Participants will need to provide blood samples, wear a continuous activity monitor, and use a smartphone application. The risks are low. DeltaG has been proven to be safe in humans, but can gastrointestinal (stomach) upset in a small proportion of people because of its bitter taste. Participants may experience improvements in their motor symptoms, sleep, sense of smell, cognitive function, and even mood.

Where is the study run from?
The John Radcliffe Hospital, Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2018 to January 2021

Who is funding the study?
TdeltaS Ltd., a spin-out company from the University of Oxford.

Who is the main contact?
1. Mr. Nicholas Norwitz (DPhil student)
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2. Prof. Michele Hu (Chief Investigator)
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Contact information

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Additional identifiers

EudraCT/CTIS number

IRAS number
256914

ClinicalTrials.gov number

Secondary identifying numbers
DeltaG PD Symptoms, IRAS 256914

Study information

Scientific Title
Supplementation with a ketone ester drink to alleviate the symptoms of Parkinson’s disease

Acronym
N/A

Study objectives
Ingestion of a ketone ester supplement (DeltaG) will improve the symptoms of Parkinson's disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved (13/05/2019), NHS Health Research Authority (Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)20 7972 2545; hra.approval@nhs.net), ref: 19/SC/0138.

Study design
Longitudinal single-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled 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
Parkinson's disease

Interventions
To ensure equal group sizes, participants will be block randomized to a ketone ester or placebo control group. Following a 2-week period during which baseline measurements will be taken (weeks -2 to 0), members of each group will be asked to ingest a drink containing either 25 ml of ketone ester (DeltaG) or an equal volume of a taste-matched control fluid four times daily for 1 month (weeks 0 to 4). Participants will also be followed for 2 weeks after the conclusion of the intervention to monitor for any lasting changes (weeks 4 to 6). Over the course of the entire 2-month period, participants will visit the study location on a fortnightly basis and undergo a series of non-invasive, minimally burdensome motor, nonmotor, and biological tests in order to monitor for changes in functional status and disease pathology. Participant compliance will also be assessed to inform future studies and to inform whether or not we will choose to extend the intervention period. Depending on the preliminary results and participants' compliance, we may want to extend the intervention by a further 2 months to monitor for cumulative (or additional) positive effects of the ketone supplement.

Intervention Type
Supplement

Primary outcome measure
1. Overall symptom severity in the drug "off" state assessed using the Movement Disorder Society-Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) at weeks 0 and 4
2. Daily activity and gait assessed using a continuous activity monitor (Axivity AX3) worn on the lower back by participants for 7 days before (weeks -2 to -1) and during (weeks 2 to 3) the intervention
3. Motor skills assessed using a smartphone application once a day
4. Olfaction assessed using the Sniffin’ Sticks 16-odor identification test at weeks 0, 4, and 6
5. Selective attention assessed using the Stroop color-word test at weeks 0, 4, and 6
6. Cognitive function assessed using the the Montreal Cognitive Assessment (MoCA) at weeks 0, 4, and 6
7. Fatigue assessed using the Fatigue Severity Scale (FSS) survey over the phone once per week during a randomly-timed compliance call
8. Quality of life of participant assessed using the PDQ-39 questionnaire at weeks 0, 4, and 6
9. Quality of life of participant's carer assessed using the PDQ-Carer questionnaire at weeks 0, 4, and 6
10. Parkinson's disease-related sleep disorder assessed using the REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ) at week 0.

Secondary outcome measures
1. Blood uric acid measured in a fasted state at weeks 0, 2, 4, and 6
2. Blood glucose measured in a fasted state at weeks 0, 2, 4, and 6
3. Blood fructosamine measured in a fasted state at weeks 0, 2, 4, and 6
4. Blood insulin measured in a fasted state at weeks 0, 2, 4, and 6
5. Blood lipids measured in a fasted state at weeks 0, 2, 4, and 6
6. Blood C-reactive protein (CRP) measured in a fasted state at weeks 0, 2, 4, and 6
7. Blood inflammatory cytokines measured in a fasted state at weeks 0, 2, 4, and 6
8. Compliance assessed by calling patients at random once per week to ask them when they last consumed the study drink and to request that they blindly (we will mask the monitor) measure their own blood ketone levels by fingerstick
9. Participant subjective comments on their experiences taking the drink assessed using a consumer-style questionnaire at week 4

Uric acid is a major circulating antioxidant that tends to be depleted in the blood of patients with Parkinson’s disease. Participants’ glucose, fructosamine, insulin, and lipids levels will afford insight into the quality of their carbohydrate metabolism and relative cardiovascular risk. This is relevant because diabetes and heart disease are also age-related diseases and often present as comorbidities alongside Parkinson’s disease. CRP and inflammatory cytokines are markers of systemic inflammation, a phenomenon characteristic of, and involved in the development of, many age-related diseases.

Overall study start date
01/10/2018

Completion date
01/01/2021

Eligibility

Key inclusion criteria
1. Diagnosis of Parkinson's disease
2. Taking L-dopa
3. Hoehn and Yahr stages 1-2
4. Fluent in English
5. Capable of giving informed consent
6. Aged 40-80

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
20 participants divided equally into two groups.

Key exclusion criteria
1. Communication impairments
2. Any disorder that the Chief Investigator deems may bias the study results or put the participant at risk

Date of first enrolment
02/02/2019

Date of final enrolment
02/10/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
John Radcliffe Hospital
Headley Way, Headington
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Sponsor information

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
TdeltaS Ltd

Results and Publications

Publication and dissemination plan
At the end of the study, the results will be presented at regional, national, and international meetings and published in medical journals. All published results and information will be anonymized.

Intention to publish date
01/07/2021

Individual participant data (IPD) sharing plan
The demographic data and individual participants' study results generated during and/or analyzed during the current study will be available upon request from Nicholas Norwitz (nicholas.norwitz@dpag.ox.ac.uk) after the study concludes and for 5 years. If participants formally

consent to have their individual data shared at the commencement of the study, it may be shared with other research teams upon justifiable request and will remain anonymized by a study-specific identification number.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.14	11/03/2020	10/08/2020	No	Yes
Protocol file	version v1.10	12/03/2020	10/08/2020	No	No
HRA research summary			28/06/2023	No	No