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The effects of liraglutide in controlling blood sugar and weight in poor-responders to bariatric surgery

Submission date
20/01/2016

Recruitment status
No longer recruiting

Registration date
20/01/2016

Overall study status
Completed

Last Edited
30/07/2019

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
Type 2 diabetes mellitus (T2DM) is a growing problem worldwide. People with T2DM have difficulty controlling their blood sugar (glucose) as they do not produce enough insulin to function properly (insulin deficiency), or that the body's cells don't react to insulin as they should do (insulin resistance). Once of the main reasons why people develop T2DM is because they are overweight or obese. Weight loss surgery, also called bariatric surgery, is a drastic measure used to help people who are dangerously overweight. There are a number of different types of bariatric surgery; however they all work by limiting the amount a person can eat or reducing the number of calories that are absorbed from food. In some patients, bariatric surgery can cause up to 30% weight loss and substantially improve blood glucose control however this is not always the case. Studies have shown that in patients where the procedures are successful, high amounts of a hormone called glucagon like peptide-1 or GLP-1 are produced. This hormone is responsible for causing insulin to be released, which reduces blood sugar. Liraglutide is a drug which has been developed to mimic the action of GLP-1. In the past, it has been given to overweight diabetics who aren't suitable for bariatric surgery, and has been found to lower blood glucose and weight. The aim of this study is to look at the effects of receiving liraglutide injections on blood glucose and weight in diabetic adults who have not responded well to bariatric surgery.

Who can participate?
Adults with T2DM who have had a bariatric surgery 12 months ago.

What does the study involve?
For the first two weeks of the study, all participants are taught how to use the injector pen device and asked to inject themselves with a dummy (placebo) every day. At the end of the two weeks, the devices are measured in order to find out how well each participant stuck to the regime. Participants are then randomly allocated to one of two groups. Participants in the first group are given pens containing liraglutide to use every day. For one week, a dose of 0.6mg/day is taken, then 1.2mg/day for the next week and then 1.8mg/day for the following week. After this, participants are given the opportunity to adjust the dose if they are experiencing a lot of

side effects. Participants in the second group are given pens containing a dummy (placebo) to use every day at the same doses as the first group. At the start of the study and then again after 26 weeks, participants in both groups attend follow up appointments so that their weight and blood sugar levels (in a blood test) can be measured.

What are the possible benefits and risks of participating?
Participants in both groups will benefit from being under the care of a specialist team which they would not normally have access to. The patients taking the liraglutide may also benefit from improvements to their diabetes management and weight loss. There is a risk of pain and discomfort from the injections, as well as when blood is taken to test blood sugar levels. There is also a risk of side effects from the liraglutide, however these will be closely monitored.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
April 2015 to October 2017

Who is funding the study?
J P Moulton Charitable Foundation (UK)

Who is the main contact?
1. Dr Belen Perez Pevida
2. Dr Alex Miras

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2014-003923-23

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
20510

Study information

Scientific Title
The GRAVITAS trial: GLP-1 Receptor Agonist interVentIon for poor responders afTer bariAtric Surgery

Acronym
GRAVITAS

Study objectives
The aim of this study is to investigate whether daily injections of GLP-1 helps to reduce blood glucose and weight in bariatric surgery patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West London & GTAC Research Ethics Committee, 21/11/2015, ref: 15/LO/0780

Study design
Randomised; 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 the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Diabetes, Metabolic and endocrine disorders; Subtopic: Type 2, Metabolic and Endocrine (all Subtopics); Disease: Diabetic Control, Metabolic & Endocrine (not diabetes)

Interventions
For the the two weeks of the run-in period (Trial Weeks 0-2), patients will be instructed on how to use the pen devices and self-administer placebo once a day. At the end of the run-in period, the pen devices will be collected and the remaining volume measured to check for patient adherence to the self-administration regime.

Participants are then randomly allocated to the intervention group or the control group in a 2:1 ratio.

Intervention group: Participants are asked to self-administer subcutanious daily injections of liraglutide. The starting dose is will be 0.6 mg/day for one week (trial week 2), 1.2 mg/day for the next week (trial week 3), and then 1.8 mg/day for the next week (trial week 4). During Trial Weeks 5-6, an assessment will be made of adverse effects, and if necessary the dose can be reduced. From Trial Week 6 onwards, participants will take their maximum tolerated dose (0.6 mg/day, 1.2 mg/day, or 1.8 mg/day).
Control group: Participants are asked to self-administer subcutanious daily injections of saline (placebo) at the same doses as the intervention group.

The clinical research team will provide patients with a capillary glucose meter, inform them of possible side effects of liraglutide (e.g. nausea, vomiting, constipation or diarrhoea, hypoglycaemia and possible dehydration), and advise them as to how to deal with them. Patients will also be informed of the rare complication of pancreatitis and will be specifically instructed to urgently report any symptoms of abdominal pain to the clinical research team.

Intervention Type
Other

Primary outcome measure
Diabetes management is assessed by measuring glycated hemoglobin (HbA1C) at baseline and 26 weeks.

Secondary outcome measures
1. Body weight is measured using scales at baseline and 26 weeks
2. Blood pressure is measured using a sphygmomanometer at baseline and 26 weeks
3. Total number of medications taken by participants is measured by self-reporting at baseline and 26 weeks
4. Insulin dose for those patients taking insulin as treatment for T2DM is measured by self-reporting at baseline and 26 weeks
5. Obesity-related comorbidities are assessed using the King’s obesity staging system at baseline and 26 weeks
6. Quality of life measured using the following questionnaires at baseline and 26 weeks:
6.1. Dutch Eating Behaviour Questionnaire (DEBQ)
6.2. Eating Disorder Examination Questionnaire (EDE-Q)

6.3. Eating Attitudes Test (EAT)
6.4. Behavioural Inhibition and Activation System (BIS / BAS) scales
6.5. Eysenck Personality Questionnaire (EPQ-R)
6.6. Beck Depression Inventory (BDI-II)
6.7. Barratt Impulsivity Scale
6.8. Three Factor Eating Questionnaire (TFEQ)
6.9. Positive and Negative Affect Schedule (PANAS)
6.10. Yale Food Addiction Scale, Power of Food questionnaire
6.11. Alcohol Use Disorders Identification Test
7. Total caloric intake and macronutrient composition is measured using food diaries at baseline and 26 weeks
8. Food related behavioral traits (e.g. ad libitum total food intake, sweet taste detection threshold, consummatory taste reward ratings, and wanting and liking for food pictures) are assessed using dietry recall, sweet taste detection testing, consummatory taste reward test and a computer task (to assess liking and wanting for different food pictures) at baseline and 26 weeks
9. Number of hypoglycaemic episodes experienced by participants is measured by self-reporting at baseline and 26 weeks

Overall study start date
24/04/2015

Completion date
01/02/2019

Eligibility

Key inclusion criteria
1. Aged between 18- and 70 years
2. 12 months after gastric bypass or sleeve gastrectomy bariatric surgery
3. Diagnosed with Type 2 diabetes mellitus
4. HbA1c greater than 6.5% (more than 48 mmol/mol) on screening
5. On Metformin ± long acting insulin
6. Able to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 80; UK Sample Size: 80

Total final enrolment
80

Key exclusion criteria
1. Diagnosis of Type 1 diabetes mellitus
2. Anatomical or endocrinological pathology causing poor weight loss or weight regain
3. Screening calcitonin of 50 ng/L or above
4. Family or personal history of multiple endocrine neoplasia type 2 or familial medullary thyroid carcinoma
5. Personal history of non-familial medullary thyroid carcinoma
6. History of acute or chronic pancreatitis
7. Uncontrolled hypertension (systolic blood pressure of 160 mmHg or above and/or diastolic blood pressure of 100
mmHg or above)
8. Estimated glomerular filtration rate (eGFR) less than30 ml/min per 1.73 m2
9. Current pregnancy
10. Inability to maintain adequate contraception

Date of first enrolment
22/01/2016

Date of final enrolment
21/07/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London
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Sponsor information

Organisation
Imperial College London

Sponsor details

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Sponsor type
University/education

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Charity

Funder Name
J P Moulton Charitable Foundation

Results and Publications

Publication and dissemination plan
Dissemination through peer review publications and patient support groups.

Intention to publish date
01/02/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Belen Perez Pevida or Dr Alex Miras.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2019	10/06/2019	Yes	No
Basic results		30/07/2019	30/07/2019	No	No
HRA research summary			28/06/2023	No	No