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The mechanism whereby an exogenous ketone drink lowers blood glucose

Submission date	Recruitment status	[X] Prospectively registered
18/01/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/03/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/05/2023	Other	

Plain English summary of protocol

Background and study aims
In both animals and humans, the infusion of acetoacetate or D-beta hydroxybutyrate (DβOHB) (also called ketone bodies) lowers blood glucose (sugar) levels. However, there is controversy on the mechanism of action behind this phenomenon and both insulin-dependent and -independent mechanisms have been proposed. This blood sugar lowering effect is greater in people with diabetes than in healthy adults and no mechanism behind this difference has been found. The aim of this study is to find out whether ketone bodies lower blood glucose by reducing the amount of available alanine for gluconeogenesis (generation of glucose).

Who can participate?
Healthy volunteers aged 18 - 70

What does the study involve?
Participants are asked to fast for 24 hours before their visit. During their visit they are asked to consume a mix of the ΔG ketone drink and water. Blood samples are collected over two hours to measure levels of glucose, BOHB, L-Alanine and L-Glutamine. The estimated volume of collected blood is less than 30 ml (or about one fl oz).

What are the possible benefits and risks of participating?
Finding the mechanism behind this phenomenon could lead to a useful new treatment for diabetes. There are no expected potential benefits for participants. Participants who complete the study will receive 50 GBP and refund of reasonable travel expenses. Inserting cannulas (tubes) for blood sampling can be uncomfortable but will always be performed by an experienced practitioner and local anaesthetic creams can be used in order to minimize any discomfort. There is a very small risk of infection, but to minimize this risk, the skin is cleaned thoroughly before the insertion. The tested dose of the ketone drink is among the lowest already studied. Doses three times greater than this have already proven to be safe. Participants receive advice on how to minimise the bad taste of the drink. In previous studies, the most reported side effects were mild nausea, abdominal distension and headache. Some participants might experience flushing which a is very well known and harmless effect of Vitamin B3

supplements and which typically resolves on its own in one or two hours. No risks or potential adverse effects are expected for the alanine supplementation groups as the dose matches the amount of alanine released by the muscle tissue in healthy adults.

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

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

Who is funding the study?
TdeltaS (UK)

Who is the main contact?
Dr Luis Adrian Soto Mota
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
DELTAGMOA2018

Study information

Scientific Title
The mechanism whereby an exogenous ketone drink lowers blood glucose

Study objectives
Ketone bodies lower blood glucose by reducing the amount of available alanine for gluconeogenesis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England - Cambridge South Research Ethics Committee, 21/06/2018, 18/EE/0115

Study design
Single-centre interventional single-dose open-label study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Glucose and ketone bodies metabolism

Interventions
Ten healthy participants will be asked to fast for 24 hours before their visit. On their visit to the Department of Physiology and Genetics of the University of Oxford, they will be asked to consume a mix of 25 ml of the ΔG ketone drink and 25 ml of water. The trialists will perform 8-point curves of blood plasma Glucose, BOHB, L-Alanine and L-Glutamine over two hours. The estimated volume of collected blood is less than 30 ml (or approximately one fl oz).

Intervention Type
Other

Primary outcome measure
Blood glucose levels, measured using blood samples collected through a venous cannula at baseline and every 15 minutes during two hours

Secondary outcome measures
Blood alanine and fatty acid levels, measured using blood samples collected through a venous cannula at baseline and every 15 minutes during two hours

Overall study start date
08/01/2018

Completion date
31/07/2018

Eligibility

Key inclusion criteria
1. Participants must be fluent in English, have no communication impairments and should be willing and able to give informed consent for participation in the trial
2. Aged 18 – 70 (inclusive)
3. With no known medical diagnosis
4. Have had no course of medication, whether prescribed or over-the-counter, in the four weeks before the first trial dose and no individual doses in the final two weeks other than over the counter analgesics, vitamins and mineral supplements or, for females, oral contraceptives
5. Female participants of childbearing potential and male participants whose partner is of childbearing potential must be willing to ensure that they or their partner mechanical or pharmacological contraception during the trial and for 3 months thereafter
6. In the Investigator's opinion, is able and willing to comply with all trial requirements
7. Willing to allow his or her General Practitioner and consultant, if appropriate, to be notified of participation in the trial

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
10

Key exclusion criteria
1. Female participant who is pregnant, lactating or planning pregnancy during the trial
2. Significant renal or hepatic impairment
3. Scheduled elective procedures requiring general anaesthesia during the trial
4. Any other significant disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the

trial, or the participant’s ability to participate in the trial
5. Participants who have participated in another research trial involving an investigational product in the past 12 weeks

Date of first enrolment
30/06/2018

Date of final enrolment
03/07/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Oxford
Department of Physiology, Anatomy and Genetics
Parks Road
Sherrington Building
Oxford
United Kingdom
OX1 3PT

Sponsor information

Organisation
TdeltaS Ltd

Sponsor details
30 Upper High Street
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Sponsor type
Industry

Website
http://tdeltas.com/

Funder(s)

Funder type
Industry

Funder Name
TdeltaS

Results and Publications

Publication and dissemination plan
Planned publication of the study results in a high-impact peer-reviewed journal in August 2019. The study protocol and statistical analysis plan will be available on request from Dr Adrian Soto Mota (adrian.soto@dpag.ox.ac.uk).

Intention to publish date
01/08/2019

Individual participant data (IPD) sharing plan
Access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections. To request it, contact Professor Kieran Clarke (info@tdeltas.com).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/11/2021	19/05/2023	Yes	No
HRA research summary			28/06/2023	No	No