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The effect of canagliflozin on the blood sugar levels of people without diabetes after weight loss surgery

Submission date 14/07/2020	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 24/07/2020	**Overall study status** Completed	
Last Edited 12/08/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Symptoms due to low sugar levels (hypoglycaemia) such as dizziness, sweating, shaking, hunger and drowsiness are commonly seen in people with diabetes, especially those who use insulin. After weight-loss surgery, these symptoms along with low sugar levels can occur in people without diabetes a few hours after they eat a meal. This happens because after weight loss surgery, some people's bodies produce more insulin (a hormone that lowers their sugar levels) than required after eating a meal. Canagliflozin, a treatment for people with type 2 diabetes, works by reducing the amount of glucose absorbed from the gut as well as by reducing the insulin that the body is producing immediately after a meal. If this is also the case after weight-loss surgery, then canagliflozin may be a treatment for people without diabetes who experience low blood sugar levels after weight-loss surgery. This study will investigate the effect of canagliflozin on blood sugar levels, insulin and other hormones in people without diabetes after they have had weight-loss surgery.

Who can participate?
Patients between 18 and 75 years of age who do not have diabetes and who have had bariatric surgery (sleeve gastrectomy or gastric bypass) 1 or more years ago

What does the study involve?
There are a total of five study visits which will take place at the Leicester Diabetes Centre, Leicester General Hospital. At the start participants will be allocated to one of two different groups at random:
Group A: canagliflozin and then routine standard care
Group B: routine standard care and then canagliflozin
Halfway through the study, participants will switch from one to the other. This is explained in more detail in the visit descriptions below.
Screening visit (Visit 0) - This visit is expected to take 2 hours
The study doctor will complete a brief physical examination, blood samples will be taken to confirm eligibility to take part in the study. These tests will include long-term blood sugar level (HbA1c), full blood count, kidney and liver function. They will also take a blood sample for a

pregnancy test (where relevant). Participants will be asked about their health history and current medications. They will be asked to complete a questionnaire asking for symptoms of low blood sugar levels (hypoglycaemia) during daily life. Before booking the rest of the visits, the researchers will check that blood results are within the study range. A member of the study team will call participants to confirm whether they are eligible to take part in the study and to arrange the next visit.
Baseline visit (Visit 1 – up to 14 days after screening visit) – This visit should last approximately 2 hours.
At this visit participants will be randomly chosen to have canagliflozin or standard care (no canagliflozin). Canagliflozin group (Group A) participants will be given four 300 mg tablets and will be asked to take one tablet each morning for four days. The first dose will be taken the morning after this visit (before the first meal of the day). A fifth tablet will be taken in clinic at visit 2 under supervision. Standard care group (Group B) participants will continue with their usual daily routine until the next appointment. The researchers will measure height, body weight, body fat percentage, blood pressure and pulse readings. They will also perform a urine pregnancy test (where relevant). They will ask about any changes to medication and document any pre-existing side effects. During this visit they will attach a small device (otherwise known as a Continuous Glucose Monitor [CGM]) onto the participant's tummy. This device will measure blood sugar levels and should be worn for 5 days (i.e. until Visit 2, described below). At this visit participants will also be asked to wear a wrist activity monitor called the 'Geneactiv'. This monitor measures physical activity and sleep. Participants will be asked to wear it 24 hours a day for 5 days (i.e. until Visit 2) on their non-dominant wrist. Once it is fitted during the study visit, participants will not need to remove it until they attend for their next visit. Participants will be shown how to check their blood sugar levels. They should do this only if they experience symptoms of low blood sugar levels. Participants will be asked to record their results in a log book provided. They will also be asked to complete a wake and sleep log and a food and drink diary for 5 days. The researchers will explain how to complete the diaries accurately. Participants will need to remember to bring the log book and the food and drink diary with them at their next visit on Day 5 (Visit 2). This visit should last approximately 2 hours.
Treatment Visits (Visit 2 and Visit 4) – These will last approximately 5 hours.
Participants will be asked to fast. This means that they will not be able to eat any food or drink any liquids, other than water, from 10 pm the night before. Participants will be asked to not to drink any alcohol or do any strenuous physical activity (activity that increases their heart rate and makes them breathe harder than normal) for 24 hours before these visits. The researchers will provide refreshments after the visit. Participants are advised to bring their own food and drink for lunch. They will check any changes to medication, confirm (where relevant) that they have taken the canagliflozin, document any effects, collect their wake and sleep log, the food and drink diary and blood glucose log book. They will remove the CGMs device and collect the wrist activity monitor. A urine pregnancy test will be carried out (where relevant). Please remember to bring along the empty canagliflozin packets (where relevant).
The researchers will measure body weight, body fat, blood pressure and pulse readings. Participants randomised to receive canagliflozin will take their fifth tablet with water while in clinic. Participants randomised to standard care will drink water without taking canagliflozin. The researchers will insert a cannula. This 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 eight blood samples. This will avoid unnecessary and repeated blood samples. A total of 100 ml of blood will be collected; this is about half a cup or 6.5 tablespoons. The researchers want to know how canagliflozin affects their blood sugar levels, insulin and hormone levels. To do this participants will be given 230 ml of milkshake drink and a choice of flavours to pick from. The drink is not suitable for people with a milk protein or soy allergy. It may not be suitable for people following a vegan or vegetarian diet. Approximately 1 week later the study nurse will

call. This should last about 15 minutes. They will discuss any symptoms participants may have had after the visits (if any). In between visits, participants will continue with their usual daily routine until their next appointment.
Visit 3 – This visit will last approximately 2 hours.
Participants originally chosen to receive canagliflozin will be switched to the standard care group. This means that they will continue with their usual daily routine until their next appointment (Visit 4). Participants originally chosen to receive standard care will be switched to receive canagliflozin. They will be given four 300 mg tablets and will be asked to take one tablet each morning for four days. This will start from the next morning and before the first meal of the day. A fifth tablet will be taken in clinic at visit 2 under supervision. All other procedures remain the same; the treatment group is the only part which changes. The same procedures conducted at the baseline visit (Visit 1) will be repeated.

What are the possible benefits and risks of participating?
By taking part in this research participants will be under the care of the study doctor(s). They are helping the researchers to understand the effects canagliflozin has on glucose and insulin levels in patients without diabetes who have undergone weight-loss surgery. This will help the researchers to understand if canagliflozin could be a potential treatment option for people who have undergone weight-loss surgery and suffer with low blood sugar levels after eating. The researchers will reimburse travel costs up to the value of £7.50 per visit. Original receipts must be provided for all expenses. During the days that participants will perform a milkshake test (visits 2 and 4) they may experience symptoms related to “dumping syndrome” or hypoglycaemia. They will be monitored at all times during visits and the clinical team will be on hand to manage any symptoms that develop. The stomach should release food and drink slowly into the small intestine. If large amounts of food are released too quickly to the small intestine, it changes hormone levels. Dumping syndrome describes a range of symptoms that occur when food is emptied too quickly from the stomach into the small intestine. It is important to note that participants might experience some of the symptoms described above at other times and not just during or after having the milkshake. During the visits that the milkshake test will take place, participants will be closely monitored for symptoms of dumping syndrome and hypoglycaemia by the clinical team. If necessary, treatment for hypoglycaemia will be provided. All medications have some unwanted effects and these will be explained to the participants before they join the study. Participants can telephone the study team if they have any unwanted side effects and require advice. Their general health will be reviewed regularly by the clinical team. They will receive a telephone call approximately 7 days after study visits where they can discuss any effects. Participants can decide to withdraw, or they may be withdrawn from the study at the discretion of the study doctor if they experience untoward side effects. The side effects of canagliflozin described below are from studies in people with diabetes. More information on the side effects can be found in the patient information sheet. Urinary tract or genital infections are common side effects in people with diabetes when using canagliflozin. Patients with peripheral vascular disease and diabetes who are taking canagliflozin are at increased risk of foot infection and ulceration. In the worst cases this can result in lower limb amputations – it is extremely unlikely that taking canagliflozin for 5 days will lead to problems with feet, especially as people with diabetes as well as people with foot ulcers and previous amputations are excluded from the study. Cases of acute kidney injury, some requiring hospitalisation and dialysis, have been reported in patients with diabetes taking canagliflozin. This is extremely unlikely to happen during the 5 days that participants will receive canagliflozin. Necrotising fasciitis is a serious bacterial infection that destroys the tissue under the skin in the area between the anus and genitals (perineum). It is a very rare event even in high-risk patients such as people with diabetes. Diabetic Ketoacidosis (DKA) occurs in people with diabetes when the body is unable to use blood sugar (glucose) because there isn't enough insulin. Instead, it breaks down fat as an alternative source of energy. This causes a build-up of a potentially

harmful by-product called ketones. DKA due to canagliflozin is rare in people with type 2 diabetes. As people with a diagnosis of diabetes will be excluded from the study, it is extremely unlikely that participants will develop this complication during the 5 days that they will receive canagliflozin.

Where is the study run from?
The Leicester Diabetes Centre, University Hospitals of Leicester NHS Trust (UK)

When is the study starting and how long is it expected to run for?
August 2018 to December 2023

Who is funding the study?
Academy of Medical Sciences (UK)

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

Contact information

Type(s)
Scientific

Contact name
Dr Dimitris Papamargaritis

Contact details
Trial Manager
Leicester Diabetes Centre – Lotus Room
Leicester General Hospital
Leicester
United Kingdom
LE5 4PW
+44 (0)116 258 8922
CONTROL@uhl-tr.nhs.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2019-004041-32

Integrated Research Application System (IRAS)
263968

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 43677, IRAS 263968

Study information

Scientific Title
The effect of canagliflozin 300 mg, in subjects without diabetes after bariatric surgery, on glucose homeostasis (the CONTROL study): a proof-of-concept, randomised, open-label, two-period crossover study

Acronym
CONTROL

Study objectives
It is hypothesised that CANA300 in patients without diabetes after RYGB or SG will reduce both the peak postprandial glucose levels and the peak postprandial insulin secretion postoperatively leading to higher nadir postprandial glucose levels.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/06/2020, Yorkshire & The Humber – Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 972 2504, +44 (0)207 104 8088, +44 (0)207 104 8018; leedswest.rec@hra.nhs.uk), REC ref: 20/YH/0123

Study design
Randomized; Interventional; Design type: Prevention, Drug

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Hypoglycaemia after eating due to weight-loss surgery

Interventions
This trial is a proof-of-concept, randomised, open-label, two-period crossover trial conducted over 39 days in male and female participants without diabetes who have undergone Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG). The objective of the study is to investigate the effect of canagliflozin 300mg once daily on glucose homeostasis in patients without diabetes after bariatric surgery.

Participants will be randomised to one of the following two treatment sequences at baseline:-
A. Canagliflozin (Invokana™) 300 mg once daily for 5 days then Standard Care (no treatment for 5 days)
B. Standard Care (No treatment for 5 days) then Canagliflozin (Invokana™) 300 mg once daily for 5 days

Participants will be stratified for procedure [1. Roux-en-Y gastric bypass, 2. Sleeve Gastrectomy].

Participants will attend a screening (familiarisation) visit prior to the start of the study followed by 4 visits over 32 days.

The first visit (visit 0) is the Screening (Familiarisation) Visit and will occur not more than 2 weeks 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 investigations for exclusion criteria. A serum pregnancy test will also take place for all female participants of childbearing potential. These samples will be processed at the pathology laboratory within the Leicester General Hospital. Demographic information, past medical and surgical history as well as concomitant medication will be collected at this visit and a general physical examination will be performed by a trained delegated clinician. A hypoglycaemia questionnaire will be filled in at the screening visit asking for symptoms of hypoglycaemia during daily life.

Visit 1 is the baseline visit lasting approximately 2 hours. Randomisation to one of the two treatment sequences will take place during this visit. Participants who are randomised to the canagliflozin 300 mg once daily group will be provided with four tablets of canagliflozin 300mg and will be asked to take one tablet daily preferably in the morning before the first meal of the day (starting from the next day in the morning). Patients randomised to no treatment will be asked to continue their usual daily life. Advice will be given to both groups, not to change their diet and daily life habits. A blinded continuous glucose monitoring (CGM) device (Dexcom G6) will be attached to the patients and they will be asked to check capillary blood glucose (CBG) levels when symptoms suggestive of hypoglycaemia occur during the study period and to document both symptoms and CBG levels at that time in their monitoring diary. Dexcom G6 device does not require validation through CBG monitoring. A qualified healthcare professional will demonstrate to them how to perform the capillary blood glucose test and how to treat episodes of hypoglycaemia. Participants will also be asked to wear a Geneactiv wrist watch monitor to capture sedentary behaviour and sleep patterns for five days, they will also complete a sleep and wake log throughout the duration of the time they wear the watch. Anthropometrics, blood pressure (BP) and pulse rate will be measured during the visit. A urine pregnancy test will be performed for all women of childbearing age at Visit 1. Changes in medications compared to baseline and reported adverse events will be documented. Participants will be advised to refrain from participating in any moderate to vigorous physical activity 24 hours before their next visit (Visit 2). A food and drink diary will be provided to the patients and they will be asked to document their meals and drinks. Procedures will be conducted and supervised by the research team comprising of study clinician and a trained healthcare assistant (HCA) or research nurse.

Visit 2 (occurs 5 days after visit 1, lasting between 4-5 hours) will take place at Leicester Diabetes Centre. Participants will be asked to come to this visit having fasted from 10 pm the night before and the study team will check the participant did not partake in moderate to vigorous physical activity for at least 24 hours before this visit. Participants randomised to canagliflozin 300 mg once daily will arrive in the morning and will receive a fifth tablet of canagliflozin 300 mg which they will ingest under supervision with 100 ml of water. Weight BP and pulse will be measured. A urine pregnancy test will be performed in women of childbearing potential who are on canagliflozin 300 mg treatment sequence. Moreover, compliance with canagliflozin 300 mg once daily during the previous days will be checked (for those on canagliflozin 300 mg sequence). Changes in medications and adverse events will be documented. Patients on the standard care (“no treatment”) sequence will drink 100 ml of water without taking canagliflozin. The CGM device, Geneactiv watch monitor will be removed and the

sleep and wake log, food and drink, and glucose diaries will be collected. A mixed meal tolerance test (MMTT) will take place 30 minutes after canagliflozin 300 mg ingestion (or 30 minutes after drinking 100 ml of water for participants on standard care ("no treatment") sequence). Participants will have a cannula inserted to allow for multiple blood samples to be collected in the fasting state (immediately before MMTT) and at 15, 30, 60, 90, 120, 150 and 180 minutes after MMTT ingestion for measurement of glucose, insulin, c-peptide, GLP-1 and glucagon. Questionnaires on dumping symptoms (53) as well as questionnaires on hypoglycaemia symptoms (54) will be completed during the MMTT.

Safety Call 1 (occurs 7 days (+ 5 days) after Visit 2) is a telephone call to the patient. The patient will be asked to report any adverse events between Visit 2 and the day of the Safety Call 1 and will be reminded to attend Visit 3.

Visit 3 (occurs 21 days (+ 5 days) after visit 2) lasts approximately 2 hours and is similar to visit 1. The only change is that participants who were allocated to canagliflozin 300 mg – standard care sequence at randomisation will now be allocated to the standard care (no treatment). Participants randomised to the standard care - canagliflozin 300 mg sequence will now be given four canagliflozin tablets and will be asked to take one tablet daily preferably in the morning before the first meal of the day (starting from the next day in the morning). The same procedures will be repeated as per Visit 1. A urine pregnancy test will be performed to all women of childbearing age at Visit 3.

Visit 4 (occurs 5 days after visit 3) lasts approximately 4-5 hours and is similar to visit 2. Participants will come to this appointment having fasted from 10 pm the night before and the study team will check the participant did not partake in moderate to vigorous physical activity for at least 24 hours before this visit or consume any alcohol in the last 24 hours. The only change is that participants who were allocated to the canagliflozin 300 mg – standard care sequence at randomisation will be allocated to "no treatment" at this visit, and they will just drink 100 ml of water without canagliflozin 30 mins before the mixed meal tolerance test. Participants randomised to canagliflozin 300 mg once daily will arrive in the morning and will receive a fifth tablet of canagliflozin 300 mg which they will ingest under supervision with 100 ml of water, 30 minutes before the mixed meal tolerance test. All the procedures will be repeated as per visit 2.

Safety Call 2 (occurs 7 days (+5 days) after Visit 4) is a telephone call to the patient. The patient will be asked to report any adverse events between Visit 4 and the day of the Safety Call 2. Safety call 2 is the end of the study.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
The difference in nadir (lowest) glucose levels between the two treatment options (canagliflozin 300 mg vs no treatment) after the standardised mixed meal test (separate analysis for subjects who have undergone RYGB and for subjects who have undergone SG). For patients who will

develop hypoglycaemia during the MMTT (defined as blood glucose levels ≤3.0 mmol/l) and the test will be stopped for safety reasons, the glucose levels at the time that the test will be completed will be taken into account as the nadir glucose level. Measured using fasting blood glucose tests at 0 minutes followed by seven further glucose blood tests after the standardised MMTT at 15, 30, 60, 90, 120 and 120 minutes during visits 2 and 4.

Key secondary outcome(s))

1. Difference in Area Under the Curve (AUC)(0-180), fasting and peak glucose levels after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using fasting blood glucose tests at 0 minutes followed by seven further glucose blood tests after the standardised MMTT at 15, 30, 60, 90, 120, 150 and 180 minutes during visits 2 and 4
2. Difference in AUC(0-180) insulin, fasting and peak insulin levels after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using blood test processed and plasma measured at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4
3. Difference in AUC(0-180) Glucagon Like Peptide-1 (GLP-1), fasting and peak GLP-1 levels after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using blood test processed and plasma measured at 0 minutes (fasting) and at 15, 30, 60, 90, 120, 150 and 180 minutes after MMTT during visits 2 and 4.
4. Difference in AUC(0-180) c-peptide, fasting and peak c-peptide levels after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using blood test processed and plasma measured at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
5. Difference in AUC(0-180) glucagon, fasting and peak glucagon levels after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using blood test processed and plasma measured at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
6. Difference in the ratio AUC(0-180) insulin/AUC(0-180) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and Insulin plasma at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
7. Difference in the ratio AUC(0-30) insulin/AUC(0-30) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and Insulin plasma at 0 min (fasting) and at 15 min, 30 min after MMTT during visits 2 and 4.
8. Difference in the ratio AUC(60-180) insulin/AUC(60-180) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and Insulin plasma 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
9. Difference in the ratio AUC(0-180) c-peptide/AUC(0-180) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and c-peptide plasma at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
10. Difference in the ratio AUC(0-30) c-peptide/AUC(0-30) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and c-peptide plasma at 0 min (fasting) and at 15 min, 30 min after MMTT during visits 2 and 4.
11. Difference in the ratio AUC(60-180) c-peptide/AUC(60-180) glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results and c-peptide plasma at60 min, 90 min, 120 min, 150 min and 180

min after MMTT during visits 2 and 4.
12. Difference in the ratio of maximum/minimum plasma glucose after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using glucose blood results at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
13. Difference in AUC(0-180) of Sigstad score and peak Sigstad score after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using questionnaire completed at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
14. Difference between AUC(0-180) of Edinburgh Hypoglycaemia Scale score and peak Edinburgh Hypoglycaemia Scale score after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using questionnaire completed at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
15. Difference at the number of mixed meal tests required to be stopped due to blood glucose levels or capillary glucose levels ≤3.0 mmol/l after MMTT between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using capillary blood tests results at 0 min (fasting) and at 15 min, 30 min, 60 min, 90 min, 120 min, 150 min and 180 min after MMTT during visits 2 and 4.
16. The amount of glucose (in grams) needed to restore euglycaemia between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG
17. Difference in %time in interstitial glucose levels <3.9 mmol/l in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
18. Difference in % time in hypoglycaemia (defined as interstitial glucose levels ≤3.0 mmol/l) in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
19. Difference in % time in interstitial glucose levels ≤2.2 mmol/l in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
20. Difference in % time in range (defined as 3.9 – 7.8 mmol/l) in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
21. Difference in % time in interstitial glucose levels between 3.9 – 10 mmol/l in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
22. Difference in % time interstitial glucose >7.8 mmol/l in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
23. Difference in % time interstitial glucose >10 mmol/l in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
24. Difference in the mean interstitial glucose in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
25. Difference in the standard deviation (SD) of the mean interstitial glucose between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG
26. Difference in the coefficient of variation (CV) (CV=SD/mean interstitial glucose) between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG
27. Difference in mean amplitude glucose excursion (MAGE) in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor results worn for 5 days at visits 2 and 4

28. Difference in the frequency and intensity of symptoms suggestive of postprandial hypoglycaemia reported by the patients during CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG
29. Difference in the number of hypoglycaemic events/day (defined as interstitial glucose levels ≤3.0 mmol/l) in CGM between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG, measured using continuous glucose monitor worn for 5 days at visits 2 and 4
30. Difference in risk of hyperglycaemia between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG calculated as the high blood glucose index (HBGI) using the EasyGV workbook (www.phc.ox.ac.uk/research/technology-outputs/easygv)
31. Difference in risk of hypoglycaemia between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG calculated as the low blood glucose index (LBGI) using the EasyGV workbook (www.phc.ox.ac.uk/research/technology-outputs/easygv)
32. Difference in physical activity [MVPA (moderate to vigorous physical activity) minutes per day and sedentary time] between the two treatment options (canagliflozin 300 mg vs no treatment) after RYGB and SG

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Age ≥18 years old but less than 75 years old
2. ≥1 year after gastric bypass (RYGB) or sleeve gastrectomy (SG)
3. Able to understand written and spoken English
4. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
36

Key exclusion criteria

1. Use of any glucose-lowering medication (including insulin)
2. Adrenal insufficiency and/or substitution with glucocorticoids
3. ALT > 1.5 times the upper normal limit
4. Moderate to severe renal impairment (eGFR< = 60 ml/min/1.73m2)
5. Individuals on loop diuretics
6. Participants with established diagnosis of postural hypotension by their GP
7. Recent active infection (over the last 10 days)
8. Current use of steroids
9. Other bariatric procedure except RYGB/SG
10. Previous revisional bariatric surgery
11. Currently pregnant or breastfeeding
12. Females of child-bearing age, unwilling to use contraception during the period of the study
13. Patients with history of Type 1 or Type 2 diabetes
14. Intolerant to the Mixed Meal Tolerance test
15. HbA1C > = 6.5% or > = 48mmol/l at screening blood tests
16. Haemoglobin (Hb) < 100 g/L at screening blood tests
17. Clinical contraindication to Canagliflozin
18. Known osteoporosis
19. Previous history of Fournier's gangrene
20. History of epilepsy
21. Known foot ulcers/previous amputation
22. Participating in another research study involving intervention within 3 months of screening
23. Having a formal previous diagnosis of postprandial hypoglycaemia
24. Being on acarbose, diazoxide, octreotide or other treatment for postprandial hypoglycaemia
25. Participants without established previous diagnosis of postprandial hyperinsulinaemic hypoglycaemia but with symptoms suggestive of frequent (defined as more than once weekly) AND severe postprandial hypoglycaemia at the screening hypoglycaemia questionnaire (severe is defined as at least two symptoms on Edinburgh Hypoglycaemia Scale (EHS) Questionnaire with intensity > 5 in a scale from 1 to 7) over the last 2 months

Date of first enrolment
31/05/2021

Date of final enrolment
31/01/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leicester Royal Infirmary
University of Leicester NHS Trust
Infirmary Square
Leicester

United Kingdom
LE1 5WW

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Research organisation

Funder Name
Academy of Medical Sciences; Grant Codes: SGL020\1002

Alternative Name(s)
The Academy of Medical Sciences

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

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?

Basic results		17/01/2025	24/01/2025	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes