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What is the effect of the natural occurring hormone kisspeptin on reproductive hormone secretion in humans?

Submission date
09/02/2020

Recruitment status
No longer recruiting

Registration date
17/02/2020

Overall study status
Ongoing

Last Edited
14/04/2025

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Infertility affects 1 in 7 couples in the UK. Unfortunately, many cases of infertility cannot be treated, which leaves affected couples with devastating psychological and social consequences. It has been known for decades that human fertility is regulated by a small part of the brain called the hypothalamus, which stimulates the release of sex hormones into the bloodstream. However until now, we have been unable to measure how well the hypothalamus works in people with infertility. This greatly limits our understanding of what causes infertility in patients.

The kisspeptins are recently identified natural hormones made in the hypothalamus, which are needed for the hypothalamus to maintain fertility. Our previous studies suggest that a single injection of kisspeptin safely stimulates the hypothalamus to release sex hormones in healthy participants without any adverse effects. An injection of kisspeptin will therefore safely tell us how well the hypothalamus is working in any given individual.

The aim of this study is to study the physiological effects of kisspeptin administration on sex hormone release in participants with normal or reduced fertility

Who can participate?
Any person aged over 16 years, with or without known problems with reproductive function.

What does the study involve?
Participants recruited will each attend at least two study visits at our clinical research unit. During each visit, they will be given either kisspeptin or GnRH or salty water through a plastic tube placed in a vein. The study visits will take place in random order. Following administration of hormone, blood samples will be taken (to measure reproductive hormone levels) through the same plastic tube up to a maximum period of 24 hours.
The participant may be asked to return for additional study visits. Each participant will be invited up to a maximum of six study visits. The additional study visits will not take place more frequently than two times per week.

What are the possible benefits and risks of participating?
There is no direct benefit to participants since participation will not have long term effects on their hormonal secretion. However, the greater understanding of the regulation of fertility resulting from this study may lead to advancements in the treatment of people with reduced fertility in the future.
There are minimal risks to taking part in the study. Kisspeptin has been given to several hundred adults by our group and others with no known reported side effects.

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

When is the study starting and how long is it expected to run for?
March 2017 to November 2027

Who is funding the study?
1. National Institute for Health Research (NIHR) (UK)
2. NIHR Imperial Biomedical Research Centre (UK)
3. Medical Research Council (UK)
4. Imperial Health Charity (UK)

Who is the main contact?
Megan Young
Megan.young1@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Megan Young

Contact details
Section of Endocrinology and Investigative Medicine
Imperial College London
6th Floor Commonwealth Building
Hammersmith Hospital Campus
Du Cane Road
London
United Kingdom
W12 0NN
+44 (0)20 3313 3242
Megan.young1@imperial.ac.uk

Type(s)
Scientific

Contact name
Dr Ali Abbara

Contact details

6th Floor, Commonwealth building
Faculty of Medicine, Department of Metabolism, Digestion and Reproduction
Imperial College London
Hammersmith Campus
London
United Kingdom
W12 0NN
+44 (0)20 3313 3242
ali.abbara@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
93319

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 93319, CPMS 12448

Study information

Scientific Title
Physiological studies of kisspeptin on reproductive hormone secretion in humans

Study objectives
The naturally occurring physiologic hormone kisspeptin acts to stimulate reproductive hormone secretion from the hypothalamus and thus it is necessary to study its effect on reproductive hormone levels in men and women with and without infertility to understand how this compares with current hormonal stimuli.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/06/2012, 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: 12/LO/0507

Study design
Interventional randomized cross over trial

Primary study design
Interventional

Secondary study design

Randomised cross over trial

Study setting(s)
Other

Study type(s)
Screening

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
Conditions that can impair fertility

Interventions
Healthy male and female participants with normal or reduced fertility will be identified from clinics and newspaper advertisements. Potential participants will be offered an invitation to a screening visit. A patient information sheet will be given to them prior to the screening visit. In the screening visit, participants will be questions with regard to their medical history and medication history as would occur in an outpatient endocrinology clinic. This visit will involve a blood test to assess the hormones in body and an ECG (electrical tracing of the heart).

Participants will each attend up to a maximum of six study visits, and be administered one of the following hormones: kisspeptin-54, Kisspeptin-10, kisspeptin-9 analogue, GnRH or saline. The hormones will be administered intravenously (directly into the blood-stream) during each visit in random order. The order of administration will be randomised using an online randomisation tool.

The maximum doses of kisspeptin administered will be 25.6nmol/kg (kisspeptin-54) and 43.2 nmol/kg (kisspeptin-10); we have already administered these identical doses during our previous studies and no adverse effects have been reported.

The gonadotrophin-releasing hormone (GnRH) test has been used safely and routinely as an NHS diagnostic test for over 25 years and has no associated adverse effects. The dose of GnRH given will be weight based at 2.5 micrograms per kilogram up to a maximum of 100mcg, followed by serial blood sampling. Since GnRH stimulates the pituitary gland directly, we can compare stimulation of sex hormone secretion following kisspeptin and GnRH in order to deduce how much actual stimulation of the hypothalamus occurs following kisspeptin administration.

Intervention Type
Other

Primary outcome measure
1. Luteinising hormone (LH) levels measured using chemiluminescent assay over 8hrs
2. LH pulsatility measured over 8hrs by blinded deconvolution analysis
2. Follicle-stimulating hormone levels measured using chemiluminescent assay over 8hrs

Secondary outcome measures

1. Testosterone levels measured using chemiluminescent assay over 8hrs
2. Oestrogen levels measured using chemiluminescent assay over 8hrs
3. Progesterone levels measured using chemiluminescent assay over 8hrs

Overall study start date
31/03/2017

Completion date
30/11/2027

Eligibility

Key inclusion criteria
1. Age over 16 years
2. Ability to give informed consent
3. Adult participants will be recruited with no known problems with reproductive function ("normal fertility")
3. Adult participants will be recruited with previous problems with reproductive function ("reduced fertility")
4. Availability to attend hospital visits during weekdays for study visits.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
250

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 reproductive hormone levels 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. Volunteers with poor venous access.
7. A history of alcoholism or substance abuse within the preceding 5 years
8. A history of major haematological, renal, thyroid or hepatic abnormalities or significant cardiovascular disease

9. A history of cancer
10. Volunteers with a medical or psychological condition that would impair their ability to participate reliably in the study or give informed consent

Date of first enrolment
31/03/2017

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London
Imperial College Academic Health Science Centre
Fulham Palace Road
London
United Kingdom
W6 8RF

Sponsor information

Organisation
Imperial College London

Sponsor details
Joint Research and Compliance Office
Imperial College London and Imperial College Healthcare NHS Trust
Norfolk Place
London
England
United Kingdom
W2 1PG
+44 (0)207 594 9459
becky.ward@imperial.ac.uk

Sponsor type
University/education

Website

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

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

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
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
Imperial Health Charity

Alternative Name(s)
Imperial Charity, IHC

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

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
01/08/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from (Professor Waljit Dhillo, w.dhillo@imperial.ac.uk, if consent from specific patients allowed for this and in line with ethical approval (the consent form was amended to allow for this for participants recruited later in the study.)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	17/11/2020	Yes	No