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The effect of increased salt intake with a meal on blood sugar levels in people without diabetes after weight-loss surgery

Submission date
09/07/2020

Recruitment status
No longer recruiting

Registration date
23/07/2020

Overall study status
Completed

Last Edited
06/01/2026

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
In people without diabetes, symptoms due to low sugar levels (hypoglycaemia) a few hours after eating is a common problem after weight-loss surgery which can be distressing. Currently, there is no good treatment available for this problem.The altered absorption of glucose from the gut after weight-loss surgery seems to be an important factor contributing to hypoglycaemia after the meal.

Studies in animals after weight-loss surgery have demonstrated that increased salt intake with a meal can modify the absorption of glucose from the gut and increase the glucose levels. If this is also the case in humans, increased salt intake with a meal may be a treatment for post-meal hypoglycaemia after weight-loss surgery.

Who can participate?
Patients over one year after gastric bypass, aged 18 - 74 years.

What does the study involve?
This study will investigate the effect of increased salt intake with a meal on glucose after weight-loss surgery in patients without diabetes. Participants will be randomised to either
Group 1: Standardised MMTT (mixed meal tolerance test) with 2 g of table salt at visit 1, followed by standardised meal without additional table salt at visit 2.
Group 2: Standardised MMTT (mixed meal tolerance test) without 2 g table salt at visit 1, followed by standardised meal with additional 2 g table salt at visit 2.

What are the possible benefits and risks of participating?
Benefits: Contributing to the scientific understanding of the effects of the intervention. The results of this study may contribute to the design of a potential treatment option to prevent low blood glucose episodes in people who have had weight loss surgery. Potential participants with hypoglycaemia may be identified during the study and will be provided with nutritional advice (after completion of the study.
Risks: Participants may experience symptoms that are related to dumping syndrome and low

blood sugar levels (hypoglycaemia). In order to reduce the risk of experiencing these symptoms, people with a diagnosis of hypoglycaemia after weight loss surgery will not be included in the study. The amount of sugar in the set meal will be a lot less compared to the usual meals that would trigger dumping syndrome. Throughout the visits, participants will be monitored at all times for any symptoms related to hypoglycaemia and dumping syndrome through study questionnaires and if low glucose levels are confirmed, the test will be stopped and participants will receive treatment for hypoglycaemia. The clinical team will also be on hand to manage any symptoms that may develop.

Where is the study run from?
Leicester Diabetes Centre (UK)

When is the study starting and how long is it expected to run for?
March 2019 to April 2024

Who is funding the study?
Novo Nordisk UK Research Foundation

Who is the main contact?
Dr Dimitris Papamargaritis, SALT@uhl-tr.nhs.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
273999

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 45812, IRAS 273999

Study information

Scientific Title
The effect of increased sodium intake with a carbohydrate-rich meal on glucose homeostasis in subjects without diabetes after bariatric surgery: A proof-of-concept, randomised, open-label, crossover study

Acronym
The SALT Study

Study objectives
Increased sodium intake with a carbohydrate-rich meal in patients without diabetes after RYGB will increase the postprandial and nadir glucose levels after RYGB through a more physiological and gradual absorption of the dietary glucose at the proximal small intestine

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/06/2020, Yorkshire & Humber- South Yorkshire Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8091; southyorks.rec@hra.nhs.uk), ref: 20/YH/0177

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of hypoglycaemia in non-diabetic people who have had a gastric bypass

Interventions
This study is a proof-of-concept, randomised, open label, crossover study conducted in male and female participants without diabetes who have undergone Roux-en-Y gastric bypass (RYGB). The objective of the study is to investigate the effect of increased sodium intake with a carbohydrate rich meal on glucose homeostasis in patients without diabetes after bariatric surgery.

Participants will be randomised to one of the following two treatment sequences at baseline:-
• Group 1: will receive a standardised MMTT (mixed meal tolerance test) with 2g of table salt at

visit 1, and then a standardised meal without additional table salt at visit 2.
• Group 2: will receive a standardised MMTT (mixed meal tolerance test) without addition of 2g table salt at visit 1, then a set meal with 2g table salt at visit 2.

Standardised MMTT (mixed meal tolerance test) will consist of 170mls of orange juice (Tropicana smooth orange juice, where the 2g of table Salt will be diluted for those on the "additional table Salt" treatment sequence) followed by 135g Blueberry Yoghurt with Granola (Yeo Valley, Blueberry Yoghurt with Crunchy Granola)

Participants will attend a screening (familiarisation) visit prior to the start of the study followed by 2 visits and then a Safety Call.

The first visit (visit 0) is the Screening (Familiarisation) Visit and will occur not more than 14 days nor less than 1 day before the Visit 1 (Baseline visit). Visit 0 (approximately 2 hours) will involve an assessment of inclusion/exclusion criteria, an explanation of study procedures and obtaining verbal and written consent from participants by a trained healthcare professional. In addition, blood will be taken for HbA1c, Full blood count (FBC), renal function and liver function as part of investigation for exclusion criteria. A urine pregnancy test will also take place for all female participants of child bearing potential. These samples will all be processed at the pathology laboratory within the Leicester General Hospital. In addition demographic information, past medical/surgical history, concomitant medication, medication history will also be collected at this visit. A General Physical examination will be performed by a trained delegated clinician.

Visit 1 is the Baseline visit lasting approximately 5 hours and will take place at Leicester Diabetes Centre. Randomisation to one of the two treatment sequences will take place during this visit. Anthropometrics (Weight(including body fat %), Height, BP, Pulse rate) will be measured. Changes in medications since screening will be documented. Urine pregnancy test will be performed in all women of childbearing potential. A cannula will be inserted to allow multiple blood samples collection. Participants randomised to standardised MMTT plus 2g additional table Salt (NaCl) treatment sequence will be asked to drink first 170mls of orange juice with 2g of table Salt (NaCl) diluted into this and then consume 135g of Blueberry Yoghurt with Crunchy Granola (Yeo Valley) under supervision. Participants randomised to standardised MMTT without additional Salt (NaCl) will be asked to drink 170mls of orange juice (without added table Salt) and then consume 135g of Blueberry Yoghurt with Crunchy Granola (Yeo Valley) under supervision. Blood samples will be collected in the fasting state (immediately before MMTT) and at 15', 30', 60', 90', 120', 150' and 180' after MMTT ingestion for measurement of glucose, insulin, c-peptide and GLP-1. Questionnaires on dumping symptoms as well as questionnaires on hypoglycaemia symptoms will be completed during the MMTT. For the 24 hours before study visits 1 and 2, participants will be asked to refrain from: completing any moderate to vigorous form of physical activity and consuming any alcohol.

Visit 2 (occurs 7 days after visit 1) lasts approximately 5 hours and is similar to visit 1. The only change is that participants who were initially allocated to standardised MMTT plus 2g additional table Salt (NaCl) will now receive the standardised MMTT without additional table salt (NaCl) sequence. Conversely, those who were initially allocated to receive the standardised MMTT without additional table salt, (NaCl) will receive the standardised MMTT with the table salt (NaCl) added. All procedure visits will be the same as Visit 1 and urine pregnancy tests will be performed for all women of childbearing age at visit 2.

Safety Call 1 (occurs 7 days after Visit 2) is a telephone call to the patient. Patient will be asked to report any adverse events between Visit 2 and the day of the Safety Call 1. Safety call 1 is the end of the study.

Intervention Type
Other

Primary outcome(s)
Nadir (lowest) glucose levels after the standardised mixed meal tolerance test after RYGB measured using blood test in the fasting state (immediately before MMTT) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT ingestion

Key secondary outcome(s))
Measured using blood test in the fasting state (immediately before MMTT) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT ingestion (unless otherwise stated):
1. Fasting and peak glucose level
2. Insulin level
3. GLP-1 level
4. c-peptide level
5. Sigstad score
6. Edinburgh Hypoglycaemia Scale score
7. Amount of glucose (in grams) needed to restore euglycaemia
8. Number of MMTTs needed to be terminated early because of hypoglycaemia (blood glucose or capillary glucose levels ≤3.0mmol/l) measured using case report forms

Completion date
30/04/2024

Eligibility

Key inclusion criteria
1. Aged >=18 years old but less than 75 years old
2. Subjects >=1 year after gastric bypass (RYGB)
3. Able to understand written and spoken English
4. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
110 years

Sex

All

Total final enrolment
12

Key exclusion criteria
1. Use of any glucose-lowering medication (including insulin)
2. Adrenal insufficiency and/or substitution with glucocorticoids
3. eGFR <=60 ml/min/173 m²
4. Recent active infection (an active infection will be any infection over the last 10 days)
5. Current use of steroids
6. Known liver cirrhosis or ALT >2 times above upper normal limit
7. Known primary or secondary hyperaldosteronism
8. Moderate or severe hypertension during screening visit (Systolic Blood Pressure >160 mmHg as average of 3 measurements)
9. Established diagnosis of congestive heart failure
10. Significant peripheral oedema on clinical examination at screening visit
11. People with allergy or intolerance to the mixed meal tolerance test (eg, milk protein allergy, lactose and gluten intolerance)
12. People following a vegan diet (mixed meal tolerance test not suitable for those following a vegan diet)
13. Other bariatric procedure except of RYGB
14. Previous revisional bariatric surgery
15. Currently pregnant or breastfeeding
16. Patients with history of Type 1 or Type 2 Diabetes
17. Patients with diagnosis of Epilepsy
18. HbA1C >=65% or >=48 mmol/l at screening blood tests
19. Haemoglobin (Hb) <100 g/l at screening blood tests
20. Participating in another research study involving intervention within 3 months of screening
21. Having a formal previous diagnosis of postprandial hypoglycaemia
22. Being on acarbose, diazoxide, octreotide or other treatment for postprandial hypoglycaemia
23. Any concurrent condition, in the judgment of investigator and/or sponsor, that could interfere with the safety and study conduct or interpretation of study results

Date of first enrolment
26/04/2021

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Leicester Diabetes Centre
Leicester General Hospital
Leicester
England
LE5 4PW

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
Novo Nordisk UK Research Foundation

Alternative Name(s)
Novo Nordisk UK Research Foundation (NNUKRF), The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

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
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		28/11/2025	06/01/2026	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			07/02/2025	No	Yes
Protocol file	version 3.8	17/11/2023	07/02/2025	No	No