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Can a ketone drink increase ATP in the brains of patients with Parkinson's disease?

Submission date
04/12/2018

Recruitment status
No longer recruiting

Registration date
07/12/2018

Overall study status
Completed

Last Edited
12/01/2021

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 second most common neurodegenerative disease in the world, affecting 2-3% of individuals >65. It is biologically defined by the death of brain neurons that release the chemical messenger dopamine and is symptomatically characterized by a variety of motor and nonmotor issues.
It is thought that PD is caused, in part, by problems in energy metabolism. Specifically, there is a decrease in the production of ATP (adenosine triphosphate) within the brain's dopamine-releasing neurons. ATP can be thought of as the energy currency of all cells, and the brain's dopamine-releasing neurons are among the most energetically demanding cells in the human body. Therefore, this decrease in ATP production contributes to an energy crisis that ultimately leads to dopamine-releasing neuron cell death in patients with PD.
While there is no cure for PD, evidence suggests that altering the brain's energy metabolism by providing neurons with a highly efficient source of fuel called ketone bodies can increase ATP levels and help to alleviate the symptoms of PD. Encouragingly, work in cell and animal models of PD has shown that ketone bodies do, in fact, prevent the death of dopamine-releasing neurons and also protect against the symptoms of PD.
Historically, the only way to meaningfully increase ketone body levels in humans has been through starvation or pseudo-starvation "ketogenic" diets. During starvation, or while on a ketogenic diet, there is a deficiency of glucose. Because the brain normally relies on glucose for fuel, evolution equipped humans with the ability to produce a highly efficient backup fuel—ketone bodies. In the absence of dietary carbohydrates, the liver produces ketone bodies from fat to fuel the brain. These ketone bodies alter brain metabolism in a manner that may protect neurons. Interestingly, human patients who adhered to a ketogenic diet for 28-days experienced impressive improvements in their PD symptoms. Unfortunately, starvation and ketogenic diets come with major drawbacks. The former is obviously not sustainable. The latter is also difficult to sustain because ketogenic diets are composed of >80% fat calories and are difficult with which to comply. Furthermore, ketogenic diets may confer cardiovascular risk.
The Clarke group at the University of Oxford has invented a ketone body dietary supplement (DeltaG) that may provide the pros of ketones without the cons of starvation or ketogenic diets. Data in healthy humans has already demonstrated that DeltaG is a tolerable and safe way to increase ketone body levels and favorably alter energy metabolism. The aim of this study is to investigate whether DeltaG can be used to increase ATP levels in the brains of patients with PD

and, thereby, perhaps help to rescue PD-sensitive dopamine-releasing neurons from energy crisis and subsequent cell death.

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

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 undergo magnetic resonance imaging at the John Radcliffe Hospital in Oxford to measure the ATP levels in their brains before, and one hour after, consuming 350mg/kg of the Clarke group's ketone supplement (DeltaG). In addition to the scan, participants will be asked to provide two blood samples taken from a venous cannula inserted into one of their arms to investigate how the ketone supplement affect the levels of circulating metabolites.

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 therapeutic interventions for patients with Parkinson's disease. The risks to participants are minimal. Perhaps the only notable risk is that it has been reported that the ketone supplement (DeltaG) can 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 FDA, is commercially available in the United States as a sports supplement, and prior work by the Clarke group has demonstrated that chronic ingestion of DeltaG at much higher doses is safe and generally well-tolerated.

Where is the study run from?
The John Radcliffe Hospital in Headington, Oxford, OX3 9DU, United Kingdom.

When is the study starting and how long is it expected to run for?
October 2018 to December 2019.

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

Protocol serial number
DeltaG PD ATP

Study information

Scientific Title
Supplementation with a ketone ester drink to increase cerebral ATP in the brains of patients with Parkinson's disease as measured by magnetic resonance spectroscopy

Study objectives
Ingestion of a ketone ester supplement (DeltaG) will increase ATP levels in the brains of patients with Parkinson’s disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/03/2019, South Central - Oxford A Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3 Block B, Lewins Mead, Bristol, BS1 2NT, UK; Tel: +44 (0)207 104 8041; Email: nrescommittee.southcentral-oxforda@nhs.net), REC ref: 19/SC/0033

Study design
Single-centre non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
12 patients with Parkinson’s disease will undergo 31-phosphorus magnetic resonance spectroscopy (31-P MRS) imaging in order to determine their baseline cerebral ATP levels. They will also have a set of bloods drawn at this timepoint to determine their glucose, lactate, insulin, free fatty acid, and beta-hydroxybutyrate baselines. Participants will then consume 350mg/kg of ketone ester supplement (DeltaG) and, one hour later, repeat the 31-P MRS and blood measurements.

Intervention Type
Supplement

Primary outcome(s)
Cerebral ATP levels measured by 31-P MRS before and one hour after ingestion of the ketone supplement

Key secondary outcome(s))

Glucose, insulin, free fatty acid, and beta-hydroxybutyrate levels measured by standard laboratory blood assays before and one hour after ingestion of the ketone supplement

Completion date
01/12/2019

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

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
10

Key exclusion criteria
1. Communication impairments
2. Contraindications for undergoing magnetic resonance imaging (metal implants, claustrophobia)
3. Any disorder that the Principal Investigator deems may bias the study results or put the participant at risk

Date of first enrolment
01/02/2019

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hopsital
Headley Way
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
TdeltaS Ltd

Funder(s)

Funder type
Industry

Funder Name
TdeltaS Ltd

Results and Publications

Individual participant data (IPD) sharing plan
To adhere to the privacy protection requirements of our ethics board, participant level data will only be available to the research team and regulation institutions upon request to the sponsor. All participant level data will be stored in password-protected computers and facilities with restricted access.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		12/01/2021	12/01/2021	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version V1.5	04/12/2018	07/12/2018	No	Yes
Participant information sheet	version v1.10	12/03/2019	10/08/2020	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes

Protocol file	version V1.2	04/12/2018	07/12/2018	No	No
Protocol file	version v1.21	06/02/2019	10/08/2020	No	No