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Pancreatic replacement therapy and glycaemic control in diabetes

Submission date
31/05/2017

Recruitment status
No longer recruiting

Registration date
31/05/2017

Overall study status
Completed

Last Edited
30/09/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Diabetes is a common chronic condition. About 6% of the UK population already have either type 1 diabetes (T1DM) or type 2 diabetes (T2DM), and one in ten adults are at risk of developing diabetes. People may develop problems due to diabetes, including diabetic eye disease, numbness in feet, kidney damage and heart problems. However, diabetes can also cause other problems that are not as easy to prevent or treat such as delayed stomach emptying after meals, and problems with the pancreas not producing enough juices to help digest food. When the pancreas doesn't produce enough of these digestive juices, patients may have gastrointestinal (stomach and intestine) symptoms including abdominal pain, bloating, diarrhoea and weight loss. This condition is called pancreatic exocrine insufficiency (PEI) and it is confirmed by doing a stool test. It is easily treated by replacing the digestive juices in a capsule, which contains enzymes for digestion (pancreatic enzyme replacement therapy – PERT). This is taken with every meal and snack and can significantly improve symptoms. This treatment may also improve blood sugar levels for people with diabetes, but we are not sure exactly how this happens. Measuring sugar levels with finger-prick tests or with HbA1c (a measure of average glucose levels over a 6 week period) does not clearly show these changes in sugar levels. The aim of this study is to find out more about how pancreatic enzyme replacement therapy may have an effect on sugar levels in patients who also have diabetes by using a new way of measuring sugar levels called a continuous glucose monitor which will measure sugar levels in much more detail.

Who can participate?
Adults aged 18 and older with either type 1 or type 2 diabetes, who have recently been diagnosed with PEI but who have not yet started treatment for this.

What does the study involve?
Participants attend four study visits. At the first visit, participants fill out a questionnaire about their gastrointestinal symptoms and have a blood test. They receive a continuous glucose monitor (a small disc that sticks to the back of the arm with a tiny fibre that is inserted under the skin) for two weeks. Participants check their blood sugar levels normally. After two weeks, participants are given a prescription for Creon. They take this for six weeks and then have another continuous glucose monitor applied for two weeks. At the last visit, the sensor is removed and participants repeat the blood test and questionnaire.

What are the possible benefits and risks of participating?
Participants may benefit by receiving a treatment which may improve their gastrointestinal symptoms. Depending on the outcome of the study, participants may also improve their sugar levels. There are no notable risks with participating as Creon is a safe drug that has been used in the NHS for several years. We are using Creon in this study in the same way as we would for people with PEI who do not have diabetes, so even after the study, or if patients decide not to take part, we will still recommend that patients take Creon. The most common side effects of Creon are gastrointestinal, but are normally due to the underlying PEI rather than the new drug. The safety of the continuous glucose monitor has been tested by the manufacturer. Occasionally the sticky patch can cause some skin itching or a mild rash. Participants may experience discomfort when providing blood samples.

Where is the study run from?
Queen Alexandra Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2017 to May 2019

Who is funding the study?
Mylan Products Ltd

Who is the main contact?
Dr Katherine Alington
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2017-001227-45

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
34410

Study information

Scientific Title
Comparison of ambulatory glucose profile prior to and during pancreatic enzyme replacement therapy in patients with diabetes and pancreatic exocrine insufficiency: a single-arm phase IV trial

Acronym
DRIVE - PEI

Study objectives
The aim of the study is to investigate whether treatment of pancreatic exocrine insufficiency in individuals with type 1 or type 2 diabetes mellitus results in improved glycaemic control.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Hampshire B, 12/06/2017, 17/SC/0224

Study design
Non-randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

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

Interventions
Participants all have type 1 or type 2 diabetes and will be newly diagnosed with pancreatic exocrine insufficiency. At the first visit, participants fill out a questionnaire about their gastrointestinal symptoms and have a blood test. Participants will wear a flash glucose monitoring sensor for 14 days to measure their baseline ambulatory glucose profile. They then commence therapy with Creon 50,000 units with meals and 25,000 units with snacks, in accordance with standard care for patients diagnosed with pancreatic exocrine insufficiency. All participants will receive the same drug and at the same dose for the same duration. Participants check their blood sugar levels normally during this time. After continuing Creon for 6 weeks, participants have a repeat flash glucose monitoring sensor applied for 14 days and the ambulatory glucose profile metrics will be compared. Improvement in symptoms will be assessed using a gastrointestinal symptom questionnaire. Additional clinical measurements including HbA1c and BMI will be taken at baseline and at 8 weeks.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Creon

Primary outcome measure
Mean glucose interquartile range measured over 14 days at baseline (weeks 0-2) and after pancreatic enzyme replacement therapy (PERT) (at weeks 8-10) as measured using the Freestyle Libre Pro flash glucose monitor.

Secondary outcome measures
1. Other ambulatory glucose profile (AGP) metrics averaged over 14 days as measured by the Freestyle Libre flash glucose monitor at weeks 6-8 of PERT therapy:
1.1. Area under the median curve (AUC)
1.2. Median
1.3. Time above target range (above 10mmol/L and above 15mmol/L)
1.4. Time in target range (TIR) (4-10mmol/L)
1.5. Time below target range (below 4mmol/L and below 3mmol/L)
1.6. Median curve instability

1.7. Specific time periods – including pre-prandial and post-prandial
1.8. Estimated HbA1c
2. GI symptoms are measured using a questionnaire at 8 weeks after starting PERT
3. Clinical measurements – HbA1c, weight, BMI are measured using venous blood sampling and physical examination at 8 weeks after starting PERT

Overall study start date
18/03/2017

Completion date
31/05/2019

Eligibility

Key inclusion criteria
1. Male or Female, aged 18 years or above
2. Diagnosed with Type 1 diabetes or Type 2 diabetes at least 1 year ago, and be receiving oral and / or insulin therapy for diabetes
3. Have 1 or more symptoms of PEI:
3.1. Diarrhoea – Bristol Stool Chart (see appendix) type 5, 6 or 7
3.2. Steatorrhoea or greasy, pale or offensive smelling stools
3.3. Weight loss
3.4. Abdominal pain or cramps
3.5. Bloating or increased flatulence
4. Low faecal elastase level <200mcg/g in last 2 years
5. Willing and able to give informed consent for participation in the study and for GP to be informed

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 20; UK Sample Size: 20

Total final enrolment
19

Key exclusion criteria
1. Currently receiving, or have ever received, PERT
2. Current prescription of or planning to commence medication (within next 2 months), other than those for diabetes, that may increase or decrease serum glucose levels such as:

2.1. Oral corticosteroids for more than 7 days
2.2. Antipsychotics
2.3. Nutritional supplements such as Fresubin®
2.4. Weight-loss medication such as orlistat
3. Diagnosed with or suspected diagnosis of:
3.1. Pancreatic malignancy
3.2. Acute pancreatitis or chronic pancreatitis
3.3. Type 3c diabetes or other Type 3 secondary diabetes
3.4. Cystic fibrosis
3.5. Previous or awaited gastric bypass (within next 2 months), pancreatic or extensive small bowel surgery
3.6. Other primary pancreatic disorder or uncontrolled liver disorder (exception: non-alcoholic fatty liver disease)
4. Current or recently resolved (within 2 weeks) acute diarrhoeal episode thought likely to be infectious or other gastroenteritis
5. Current of previous chronic alcohol excess
6. Currently pregnant, recently postpartum (within 6 months) or planning pregnancy before end of study date
7. Currently using a modified diet under dietetic supervision, such as FODMAP
8. Currently receiving supported nutrition, including via nasogastric tube, gastrostomy tube or parenteral nutrition
9. Known allergy to Creon® or any of its components
10. Objection to porcine origin of pancreatin
11. Known allergy to Freestyle Libre Pro adhesive pad
12. Already enrolled, or recently (within 6 weeks) taken part in, another study that may affect glycaemic control or that may affect digestion or absorption or another aspect of the GI system or nutrition

Date of first enrolment
01/06/2017

Date of final enrolment
01/03/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Alexandra Hospital
Portsmouth Hospitals NHS Trust
Portsmouth
United Kingdom
PO6 3LY

Sponsor information

Organisation
Portsmouth Hospitals NHS Trust

Sponsor details
De La Court House
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Sponsor type
Hospital/treatment centre

Website
www.porthosp.nhs.uk/departments/Research/research-innovation.htm

ROR
https://ror.org/009fk3b63

Funder(s)

Funder type
Industry

Funder Name
Mylan Products Ltd

Results and Publications

Publication and dissemination plan
The results of the study will be submitted for publication in a peer-reviewed journal.

Intention to publish date
21/12/2019

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			30/09/2022	No	No
Protocol file	version 2.0	22/05/2017	30/09/2022	No	No
HRA research summary			28/06/2023	No	No