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Can a pancreatic hormone be used to treat pancreatogenic diabetes?

Submission date
17/01/2019

Recruitment status
No longer recruiting

Registration date
28/01/2019

Overall study status
Completed

Last Edited
05/07/2019

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The pancreas is the organ in the human body that secretes the hormone insulin which controls blood sugar levels. If the pancreas is damaged, or if the pancreas is removed during surgery, patients develop a type of diabetes called Pancreatogenic Diabetes (PD for short). Patients with PD, unlike the more common types of diabetes, suffer from much more variable blood sugar levels with very high followed by extremely low blood sugar levels which can kill. The reason for such swinging blood sugar levels is due to the lack of a pancreatic hormone called pancreatic polypeptide (PP), which reduces the liver's sensitivity to the action of insulin. Replacing PP in patients with PD improves the sensitivity of the liver to insulin, reducing the amount of insulin they need to control their diabetes and reducing the likelihood of low blood sugar. We have devised a new 'analogue' of PP, which can be injected under the skin, and which lasts for a longer time than PP itself. In this project, we are going to study patients with PD where we will test the PP analogue PP 1420 for its ability to improve liver insulin sensitivity. If this is shown to occur, then PP 1420 can be quickly developed as a treatment for patients with PD to help reduce high blood sugar levels, and to help prevent low blood sugar levels. The aim of this study is to study whether PP 1420 improves insulin sensitivity in patients with PD.

Who can participate?
Volunteers must have Pancreatogenic Diabetes, i.e. diabetes due to pancreatic disease or surgery to the pancreas. They must be adults aged between 18-75.

What does the study involve?
Volunteers will come in for three study visits, each of which will involve an overnight stay and an all-day study. At each visit, volunteers will come in overnight and will be given drip of specially labelled, non-radioactive sugar water starting at 7 am. At 9 am they will receive either an injection of 0.9% saline (harmless salt water), 2 mg of the PP 1420 analogue, 4 mg of the PP 1420 analogue. They will not be told which injection is which, and all volunteers will receive all three treatments at some time during the three study visits. Volunteers will then be given more sugar water and a drip of insulin. They will have regular blood samples taken from a plastic tube in their arm to measure blood sugar levels. At the end of the day, at 4 pm, all the drips will be stopped. After two hours' observation, volunteers will be allowed to go home.

What are the possible benefits and risks of participating?
There will be no direct benefit from participating. Possible risks from participating include instability of blood sugar levels (too low or too high), nausea arising after the PP 1420 injection.

Where is the study run from?
The study is sponsored by University College London. It will be run from two centres: Royal Free London NHS Foundation Trust (affiliated with University College London) and Imperial Healthcare NHS Trust.

When is the study starting and how long is it expected to run for?
The study is anticipated to start 1/3/2019 and last to 1/4/2020.

Who is funding the study?
The study is funded by the Moulton Charitable Foundation.

Who is the main contact?
Dr Bernard Khoo (b.khoo@ucl.ac.uk)

Contact information

Type(s)
Scientific

Contact name
Dr Bernard Khoo

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Protocol serial number
UCLIC-PP1420-2018

Study information

Scientific Title
A randomised placebo-controlled study of the pancreatic polypeptide analogue PP 1420 in patients with pancreatogenic diabetes (a pilot study)

Acronym

PP 1420 in PD

Study objectives
Administration of an exogenous single dose of human Pancreatic Polypeptide analogue PP 1420 will increase hepatic insulin sensitivity in patients with Pancreatogenic Diabetes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/03/2019, London - City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, UK; Tel: +44 (0) 2071048033/53; Email: nrescommittee.london-cityandeast@nhs.net), REC ref: 19/LO/0315

Primary study design
Interventional

Study design
Interventional single-blinded randomised controlled cross-over study, multicentre

Study type(s)
Other

Health condition(s) or problem(s) studied
Pancreatogenic Diabetes

Interventions
There will be three interventions, all delivered as single subcutaneous injections:
1. 0.9% saline placebo.
2. Pancreatic polypeptide analogue PP 1420, 2 mg.
3. Pancreatic polypeptide analogue PP 1420, 4 mg.

Volunteers will be asked to come in for three study visits involving an overnight stay and a full day study. At randomisation the volunteers will be assigned to one of six treatment sequences in a balanced fashion (i.e. two patients each will be assigned to each treatment sequence).

1st study visit 2nd study visit 3rd study visit
A 0.9% saline (placebo) PP 1420 2 mg PP 1420 4 mg
B 0.9% saline (placebo) PP 1420 4 mg PP 1420 2 mg
C PP 1420 2 mg 0.9% saline (placebo) PP 1420 4 mg
D PP 1420 4 mg 0.9% saline (placebo) PP 1420 2 mg
E PP 1420 2 mg PP 1420 4 mg 0.9% saline (placebo)
F PP 1420 4 mg PP 1420 2 mg 0.9% saline (placebo)

On the morning of the study visit, an euglycaemic hyperinsulinaemic clamp study will be commenced at 0700h (T=-120 mins) with a primed continuous infusion of [6,6-2H2] glucose, a stable isotope tracer. Baseline samples will be taken between T=-30 mins and T=0 mins to measure the baseline [6,6-2H2] glucose enrichment. At 0900h (T=0 mins) the PP 1420 or saline placebo will be given as a single subcutaneous injection according to the treatment sequence. A

two-step euglycaemic hyperinsulinaemic clamp study protocol will be commenced at T=+30 mins. The study visit will stop at 1600h. Volunteers will be discharged home after a two hour observation period.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Pancreatic Polypeptide 1420 (Pancreatic polypeptide analogue)

Primary outcome(s)
Hepatic insulin resistance will be measured using endogenous glucose production as assessed during an euglycaemic hyperinsulinaemic clamp commenced 120 mins before the intervention is given.

Key secondary outcome(s)
1. Peripheral insulin resistance will be measured using the following parameters as assessed during an euglycaemic hyperinsulinaemic clamp commenced 120 mins before the intervention is given:
1.1. Glucose uptake (Rd)
1.2. Metabolic clearance rate (MCR)

Completion date
01/04/2020

Eligibility

Key inclusion criteria
1. Aged 18-75
2. Diagnosed with pancreatogenic diabetes (PD) on the basis of:
2.1. WHO 2006 and 2011 criteria defining diabetes mellitus: fasting plasma glucose of ≥7.0 mmol /L, 2-hour plasma glucose of ≥11.1 mmol/L after a 75g oral glucose load is consumed, and/or HbA1c ≥48 mmol/mol.
2.2. Evidence of pancreatic exocrine deficiency: faecal pancreatic elastase levels below local reference limits.
2.3. Abnormal pancreatic morphology on imaging by CT, ultrasound or MRI scanning.
2.4. No evidence of diabetic autoimmune disease, e.g. negative anti-glutamic acid decarboxylase antibodies
2.5. Deficient PP response to a mixed meal tolerance test (<2-fold elevation in PP levels from baseline to peak).
3. Treated with insulin or oral hypoglycaemics for diabetes, doses stable (less than ±10% change in previous 3 months)

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
All

Key exclusion criteria
Current pregnancy (positive urinary ß-hCG test)

Date of first enrolment
01/03/2019

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital, Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Imperial College Healthcare NHS Trust
Hammersmith Hospital, Du Cane Road
London
United Kingdom
W12 0NN

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Moulton Charitable Foundation

Results and Publications

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 Bernard Khoo (b.khoo@ucl.ac.uk). The data provided will be pseudoanonymised using a subject code and will include datasets relating to the sample data from the euglycaemic hyperinsulinaemic clamp.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No