ISRCTN13848689 https://doi.org/10.1186/ISRCTN13848689

Sumatriptan (a drug used for the treatment of migraine) and blood sugar

Submission date
29/01/2021

Recruitment status
No longer recruiting

Registration date
01/02/2021

Overall study status
Completed

Last Edited
01/02/2021

Condition category
Nutritional, Metabolic, Endocrine

[_] 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
Sumatriptan is a drug widely used for migraine treatment and data from mouse models show that it decreases appetite and lowers glucose. This glucose lowering effect of sumatriptan has not been studied in humans yet. In this study, we aim to establish in healthy overweight adults whether a single tablet of sumatriptan can improve:
1. sensitivity of the body to insulin (a hormone which regulates your blood glucose level), and/or
2. release of insulin from the pancreas
The results of this study might help design more targeted studies in people with diabetes. If ultimately proven effective, sumatriptan or similar treatments could be used in diabetes (including those treated with insulin as an “add-on” treatment) to improve glucose levels and reduce the risk of complications and substantial healthcare costs associated with this.

Who can participate?
Adults aged 18 – 65 years, who are overweight but otherwise healthy.

What does the study involve?
Participation will involve a screening visit (to determine if you are eligible) and 2 visits at which you will have a single dose of either sumatriptan or placebo (tablet without active drug) and studies with glucose and insulin infusion will be performed together with blood tests as detailed below. Drugs will be given in a random order (first sumatriptan and then placebo or vice versa) one at visit 1 and one at visit 2. This study is blinded so neither you nor the study doctors and nurses will know which tablet you had at which visit. This will allow us to assess the effects of the drug using a rigorous scientific approach. During the study you will be looked after by healthcare professionals (doctors and research nurses) trained in clinical research and the methods described below.
We wish to examine how the body handles glucose and insulin in overweight healthy volunteers (aged 18-65 years) after taking a single dose of sumatriptan or placebo. There will be three visits:
1. Screening visit
We will assess if you are eligible to participate by asking questions about your medical history, and performing a clinical examination. Your height and weight will be measured and a sample of your blood and urine will be taken. The results will be reviewed, and you will be informed if you are eligible to attend the subsequent visits. The visit is expected to take around 1 hour.

2. Visit 1
Visits will take place in the morning and you will need to come fasted (nothing to eat or drink except water from approximately 22:00 h the night before the visit). At the visit you will be given the assigned medication (sumatriptan or placebo). One intravenous cannula will be placed in each arm. The whole study visit will be performed over approximately 3 hours. You will first receive an infusion of glucose and blood samples will be taken at pre-defined time points (from the cannula). After 1 hour you will receive an infusion of insulin and blood samples will be taken at pre-defined time points. You will simultaneously receive an infusion of glucose to keep your blood glucose stable until the end of the procedure for the next 2 hours.
3. Visit 2
This is the same as Visit 1, the only difference being that the assigned medication will be the opposite of what you had at Visit 1 (i.e. if you had sumatriptan you will receive placebo and vice versa). All the visit procedures will be repeated as described in Visit 1 above.
At all visits you will be looked after by healthcare professionals (doctor and research nurses) trained in clinical research and the method described above. This study plan has been reviewed by our diabetes Patient and Public Involvement group (GRACED- Group for Research and Clinical Experience in Diabetes)- an independently chaired and functioning group established from volunteers attending the Wolfson Diabetes Endocrine Clinic in Cambridge.

What are the possible benefits and risks of participating?
Benefits: This study will not benefit you directly . However, the results of this study and your experience will help us develop targeted studies in people with diabetes to further explore the impact of sumatriptan on glucose levels in diabetic populations and if shown to be effective sumatriptan has the potential to be used as one of the treatment options in diabetes.
Risks: The procedure risks include. not being able to insert an intravenous cannula on the first attempt, bruising, skin irritation and infection. Well trained staff, standardised protocols and aseptic technique are used to minimise these risks. Other risks include well established side effects of sumatriptan. Side-effects of sumatriptan occurring between 1/100 to 1/10 people include: dizziness, sensation disturbance, temporary increase in blood pressure, flushing, shortness of breath, nausea and vomiting. However, the likelihood of these side-effects is very small given that only one dose is taken in this study and if these do occur they are likely to last for a short period. Glucose infusion may cause nausea and if this happens the procedure will be stopped. Furthermore, we would like to advise you not to take a type of drug called selective serotonin reuptake inhibitor (SSRI; used for the treatment of depression) immediately after the procedure as there is an extremely small risk of developing serotonin syndrome (high blood pressure, fast heart rate, increased temperature, tremor, sweating, diarrhoea) if sumatriptan and SSRI are used together. We will review your medication at each visit to identify any potential risk and advise you accordingly.

Where is the study run from?
University of Cambridge Transnational Research Facility (UK)

When is the study starting and how long is it expected to run for?
December 2020 to July 2021

Who is funding the study?
Diabetes Research and Wellness Foundation (UK)

Who is the main contact?
Dr Rajna Golubic, rg380@medschl.cam.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Rajna Golubic

ORCID ID
https://orcid.org/0000-0003-0419-9582

Contact details
MRC Wellcome Institute of Metabolic Science
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 74847
rg380@medschl.cam.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
277675

Central Portfolio Management System (CPMS)
47125

Protocol serial number
A095470

Study information

Scientific Title
Effects of serotonin receptor agonism on blood glucose lowering: Proof of concept in humans

Study objectives
A single dose of sumatriptan (100 mg) significantly increases insulin sensitivity and/or insulin secretion compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/12/2020, Camden and King's Cross Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 104 8277; CamdenandKingsCross.REC@hra.nhs.uk), ref: 20/LO/1122

Primary study design

Interventional

Study design
Random order double blinded placebo-controlled cross-over design

Study type(s)
Other

Health condition(s) or problem(s) studied
Overweight adults with no known co-morbidities

Interventions
All subjects will undergo a screening visit. This will include an assessment of inclusion/exclusion criteria, physical exam, alcohol and substance screening test, pregnancy test for women and routine blood tests (full blood count, urea and electrolytes, HbA1C, liver function tests, blood borne viruses).

The assessment of insulin sensitivity and insulin secretion usually requires separate study days. In this study, we aim to combine these into a single 3 hour physiological study combination (FSivGTT followed by a hyperinsulinaemic euglycaemic clamp (HEC) sometimes termed a “Botnia clamp”).

Participants will attend 2 visits receiving either sumatriptan (100 mg) or placebo in a random order by a coin toss.

At each visit the participant will arrive fasted. After taking either sumatriptan (100 mg) or placebo one intravenous cannula will be placed in each arm.
Participants will receive an infusion of glucose and blood samples will be taken at pre-defined time points (from the cannula). After 1 hour particpatns will receive an infusion of insulin and blood samples will be taken at pre-defined time points. Participants will simultaneously receive an infusion of glucose to keep your blood glucose stable until the end of the procedure for the next 2 hours.
There will be up to 4 weeks between visit 1 and visit 2.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
1. Insulin sensitivity - expressed as M-value calculated from the hyperinsulinaemic euglycaemic clamp component of the Botnia clamp at visit 1 and visit 2
2. Insulin secretion - calculated from the frequently sampled intravenous glucose tolerance test component of the Botnia clamp at visit 1 and visit 2

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/07/2021

Eligibility

Key inclusion criteria
1. Being able to provide written informed consent
2. Age between 18 and 65 years
3. Body Mass Index (BMI) ≥25 kg/m² and <30 kg/m² for non-Asian individuals; BMI ≥23 kg/m² and <25 kg/m² for Asian individuals according to the BMI classification by the World Health Organization (WHO)
4. HbA1C <48 mmol/mol at screening
5. Subject must not use any regular prescribed medications (this excludes simple analgesia used as needed)
6. Subject must not use any over the counter supplements targeting metabolism
7. Subject must not have any acute or chronic disease which in the opinion of the investigator may affect the study outcome
8. Subject must not be a current smoker
9. No history of substance abuse or excess alcohol consumption (>14 units/week)
10. Women of childbearing age must have a negative pregnancy test at screening and must not be breastfeeding
11. Women of childbearing age who are sexually active with a male partner must use highly effective contraceptive methods

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Use of any regular medications
2. Use of illicit drugs
3. Use of any over the counter supplements affecting metabolism
4. Diagnosis of any acute/chronic disease
5. Current smoking or excess alcohol consumption (>14 units/week)
6. Current pregnancy or lactation
7. Abnormal findings on physical exam or routine blood tests at screening (full blood count, urea and electrolytes, HbA1C, liver function tests)
8. Concurrent participation in another trial with an investigational product
9. History of anaphylaxis

Date of first enrolment
04/01/2021

Date of final enrolment
01/06/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Cambridge Transnational Research Facility
Hills Road
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Charity

Funder Name
Diabetes Research and Wellness Foundation

Alternative Name(s)
Diabetes Research & Wellness Foundation, Diabetes Research and Wellness Foundation UK, DRWF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version V2	01/11/2020	01/02/2021	No	Yes
Protocol file	version V2	01/11/2020	01/02/2021	No	No