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Are gut hormone changes the reason why the long-limb gastric bypass is more effective than the standard limb gastric bypass in improving type 2 diabetes mellitus?

Submission date
29/07/2015

Recruitment status
No longer recruiting

Registration date
30/07/2015

Overall study status
Completed

Last Edited
18/08/2023

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Obesity is the main cause of the world wide epidemic of diabetes. Weight loss, or bariatric, surgery produces major and sustained weight loss and is being increasingly used to treat obese diabetic patients. There was initial optimism that these procedures might cure all diabetes. However, the gold-standard operation, standard gastric bypass, effectively cures diabetes in only 4 out of 10 patients. To design a safer and more successful procedure we need to understand how bariatric surgery works to improve diabetes. Hormones from the gut are released when we eat food. They control how the body uses the food it absorbs. For example they release the sugar lowering hormone insulin, and also greatly reduce appetite, which is why one feels less hungry after eating a meal. We have discovered that the good effects of bariatric surgery, and in particular the gastric bypass, are mainly due to increased release of gut hormones, reducing patients appetite and improving the release of insulin. In this project we will be testing a new procedure called the long-limb gastric bypass. It is designed particularly to be better at helping the diabetes in overweight patients, while being as safe as the currently available standard gastric bypass. We now want to show that this new procedure works better than the standard gastric bypass by causing an even bigger increase in the release of gut hormones and therefore insulin.

Who can participate?
Obese adults (aged 18-70 years) with type 2 diabetes.

What does the study involve?
Participants are randomly assigned into one of two groups. Those in group 1 have a standard-limb gastric bypass. Those in group 2 have a long-limb gastric bypass. Using a newly developed technique (mass spectroscopy) we then measure the differences in gut hormone secretion between the new long-limb and the standard gastric bypass. We also use a well-tested insulin sensitivity procedure (glucose clamp), both to confirm and to investigate how and why each participants diabetes has improved after the surgery.

What are the possible benefits and risks of participating?
The measurements we will be making are non-invasive and safe. The only discomfort comes from inserting a cannula to take blood samples.

Where is the study run from?
Imperial College London, Hammersmith Hospital (lead centre) and King's College London (UK)

When is the study starting and how long is it expected to run for?
August 2015 to February 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Alex Miras

Contact information

Type(s)
Public

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
19153

Study information

Scientific Title
Are gut hormone changes the reason why the long-limb gastric bypass is more effective than the standard limb gastric bypass in improving type 2 diabetes mellitus? A randomised controlled trial

Acronym
LONG LIMB

Study objectives
The aim of this study is to show that a new bariatric surgery, the long-limb gastric bypass, is more effective at treating diabetes in people with obesity than the standard-limb gastric bypass.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West London & GTAC, 29/06/2015, ref: 15/LO/0813

Study design
Randomized; Double blind; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Topic: Diabetes; Subtopic: Type 2; Disease: Diabetic Control, Obesity

Interventions
Bariatric surgery, either the standard--limb or long--limb gastric bypass
Study Entry : Registration and one or more randomisations

Intervention Type
Procedure/Surgery

Primary outcome measure
Current primary outcomes as of 29/04/2019:
Peak plasma GLP-1 concentration as measured by laboratory assays at baseline and at 2 weeks after intervention.

Previous primary outcomes as of 10/01/2017:
Mechanistic primary outcome: Peak plasma GLP-1 level as measured by laboratory assays at baseline and at the point of 20% weight loss.

Clinical primary outcome: Glycated haemoglobin (HbA1c) as measured by laboratory assays at baseline and 1 year.

Previous primary outcome:
Change in peak GLP--1 level; Timepoint(s): After the mixed meal tolerance test.

Secondary outcome measures
Current secondary outcome measures as of 29/04/2019:
1. Plasma levels of glucose, insulin, c-peptide, gut hormones, bile acids, FGF-19 and 21 after the mixed meal tolerance test are measured using laboratory assays at baseline, within 2 weeks and at the point of 20% weight loss
2. Rate of glucose appearance (Ra) and disposal (Rd) in the euglycaemic hyperinsulinaemic clamp is measured using mass spectroscopy/metry at baseline, within 2 weeks and at the point of 20% weight loss.
3. Faecal caloric content is measured using calorimetry at baseline, 20% weight loss and at 1 year
4. 4. Blood, urine and faecal microbial diversity and metabolomics are measured using mass spectroscopy/metry at baseline, within 2 weeks and at the point of 20% weight loss.
5. Total caloric intake and macronutrient composition is measured using dietary records at baseline and at 1 year
6. HbA1c is measured using by laboratory assays at baseline and 1 year
7. Total number of medications are measured using health records at baseline and 1 year
8. Rate of patients achieving diabetes remission is measured using HbA1c and number of medications at 1 year
9. Body weight is measured using scales at baseline and 1 year
10. Systolic, diastolic blood pressure and pulse are measured using a sphygmomanometer at baseline and 1 year
11. Serum fasting lipids are measured using laboratory assays at baseline and 1 year
12. Medical, surgical, nutritional and psychological complications are measured using health records at 1 year

13. Adverse events are measured using health records at 1 year
14. Glycated haemoglobin (HbA1c) as measured by laboratory assays at baseline and 1 year.

Previous secondary outcome measures:
1. Plasma levels of glucose, insulin, c-peptide, gut hormones, bile acids, FGF-19 and 21 after the mixed meal tolerance test are measured using laboratory assays at baseline, within 2 weeks and at the point of 20% weight loss
2. Rate of glucose appearance (Ra) and disposal (Rd) in the euglycaemic hyperinsulinaemic clamp is measured using mass spectroscopy/metry at baseline, within 2 weeks and at the point of 20% weight loss.
3. Faecal caloric content is measured using calorimetry at baseline, 20% weight loss and at 1 year
4. 4. Blood, urine and faecal microbial diversity and metabolomics are measured using mass spectroscopy/metry at baseline, within 2 weeks and at the point of 20% weight loss.
5. Total caloric intake and macronutrient composition is measured using dietary records at baseline and at 1 year
6. HbA1c is measured using by laboratory assays at baseline and 1 year
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8. Rate of patients achieving diabetes remission is measured using HbA1c and number of medications at 1 year
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13. Adverse events are measured using health records at 1 year

Overall study start date
01/02/2015

Completion date
14/08/2018

Eligibility

Key inclusion criteria
1. Both genders
2. Age 18-70 years
3. Type 2 diabetes mellitus
4. Obesity
5. HbA1c>7.0%
6. On glucose-lowering medication

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Total final enrolment
53

Key exclusion criteria
1. Contraindications to bariatric surgery
2. Type 1 diabetes
3. Pregnancy or breastfeeding
4. Recent blood donation

Date of first enrolment
31/07/2015

Date of final enrolment
01/02/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London, Hammersmith Hospital (lead centre)
Du Cane Road
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Study participating centre
King's College London
Denmark Hill
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Sponsor information

Organisation
Imperial College London

Sponsor details
Joint Research Compliance Office
Charing Cross Hospital
Fulham Palace Road
London
England
United Kingdom
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

The results of this project will be published in high quality peer-reviewed journals with a wide medical and scientific readership which will allow the detail of the trial to be scrutinized by the medical and scientific community at large. The results of the study will be presented at national and international scientific meetings. All of the applicants are experts in their field and regularly lecture to professional and lay audiences on these topics. We will also disseminate our findings via the press offices of Imperial College London and King's College London and associated NHS Trusts. Crucially, the clinical results of the trial will be disseminated through our research teams and institutions to NHS England service providers and policymakers.

Intention to publish date

01/02/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		06/11/2020	23/09/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/02/2021	18/08/2023	Yes	No