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How do hormones affect reproduction and metabolism in people with type 2 diabetes and people who do not have type 2 diabetes?

Submission date
29/11/2019

Recruitment status
No longer recruiting

Registration date
09/12/2019

Overall study status
Completed

Last Edited
26/02/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Up to 40% of people who are obese and/or have type 2 diabetes have low reproductive hormone levels (hypogonadism) and therefore have reduced sexual function and reduced fertility. Also, having low reproductive hormone levels is associated with lower insulin secretion and higher insulin resistance in people with type 2 diabetes. Some hormones have been shown to be essential for fertility in animals and humans, whilst other hormones have been shown to affect the amount of insulin produced, appetite and body weight in animals and humans (but some of these effects might be different in different genders). Identifying hormones that can control both reproduction and metabolism may lead to better treatments for fertility disorders.

Aims
Part A of the study will investigate if hormones, which are known to affect insulin and food intake and are produced in the gut (i.e. glucagon, glucagon-like peptide-1, oxyntomodulin, peptide-YY and substance P) can affect reproductive hormones.
Part B will investigate if certain reproductive hormones (i.e. kisspeptin and neurokinin B) can improve the ability of the body to respond to glucose how these hormones affect appetite, the quantity of food eaten and how much energy people use.

Who can participate?
Men and women aged 18 – 60 years who are obese and/or have type 2 diabetes and are non-smokers.

What does the study involve?
People will only be allowed to take part in both parts of the study at the same time.
In Part A, people who participate will come to the research facility for up to six visits. During one visit they will be given salty water through a plastic tube placed in a vein and during each of the other visits they will receive (through a plastic tube placed in a vein) a different hormone produced by the gut, which has been dissolved in salty water. The study visits will take place in a random order. During all study visits, blood samples will be taken (to measure hormone, glucose and insulin levels) through a plastic tube placed in a different vein.

In Part B, people who participate will come to the research facility for up to three pairs of visits. They will be asked to fast overnight before each study visit. For each pair of study visits, during one visit they will be given kisspeptin or neurokinin B (through a plastic tube placed in a vein) and salty water (through a plastic tube placed in a vein) on the other study visit. During one pair of study visits, they will be asked to drink a sugary drink. During the second pair of study visits, they will be given a sugar solution into a vein (via a plastic tube) with a small dose of insulin given to some people. During the third pair of study visits, they will be asked to rate their hunger levels, they will be given a meal to eat and in some cases measurements of how much energy they are using will be performed. During all study visits, blood samples will be taken (to measure hormone, glucose and insulin levels) through a plastic tube placed in a different vein.

What are the possible benefits and risks of participating?
BENEFITS - The information that we get from this study will help us to understand how to treat patients who suffer from type 2 diabetes, obesity and/or fertility problems.
RISKS - It is possible that mild nausea may occur. The insertion of the cannula may cause minor discomfort or superficial bruising. Some gut hormones can affect blood sugar but these effects do not last long. We will monitor blood sugar during the infusions and make sure that participants blood sugar is ok before they leave.

Where is the study run from?
Imperial College Academic Health Science Centre, UK

When is the study starting and how long is it expected to run for?
May 2019 to February 2023

Who is funding the study?
1. National Institute for Health Research, UK
2. Medical Research Council, UK
3. NIHR Imperial Biomedical Research Centre, UK
4. Society for Endocrinology, UK
5. Imperial College London, UK

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
16HH3156; CPMS 20865

Study information

Scientific Title
Physiological studies of hormones which control metabolism and reproduction

Acronym
REPROMET

Study objectives
The study aims to answer the questions:
Part A: Do gut hormones affect reproductive hormone secretion?
Part B: Do reproductive hormones affect gut hormones, glucose, insulin, appetite, food intake and energy expenditure?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/04/2016, West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)207 104 8124; NRESCommittee.London-WestLondon@nhs.net), ref: 16/LO/0391

Study design
Single-blinded randomized two-way crossover study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
http://imperial.crf.nihr.ac.uk/studies/repromet/

Health condition(s) or problem(s) studied
Reproductive hormone effects

Interventions
Part A: Intravenous infusion of vehicle during one study visit and intravenous infusion of a gut hormone (i.e. glucagon, glucagon-like peptide-1, oxyntomodulin, peptide-YY or substance P) during a separate study visit. Infusion order will be randomly assigned

Part B (participants will be involved in one or more of the following):
1: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order will be randomly assigned. Oral glucose tolerance tests (OGTT) will be performed during both study visits
2: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order will be randomly assigned. Intravenous glucose tolerance tests (IVGTT) will be performed during both study visits
3: Intravenous infusion of vehicle during one study visit and intravenous infusion of a reproductive hormone (kisspeptin or neurokinin B) during a separate study visit. Infusion order

will be randomly assigned. Mixed meal tolerance tests (MMTT) will be performed during both study visits

Randomisation:
Part A – An online random number generator (www.random.org) will be used to generate numbers for each participant at the time of study entry. Participants with an even number will receive vehicle infusion first and glucagon-like peptide-1 (GLP-1) infusion second. Participants with an odd number will receive GLP-1 infusion first and vehicle infusion second. This process will be repeated for paired peptide-YY infusion and vehicle infusion visits; glucagon infusion and vehicle infusion visits; oxyntomodulin infusion and vehicle infusion visits; and substance P infusion and vehicle infusion visits.

Part B – An online random number generator (www.random.org) will be used to generate numbers for each participant at the time of study entry. Participants with an odd number will receive kisspeptin infusion first and vehicle infusion second. Participants with an even number will receive vehicle infusion first and kisspeptin infusion second. This process will be repeated for paired neurokinin B infusion and vehicle infusion visits

Intervention Type
Other

Primary outcome measure
Part A:
1. Luteinising hormone (LH) pulsatility, LH levels, follicle-stimulating hormone levels and testosterone levels in males measured using blood tests during the vehicle and hormone infusions
2. Oestrogen and progesterone levels in females measured blood tests during the vehicle and hormone infusions

Part B:
1. OGTT/IVGTT/MMTT insulin and glucose levels measured using blood tests during vehicle and hormone infusions
2. OGTT/IVGTT/MMTT insulin secretion measured using blood tests during vehicle and hormone infusions
3. OGTT/IVGTT/MMTT insulin sensitivity and disposition indices measured using blood tests during vehicle and hormone infusions
4. MMTT food intake measured using scales during vehicle and hormone infusions
5. MMTT Energy expenditure measured using calorimetry and infrared thermography during vehicle and hormone infusions

Secondary outcome measures
Part B: Pre- and post-meal nausea, hunger and fullness ratings measured using visual analogue scales during hormone and vehicle infusions.

Overall study start date
23/05/2016

Completion date
01/02/2023

Eligibility

Key inclusion criteria
1. Aged 18 – 60 years
2. Male or female
3. Stable body weight for the preceding 3 months
4. 12-lead ECG with no clinically significant abnormalities as judged by the investigators
5. Full blood count, urea and electrolytes, thyroid function tests, liver function tests and glucose within 2 x the upper limit of normal
6. Conditions that predispose subfertility: BMI >25, Pre-diabetes, Type 2 diabetes

Participant type(s)
Mixed

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
200

Total final enrolment
78

Key exclusion criteria
1. History of any medical, psychological or other condition, or use of any medications, including over-the-counter products, which, in the opinion of the investigators, would either interfere with the study or potentially cause harm to the volunteer
2. Pregnancy or breastfeeding
3. History of hypersensitivity to any of the components of the infusions
4. Treatment with an investigational drug within the preceding 2 months
5. Volunteers who have or intend to donate blood or blood products within three months before or following study completion
6. A history of alcoholism or substance abuse within the preceding 5 years
7. A history of major haematological, renal, thyroid or hepatic abnormalities or significant cardiovascular disease
8. A history of cancer
9. Volunteers with a medical or psychological condition that would impair their ability to participate reliably in the study or give informed consent
10. Smoker

Date of first enrolment
23/05/2019

Date of final enrolment
01/02/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College Academic Health Science Centre
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Sponsor information

Organisation
Imperial College London

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Sponsor type
University/education

Website
http://www3.imperial.ac.uk/clinicalresearchgovernanceoffice

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

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
NIHR Imperial Biomedical Research Centre

Alternative Name(s)
NIHR Imperial BRC, Imperial Biomedical Research Centre, BRC

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Funder Name
Society for Endocrinology

Alternative Name(s)
SFE

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Imperial College London

Alternative Name(s)
Imperial College of Science, Technology and Medicine, Imperial College London, UK, Imperial College London, London, England, Imperial College London in United Kingdom, imperialcollege, ICL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
NIHR Academy; Grant Codes: RP-2014-05-001

Results and Publications

Publication and dissemination plan
Results will be published and presented at conferences in phases following completion of each phase of the study.

Intention to publish date

16/08/2018

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available as this study is a physiological study.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Effects of Peptide YY on the reproductive axis in healthy young men	01/03/2020	03/12/2019	Yes	No
Results article	Effects of kisspeptin on glucose-stimulated insulin secretion, metabolites, gut hormones, appetite and food intake in healthy men	01/12/2018	03/12/2019	Yes	No
Protocol file	version V2	18/03/2019	09/12/2019	No	No
Results article	Effects of kisspeptin on food intake in women with overweight or obesity	11/04/2023	17/04/2023	Yes	No
HRA research summary			28/06/2023	No	No
Results article	Acute effects of glucagon on reproductive hormone secretion in healthy men	01/06/2020	26/02/2024	Yes	No
Results article	Effects of glucagon-like peptide-1 on the reproductive axis in healthy men	01/04/2020	26/02/2024	Yes	No