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Can an endoscopic treatment of the small bowel make women with polycystic ovarian syndrome start having periods?

Submission date
23/10/2017

Recruitment status
No longer recruiting

Registration date
10/11/2017

Overall study status
Completed

Last Edited
27/09/2019

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Polycystic ovarian syndrome (PCOS) is a very common condition affecting women. Women with PCOS have irregular periods, infertility, increased male hormone levels (testosterone), increased hair growth and obesity. More than half of women with PCOS are unable to respond normally to insulin (insulin resistance). Insulin is a hormone involved in lowering blood sugar and as a result these women can develop raised blood sugar levels and diabetes. Treatments that improve their sensitivity to insulin have been shown to help women with PCOS start having regular periods and eventually get pregnant. This study investigates the use of a new non-surgical device, the Revita System, which has been shown in early studies to safely and effectively improve blood sugar control in diabetic patients. The system, which entails heating up the duodenum (duodenal mucosal resurfacing), uses a device manufactured by Fractyl Laboratories and has the CE (European Conformity) mark for the treatment of metabolic disease. The aim of this study is to investigate if the use of this device in women with PCOS and insulin resistance can make these women more sensitive to insulin and also if it will help them have more regular periods.

Who can participate?
Females aged 18-45 who have been diagnosed with PCOS.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the treatment. The Revita System consists of two parts, a tube and a console unit. The tube is attached to the console and this is introduced into the upper part of the gut (food pipe, stomach and first part of the small bowel called the duodenum). A special x-ray movie (fluoroscopy) will also be used to make sure the device is positioned in exactly the right place during the procedure. At the same time, a flexible camera called an endoscope is used to look inside the duodenum. First, the catheter is used to inject salt water (saline) into the inner layer of the gut wall to protect the underlying muscle. Second, the balloon at the end of the catheter is filled with hot water to heat the inner lining (mucosa) of the duodenum. The procedure is performed

under general anaesthesia. Those in the second group receive the “sham” procedure. Participants are followed up for six months where they are followed up to see if their reproductive outcomes have improved and to assess their body composition.

What are the possible benefits and risks of participating?
Participants may benefit from the treatment as it may enable them to get pregnant without exposing them to the side effects of long term medications or the complications of invasive interventions. The risks of the Fractyl Revita SystemTM and the procedure are as follows: discomfort and bruising at the cannulae insertion sites, abdominal bloating and discomfort following the procedure, sore throat after endoscopy, diarrhea. Some infrequent risks include: narrowing of the small bowel after the procedure (stenosis), which may require another endoscopy to dilate and low blood sugar during the clamp test which will be promptly treated. Rare or theoretical risks may include: perforation (a tear in your GI tract), pancreatitis (inflammation of your pancreas), low blood sugars after treatment, risks from x-ray radiation, radiation damage the DNA which may, very rarely, cause cancer (0.008% or 1 in 12,500). and general anaesthesia risks.

Where is the study run from?
1. Imperial College London Hammersmith Hospital (UK)
2. St Mary's Hospital (UK)
3. King's College Hospital (UK)
4. West Middlesex Hospital (UK)
5. University Hospital Coventry (UK)

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

Who is funding the study?
Fractyl Laboratories Inc. (UK)

Who is the main contact?
1. Miss Vasha Kaur (Public)
vasha.kaur@nhs.net
2. Dr Belen Pevida (Scientific)
vasha.kaur@nhs.net

Study website
https://www.clinlife.com

Contact information

Type(s)
Public

Contact name
Miss Vasha Kaur

Contact details
Imperial Clinical Research Facility
Hammersmith Hospital
Du Cane Road

London
United Kingdom
W12 0HS
+44 7710067018
vasha.kaur@nhs.net

Type(s)
Scientific

Contact name
Dr Belen Perez Pevida

Contact details
Imperial Clinical Research Facility
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS
+44 7710067018
belen.pevida@nhs.net

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
35208

Study information

Scientific Title
Investigation of the metabolic effects of duodenal resurfacing on insulin resistant women wIth polycystic ovarian syndrome

Acronym
DOMINO trial

Study objectives
The aim of this study is to investigate both whether the Fractyl Revita SystemTM, a non-invasive device, can increase insulin sensitivity using gold-standard methodologies and also whether it can help women of reproductive age start menstruating.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Dulwich Research Ethics Committee, 07/08/2017, ref: 17/LO/1095

Study design
Randomised; Interventional; Design type: Treatment, Radiotherapy, Dietary

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Specialty: Metabolic and endocrine disorders, Primary sub-specialty: Metabolic and endocrine disorders; UKCRC code/ Disease: Metabolic and Endocrine/ Metabolic disorders

Interventions
DOMINO is a prospective double-blinded randomised controlled trial comparing the Fractyl Revita duodenal mucosal resurfacing device to a sham procedure in women with PCOS to ascertain its effect on insulin sensitivity and to assess its impact on menstruation.

Participants are randomly allocated to receiving the intervention or to having the sham procedure.

The intervention involves an endoscopic procedure under general anaesthesia, generally as a day-case procedure. A balloon attached to a sterile, single-use catheter is inserted endoscopically. Saline is injected into the submucosa of the duodenum to create a thermal barrier and through the use of hot water inside a balloon thermally ablates ~10cm of the duodenal mucosa at a time from an area distal to the papilla up to the ligament of Treitz. Limited fluoroscopy is used during catheter placement and location certification during treatment. A lead apron will be placed on the abdomen and pelvis during the procedure to protect the reproductive organs. The total procedure time is approximately 70 minutes.

The sham procedure will consist of placing the DMR Catheter into the duodenum under general anaesthesia and leaving it in place for a minimum of 45 minutes and then removing it from the patient.

All participants will be followed up for six months during which they will be invited for blood tests, body composition studies and OGTT at 2 weeks post procedure and at 12 weeks post procedure. At 12 weeks post-procedure they will also have a euglycaemic hyperinsulinaemic

clamp. From weeks 12 to 2, participants will be invited to attend for a reproductive blood tests and a pelvic ultrasound scan. At 6 months, participants will be invited for their final visit and will undergo blood tests and a body composition study.

Intervention Type
Other

Primary outcome measure
1. Reproductive outcomes are assessed as the number of ovulatory cycles over the study period defined by the increase in serum progesterone followed by menstrual bleeding. This will be assessed with:
1.1. Reproductive blood tests measured at baseline, once or twice weekly from weeks 12-24 post-procedure and 6-month clinical visit
1.2. Weekly pelvic ultrasound scan from weeks 12-24 post-procedure
2. Metabolic outcome are measured using hepatic and peripheral insulin sensitivity at baseline and at 12 weeks post procedure with:
2.1. Euglycaemic-hyperinsulinaemic clamp and
2.2. Oral glucose tolerance test.

Secondary outcome measures
1. Body weight is measured using a weighing scale at baseline, at the early post-procedure visit, at 12 weeks post-procedure and at 6-months
2. Body composition is measured using the Tanita machine at baseline, at the early post-procedure visit, at 12 weeks post-procedure and at 6-months
3. Post-prandial glucose, insulin and c-peptide excursions is measured using biochemical lab studies at the screening visit, baseline visit, early post-procedure visit, 12-week post-procedure visit
4. Reproductive hormone profile is measured using biochemical lab studies at the screening visit, baseline visit, early post-procedure visit, 12 week post-procedure visit, once / twice weekly visits from weeks 12-24 and the 6-month clinical visit
5. Ovarian follicle development is measured using weekly pelvic ultrasound scan from weeks 12-24 post-procedure
6. Liver function tests and lipid profile are measured using biochemical lab studies at the screening visit, baseline visit, early post-procedure visit, 12 week post-procedure visit, once / twice weekly visits from weeks 12-24 and the 6-month clinical visit
7. Number of medications and adverse events are recorded from the patient's history and clinical examination at every visit
8. Blood pressure readings are recorded clinically using a digital sphygmomanometer and assessed at every visit. Heart rate measurements are recorded with a finger probe and assessed at every visit

Overall study start date
01/12/2017

Completion date
01/06/2019

Eligibility

Key inclusion criteria

1. Female participants
2. Age 18-45
3. Body mass index (BMI) ≥ 30 kg/m2
4. Diagnosis of PCOS based on the NIH Criteria. Require ALL of the following:
4.1. Menstrual irregularity (anovulation or >35 day cycle)
4.2. Clinical or biochemical hyperandrogenism
4.3. Exclusion of other causes other aetiologies of menstrual dysfunction (e.g. thyroid dysfunction, hyperprolactinaemia)
5. Insulin resistance as defined by a 2-hour oral glucose tolerance test glucose concentration of 7.8 mmol/l and/or HOMA-IR ≥ 3.0.
6. Willing to comply with study requirements and able to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Key exclusion criteria
1. Type 1 or Type 2 diabetes mellitus
2. 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. These includes:
2.1. Active H. pylori infection (Participants with active H. pylori may continue with the screening process if they are treated via medication and re-testing verifies the condition has resolved.)
2.2. Previous gastrointestinal surgery that could affect the ability to treat the duodenum such as subjects who have had a Billroth 2, Roux-en-Y gastric bypass, or other similar procedures or conditions
2.3. History of chronic or acute pancreatitis
2.4. Known active hepatitis or active liver disease
2.5. Symptomatic gallstones or kidney stones, acute cholecystitis or history of duodenal inflammatory diseases including Crohn’s Disease and Celiac Disease
2.6. History of coagulopathy, upper gastro-intestinal bleeding conditions such as ulcers, gastric varices, strictures, congenital or acquired intestinal telangiectasia
2.7. Use of anticoagulation therapy (such as warfarin) which cannot be discontinued for 7 days before and 14 days after the procedure
2.8. Use of P2Y12 inhibitors (clopidogrel, pasugrel, ticagrelor) which cannot be discontinued for 14 days before and 14 days after the procedure. Use of aspirin is allowed.

2.9. Unable to discontinue NSAIDs (non-steroidal anti-inflammatory drugs) during treatment through 4-weeks post procedure phase
2.10. Taking corticosteroids or drugs known to affect GI motility (e.g. Metoclopramide)
2.11. Persistent anaemia, defined as haemoglobin< 10 g/dl
2.12. eGFR < 30 ml/min/1.73m2
2.13. Active systemic infection
2.14. Active malignancy within the last 5 years
2.15. Poor candidates for surgery or general anaesthesia
2.16. Active illicit substance abuse or alcoholism
3. Medications affecting insulin sensitivity (oral steroids, metformin, thiazolidinediones, atypical antipsychotics, hormonal contraceptives, weight loss medication) at screening or 6 months previously.
4. Other causes of anovulation (e.g. hypothyroidism, adrenal or pituitary disorders)
5. More than 6 menstrual bleeds within the previous 12 months
6. Current pregnancy or breastfeeding at screening or 6 months previously
7. Smoking at screening or 6 months previously
8. Without access at home to a telephone or other factor likely to interfere with ability to participate reliably in the study
9. Donated blood during the preceding 3 months or intention to do so before the end of the study
10. Any other mental or physical condition which, in the opinion of the Investigator, makes the subject a poor candidate for clinical trial participation

Date of first enrolment
15/12/2017

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
St Mary's Hospital
Praed Street

London
United Kingdom
W2 1NY

Study participating centre
King's College Hospital
Denmark Hill
Brixton
London
United Kingdom
SE59RS

Study participating centre
West Middlesex Hospital
Twickenham Road
Isleworth
United Kingdom
TW7 6AF

Study participating centre
University Hospital Coventry
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Sponsor information

Organisation
Imperial College of Science, Technology and Medicine

Sponsor details
Joint Research Compliance Office
Imperial College London & Imperial College Healthcare NHS Trust
Room 215, Level 2
Medical School Building
Norfolk Place
London
England
United Kingdom
W2 1PG

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
Fractyl Laboratories Inc.

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed high-impact journal is anticipated around 1 year following the end of the trial. This will be finalised following the end of the trial.

Intention to publish date
01/06/2020

Individual participant data (IPD) sharing plan
As of 18/12/2018:
The datasets generated during and/or analysed during the current study will be available upon request from Dr Alex Miras, a.miras@nhs.net . They will become available after publication of the results of the trial. They will be anonymised and there will be no ethical or legal restrictions.

Previous IPD sharing statement:
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v2	30/11/2018	30/11/2018	No	Yes
Protocol file	version v2	30/11/2018	30/11/2018	No	No
Participant information sheet	version v3.0	01/07/2019	23/09/2019	No	Yes
Protocol file	version v3.0	01/06/2019	23/09/2019	No	No

Statistical Analysis Plan	version v1.0	01/06/2019	23/09/2019	No	No
HRA research summary			28/06/2023	No	No