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Can a ketone drink improve exercise performance in patients with Parkinson's disease?

Submission date
26/11/2018

Recruitment status
No longer recruiting

Registration date
07/12/2018

Overall study status
Completed

Last Edited
17/02/2021

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Parkinson's disease (PD) is the world's most common brain disease that affects motor function. The four main symptoms of PD are shaking, rigidness, problems with posture, and slowness of movement. These symptoms tend to get worse over time and are likely to affect all patients at some point during the disease process.
Research has focused on exercise as a way to slow, and even improve, the symptoms associated with PD. However, the effectiveness of exercise is limited by the fact the PD impairs a person's ability to move and do exercise. Any therapeutic that could, even temporarily, improve physical ability could help to establish a positive loop where increased exercise capacity leads to improvement of the disease symptoms, which then improves physical functioning, and so on.
The Clarke research team at the University of Oxford has invented a ketone body dietary supplement (DeltaG) that may be able to stimulate such a positive loop. Results suggest that DeltaG alters energy metabolism and significantly increases exercise performance in human athletes. In this study, we want to investigate whether the performance-enhancing effects in athletes translate into persons struggling with PD.

Who can participate?
Patients with Hoehn and Yahr stage 1 or 2 Parkinson's disease who are between the ages of 40 and 80 years, who are fluent in English, and who have no history of heart disease.

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 perform an exercise test on a fixed-power stationary bicycle in which they begin cycling for 5 minutes at 100 Watts, after which the power requirement will increase by 25 Watts every 3 minutes until the participant stops pedaling voluntarily from exhaustion. Participants will perform the test 30 minutes after consuming either 350 mg/kg of ketone ester drink (DeltaG) or a control drink. Each participant will perform

the test twice, once after consuming the DeltaG and once after consuming the control drink. The two tests will be separated by one week.
During the exercise test, participants will be asked to wear a face mask and heart rate monitor so that we can assess heart and lung function. Finally, participants will be asked to provide blood samples to investigate how the ketone ester and exercise affect metabolic processes.

What are the potential benefits and risks of participating?
There are not expected to be direct benefits for participants, although the results of the research could inform treatment options for patients with Parkinson's disease. The risks to participants are minimal. The ketone supplement (DeltaG) might cause diarrhea, abdominal distension, and nausea. However, these gastrointestinal side effects are both rare and mild. DeltaG has 'Generally Regarded As Safe' (GRAS) certification from the US FDA and is commercially available in the United States as a sports supplement. Research has shown that repeated consumption of DeltaG at much higher doses is safe and generally well-tolerated.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2018 to January 2020.

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)
nicholas.norwitz@dpag.ox.ac.uk
2. Prof. Michele Hu (Chief Investigator)
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Additional identifiers

Integrated Research Application System (IRAS)
257795

Protocol serial number
DeltaG PD Exercise

Study information

Scientific Title
Supplementation with a ketone ester drink to improve exercise performance in patients with Parkinson's disease as measured by a cycle ergometer ramp test

Acronym
N/A

Study objectives
Ingestion of a ketone ester supplement (DeltaG) will improve exercise performance in patients with Parkinson's disease. Therefore, we will report the DeltaG versus control differences on the following parameters: patients' times to exhaustion, maximum work outputs, and cardiopulmonary test measures. We will also report on the effects of DeltaG and exercise on the levels of circulating metabolites.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved (23/07/2019), 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/0032.

Primary study design
Interventional

Study design
Cross-over single-blind placebo-controlled trial

Study type(s)
Treatment

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

Interventions
In this cross-over placebo-controlled trial, participants (n=15) will perform an exercise test on a fixed-power cycle ergometer in which they begin cycling for 5 minutes at 100 Watts, after which the power requirement increases by 25 Watts every 3 minutes until the participant stops pedaling voluntarily from exhaustion. Participants will be asked to come in before breakfast after an overnight fast and perform the test 30 minutes after consuming either a ketone drink or a taste-matched isocaloric control drink. The ketone drink will contain 25 g of ketone ester (DeltaG) and 45 g of dextrose and the control drink will contain 30 g of dextrose, 30 g of fructose, 15 g of maltodextrin, and 1.5 ml Symrise bitter flavor; product code: SY648352. Each participant will perform the test twice, once after consuming the ketone drink and once after consuming the control drink. The two tests will be separated by a one-week washout period and will be ordered randomly based on the flip of a coin.

During the exercise, participants will be asked to wear a face mask and heart rate monitor so that cardiopulmonary function (objective measures of exercise capacity) can be assessed. Finally, participants will provide blood samples immediately before consuming the study drinks, immediately before exercise, and immediately after exercise to investigate how DeltaG, in combination with carbohydrates and exercise, affects circulating levels of glucose, lactate, free fatty acid, and the ketone body beta-hydroxybutyrate.

Intervention Type
Supplement

Primary outcome(s)

1. Time to exhaustion (Te)
2. Maximum wattage achieved by participants (Wmax)
3. Maximum heart rate (HRmax) assessed by heart rate monitor worn during the test
4. Oxygen consumption (VO2max) assessed using a respiratory gas capture face mask worn during the test
5. Respiratory exchange ratio (RER) assessed using respiratory gas capture face mask worn during the test.

Key secondary outcome(s)
1. Blood glucose level
2. Blood lactate level
3. Blood free fatty acid level
4. Blood beta-hydroxybutyrate level
These will be measured using samples taken from a venous cannula inserted into one of the participants' arms immediately before consuming the study drink, immediately before exercise (30 minutes after consuming the study drink), and immediately after exercise.

Completion date
21/01/2020

Eligibility

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

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
16

Key exclusion criteria
1. Communication impairments
2. History or indications of cardiovascular disease
3. Any other disorder that the Principal Investigator deems may bias the study results or put the participant at risk

Date of first enrolment
01/01/2019

Date of final enrolment
01/01/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Brookes University
Headington Campus
Oxford
United Kingdom
OX3 0BP

Sponsor information

Organisation
TdeltaS Ltd

Funder(s)

Funder type
Industry

Funder Name
TDeltaS Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The demographic data and individual participants' study results 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?
Results article	results	30/09/2020	17/02/2021	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version V1.4	04/12/2018	07/12/2018	No	Yes
Participant information sheet	version V1.5	08/12/2018	10/12/2018	No	Yes
Participant information sheet	version V1.7	24/02/2019	10/08/2020	No	Yes
Protocol file	version V1.4	04/12/2018	07/12/2018	No	No
Protocol file	version V1.5	08/12/2018	10/12/2018	No	No
Protocol file	version v1.12	21/05/2019	10/08/2020	No	No