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The effect of consuming a fat-rich snack before a meal on blood sugar levels in people without diabetes after weight loss surgery

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18/03/2021

Recruitment status
No longer recruiting

Registration date
19/03/2021

Overall study status
Completed

Last Edited
31/01/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] 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
After weight-loss surgery such as sleeve gastrectomy, low blood sugar (hypoglycaemia) symptoms are a common problem for people without diabetes after eating a sugary meal, which can be very distressing. Symptoms include dizziness, sweating, shaking, hunger and drowsiness. They happen when food passes too quickly into the distal small intestine due to changes in the stomach structure after surgery. Glucose from food is absorbed quickly and too much insulin is released. This contributes to post-meal hypoglycaemia. Currently there is no good treatment available for this problem and the underlying cause is unclear.
Evidence suggests that eating a fat-rich snack (preload) 30 minutes before a sugary meal can change how fast glucose is absorbed and insulin is released in patients with and without diabetes. If this is the case then introducing a fat-rich snack to participants who have had a sleeve gastrectomy could be a potential option to treat post-meal hypoglycaemia. The aim of the study is to find out whether a fat-rich snack, consumed 30 minutes before a sugary meal, could be a potential treatment option for low blood sugar levels after the meal in participants that have undergone sleeve gastrectomy.

Who can participate?
Patients above 18 years old who do not have diabetes, have undergone sleeve gastrectomy at least 1 year ago and not taken part in any interventional research studies within the last 3 months.

What does the study involve?
The study requires participants to attend the Leicester Diabetes Centre (Leicester General Hospital) for three study visits over a period of around 3 weeks.

Screening visit (Visit 0) :
During this visit the study doctor will conduct a brief physical examination and will collect blood samples for long-term blood glucose (HbA1c) unless there is a result available in medical records from a test done within the last 3 months, blood count, blood pressure, pulse rate, kidney and liver function. The researchers will carry out a urine pregnancy test where relevant.

Participants will be asked about their health history, any current medications that they are taking and background information such as age, race and gender etc.
Participants have to wait on blood results to confirm they are eligible to take part in the rest of the study, if they are they will then be contacted to arrange their next two appointments.

Baseline (Visit 1 – 1 to 14 days after screening visit)
For this visit participants are asked to come in a fasted state, which means that they will not be able to eat or drink anything other than water from 11 pm the night before. They will also be asked not to drink any alcohol, or perform any exercise that raises their breathing or heart rate more than normal in the 24 hours before this visit. Participants will also be asked to avoid taking paracetamol for 48 hours before this visit and will be asked to confirm that they have adhered to these requests at the start of the visit.
The visit will last about four to five hours. Participants' height, weight, body fat percentage, blood pressure and pulse rate are measured and female participants of childbearing potential will be asked to complete a urine pregnancy test (Pregnant women will be excluded from the study as pregnancy can affect glucose levels and subsequently the results of the study). The researchers will check if there have been any changes to the participants' medication or health since their screening visit . They will then insert a cannula which is a very small, flexible tube which is placed into one of the veins, usually in the back of the hand or in the arm. One end sits inside the vein and the other end has a small valve that looks a bit like a tap. The researchers will use the cannula to take 11 different blood samples over the course of 3.5 hours (3 times before the meal and 8 times after the meal) meaning that they will avoid unnecessary and repeated blood samples. A total of 138 ml of blood will be obtained; this is slightly more than half a cup or around 8 tablespoons.
Participants will be randomly allocated (like flipping a coin) to one of the two study groups. Group 1 will have the 28 g of nuts with 80 ml of water (preload) 30 minutes before the milkshake (with 1g dissolvable paracetamol). Group 2 will have 100 ml water and then the milkshake without 28 g of nuts (with 1g dissolvable paracetamol). Participants will be supported to complete two short questionnaires that will be completed at the same time points as the blood samples (they will be completed just after the blood sample has been obtained; 11 times in total). The team will offer light refreshments once participants have completed the tests, but they are advised to bring along their own food and drink for lunch if they would like to consume after the completion of the study as study visits will last around 4-5 hours.

Follow-up (Visit 2 – 7 days after Visit 1)
This visit will also last between 4 and 5 hours and you must fast from 11 pm the night before (water is permitted), refrain from drinking any alcohol or doing any exercise that raises heart rate too much for at least 24 hours prior to the visit and must not consume any paracetamol for at least 48 hours prior to the visit. Participants will be asked to confirm that they have adhered to these requests at the start of the visit and whether there have been any changes to their health and/or medications since Visit 1. This visit will be the same as visit 1 including the blood tests, questionnaires, and measurements described above. Participants will be in the same group that they were allocated at visit 1. The only difference in this visit is whether or not they will eat the fat-rich snack (28 g nuts with 80 ml water), before the milkshake. Group 1 will have 100 ml water 30 minutes before the milkshake (with 1 g dissolvable paracetamol). Group 2 will have the 28 g of nuts with 80 ml of water (preload) 30 minutes before the milkshake (with 1 g dissolvable paracetamol). The blood tests and questionnaires will then be repeated.

What are the possible benefits and risks of participating?
Although there are no direct benefits from taking part, participants' general health will be reviewed by the study doctor during the study. Whilst the tests in the study are not designed for clinical diagnosis, in the unlikely event that the researchers find an abnormality, this will be

discussed directly with participants. With consent, they will also pass these results onto their GP and healthcare professionals, with the aim of organising appropriate care and treatment.
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.
Participants with hypoglycaemia may be identified during the study and will be provided with nutritional advice (after completion of the study).
During the visits participants could have symptoms that are related to dumping syndrome and low blood sugar levels (hypoglycaemia). This happens when food is emptied too quickly from the stomach into the small intestine. It literally “dumps” food too quickly into the small intestine and can lead to the following symptoms: feeling bloated, nausea, vomiting, abdominal cramps, diarrhoea, flushing, dizziness, light-headedness, rapid heart rate.

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 2020 to January 2024

Who is funding the study?
1. Health Education East Midlands Starter Grant (UK)
2. National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
282343

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 47865, IRAS 282343

Study information

Scientific Title
The impact of a fat-rich preload before a carbohydrate-rich meal on glucose homeostasis in patients without diabetes after sleeve gastrectomy: a proof-of-concept, randomized, open-label, crossover study

Acronym
CARLOTA

Study objectives
It is hypothesized that a fat-rich preload, consumed 30 minutes before a carbohydrate-rich meal, in patients without diabetes after sleeve gastrectomy (SG), will lead to higher postprandial nadir glucose levels by reducing peak postprandial glucose levels and postprandial insulin secretion due to a reduced rate of gastric emptying.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/01/2021, Yorkshire & The Humber- Bradford Leeds Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8083, +44 (0)207 104 8088, +44 (0)207 104 8109; bradfodleeds.rec@hra.nhs.uk), REC ref: 20/YH/0339

Study design
Randomized; Interventional; Design type: Treatment, Dietary, Management of Care

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Patients without diabetes after sleeve gastrectomy

Interventions
This trial is a proof-of-concept, randomised, open-label, crossover trial conducted over 29 days in male and female participants without diabetes who have undergone sleeve gastrectomy (SG).

Participants will be randomised to one of the following two treatment sequences at baseline: Group 1 will receive a fat-rich pre-load and 80 ml of water 30 minutes before the standardised MMTT with 1 g dispersible paracetamol at visit 1, and then 100 ml of water 30 minutes before the standardised MMTT with 1g dispersible paracetamol without a fat-rich preload at visit 2. Group 2 will receive 100 ml of water 30 minutes before the standardised MMTT with 1 g dispersible paracetamol without a fat-rich preload at visit 1, then a fat-rich pre-load and 80 ml of water 30 minutes before the standardised MMTT with 1 g dispersible paracetamol at visit 2.

The fat-rich preload will consist of 28 g of nuts plus 80 ml of water and will be consumed over 10 minutes. When participants have 100 ml of water without 28 g nuts this is as 100 ml of water is a similar volume to 28 g of nuts plus 80 ml of water.

The set meal [or otherwise standardised mixed meal tolerance test (MMTT)] will consist of a liquid oral supplement (Nutricia Fortisip Milkshake, 220 ml, 330 kcal, 12.76 g fat, 40.5 g carbohydrates, 13.2 g protein) and will also be consumed over 10 minutes. One (1) gram paracetamol will be dispersed into 20ml of water and will be added to the set meal in order for a paracetamol absorption test (an index of gastric emptying) to take place.

Participants will attend a screening (familiarisation) visit prior to the start of the study followed by two visits over 8 (+7) days.

The first visit (visit 0) is the screening (familiarisation) visit and will occur approximately 2 weeks before Visit 1 (Baseline visit). Visit 0 (~2 hours) will comprise an eligibility assessment and a written informed consent obtained by an appropriately trained and delegated individual. In addition, blood samples will be obtained for HbA1c, full blood count (FBC), renal function and liver function. A urine pregnancy test will also take place for all female participants of childbearing 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 and 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 4-5 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. A 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 Group 1 will be asked to consume 28g of nuts with 80mls of water over 10 minutes under supervision (30 minutes before initiation of MMTT). Participants randomised to Group 2 will be asked to consume 100mls of water (similar volume to 28g of nuts plus 80mls of water) over 10 minutes under supervision (30 minutes before initiation of MMTT). Blood samples (for glucose, insulin, GLP-1 and paracetamol levels) will be collected via cannula: before the consumption of the fat-rich preload/water (-30’), before (-15’) and immediately before (0’) the MMTT and then 15, 30, 45, 60, 90, 120, 150 and 180 minutes after the MMTT consumption. Questionnaires on dumping symptoms and hypoglycaemia symptoms will be completed during the MMTT at the same time points that each blood sample is drawn; the questionnaires will be completed immediately after the blood draw.

Visit 2 (7 days after visit 1) will last approximately 4-5 hours and will be similar to visit 1. The only change is that participants who were allocated to Group 1 (standardised MMTT (plus 1g dispersible paracetamol) with a fat-rich preload) will now consume the standardised MMTT (plus

1g dispersible paracetamol) without the fat-rich preload sequence and vice versa will apply for those in Group 2. The rest of the procedures will be repeated as per Visit 1. A urine pregnancy test will be performed on all women of childbearing potential at Visit 2.

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. Participants will also be asked to refrain from consuming paracetamol 48 hours before study visits.

Intervention Type
Other

Primary outcome(s)
The difference in nadir (lowest) glucose levels after the standardised MMTT with or without a fat-rich preload after SG for a two-period crossover design. Data will be collected at timepoints (minutes) -30' (immediately before brazil nut consumption), -15, 0 (immediately before MMTT meal consumption), 15, 30, 45, 60, 90, 120, 150, 180 minutes after MMTT consumption. The AUC [(Area Under the Curve) calculated using trapezium rule] will be used for summarising the response to the additional fat-rich preload before the standardized mixed meal tolerance test. Paired t-test or equivalent non-parametric tests will be used to analyse the AUC and the difference in nadir glucose levels.

Key secondary outcome(s))
1. Insulin, Glucagon-Like Peptide-1 and paracetamol levels measured using biochemical analysis of blood samples at the following timepoints at visits 1 and 2: immediately before initiation of consumption of the fat-rich preload/water (-30), before (-15) and immediately before (0) the MMTT and 15, 30, 45, 60, 90, 120, 150 and 180 minutes after the MMTT consumption (to correspond with the glucose measurements).
2. Symptoms of hypoglycaemia during the mixed meal tolerance test measured using the Edinburgh Hypoglycaemia Scale (EHS) at visits 1 and 2; timepoints -30 (before consumption of the fat-rich preload/water), -15, 0 (immediately before consumption of MMTT), 15 (after consumption of the last mouthful of the MMTT), 30, 45, 60, 90, 120, 150, 180 minutes. This will be completed at the timepoints above once blood samples have been drawn.
3. Symptoms of dumping measured using the Sigstad dumping score during the mixed meal tolerance test at visits 1 and 2: timepoints -30 (before consumption of the fat-rich preload/ water), -15, 0 (immediately before consumption of MMTT), 15 (after consumption of the last mouthful of the MMTT), 30, 45, 60, 90, 120, 150, 180 minutes. This will be completed at timepoints above once blood samples have been drawn.

Completion date
31/01/2024

Eligibility

Key inclusion criteria
1. Aged ≥18 years old
2. ≥1 year after sleeve gastrectomy (SG)
3. Able to understand written and spoken English
4. Able to give informed consent
5. Happy for their GP to be notified of their study participation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
10

Key exclusion criteria
1. Use of any glucose-lowering medication (including insulin)
2. Adrenal insufficiency and/or substitution with glucocorticoids
3. eGFR ≤45 ml/min/1.73 m²
4. Weight ≤50 kg
5. Recent active infection (an active infection will be any infection over the last 10 days)
6. Current use of steroids
7. Known liver cirrhosis or ALT >2 times above the upper normal limit
8. People with allergy or intolerance to the mixed meal tolerance test (e.g., milk protein allergy, lactose and gluten intolerance), to paracetamol or to nuts
9. People who are on regular painkillers (codeine phosphate, paracetamol, morphine or NSAIDS)
10. Other bariatric procedure except for SG
11. Previous revisional bariatric surgery
12. Hb <100 g/l at screening blood tests
13. HbA1C ≥6.5% or ≥48 mmol/l at screening blood tests
14. Currently pregnant or breastfeeding
15. Patients with a history of type 1 or type 2 diabetes
16. Patients with a diagnosis of epilepsy
17. Participating in another research study involving intervention within 3 months of screening
18. Having a formal previous diagnosis of postprandial hypoglycaemia
19. Currently on metoclopramide, domperidone or colestyramine as they can affect paracetamol absorption as per SPC (Summary of Product Characteristics) for paracetamol
20. Currently on acarbose, diazoxide, octreotide or other treatment for postprandial hypoglycaemia
21. 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
31/01/2022

Date of final enrolment
31/10/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Leicester NHS Trust
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Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200289

Funder Name
Health Education East Midlands Starter Grant

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study 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?
HRA research summary			28/06/2023	No	No
Plain English results			31/01/2025	No	Yes
Protocol file	version 2.4	22/09/2023	31/01/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes