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Effect of lowering fatty acids levels with acipimox treatment on post-meal fat levels and insulin resistance in women with polycystic ovary syndrome and diabetes compared to healthy subjects

Submission date	Recruitment status	[ ] Prospectively registered
06/11/2013	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
04/12/2013	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
13/06/2019	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Type 2 diabetes mellitus (type 2 DM) is well known to be associated with increased risks of high blood pressure, angina, heart attack and stroke. Polycystic ovary syndrome (PCOS) is a common hormone problem in young women and, as a result of it, they can experience irregular periods, reduced fertility, acne and increased body hair. Research suggests that they could have a high risk of diabetes and cardiovascular disease such as high blood pressure, angina, heart attack and stroke. One of the reasons for the increased cardiovascular risk in these patients is the presence of high bad cholesterol and low good cholesterol levels in the circulation, and insulin resistance. The fat from the diet is transported from the stomach into the blood and then cleared up by the liver, muscles and fat tissues to store or use as an energy source. Delayed removal of fat from the blood after a meal has been known to happen in diabetes and PCOS patients. According to previous studies, high fat level in the blood after a meal is an independent risk factor for cardiovascular disease. In addition, the high fat level may worsen insulin resistance and glucose levels. However why this happens in patients with type 2 DM and with PCOS, and whether lowering fat level improves insulin resistance are still not known. That is why we plan to do this research study.

Who can participate?
This study will recruit 10 premenopausal healthy women, 10 premenopausal women with polycystic ovary syndrome and 10 premenopausal women with type 2 diabetes mellitus.

What does the study involve?
The study includes 4 visits to the Diabetes Centre, Hull Royal Infirmary (UK).
Screening visit (Visit 1): Visit 1 is designed to obtain informed consent from you and to find out if you are eligible for the study. The screening includes a brief medical history (including pre-existing medical conditions, medicines you are currently taking, smoking status and alcohol

intake), physical examination (measurement of height, weight, hip and waist circumference and blood pressure), the baseline blood tests and an oral glucose tolerance test if participants are not known to have diabetes and wish to enter the study in control arm or PCOS arm. An oral glucose tolerance test involves measuring the blood sugar level at baseline and at 120 minute after taking 75g of glucose solution following overnight fasting.
Visit 2: A meal test to determine fat clearance after a meal will be done in this visit. Participant will be asked to fast overnight from 1900 hour (7pm) the day before this visit, though water is allowed. A meal made of milk, cereals, cream, cheese and bread, and an emulsion with carbon labelled fat will be provided. Blood samples will be taken half hourly for the first 3 hours and hourly for 3 hours through the inserted cannula at the forearm. Breath samples will be taken every hour for 6 hours and 4 more breath samples at home. The breath test is simple and it is basically exhaling breath for a few seconds into a test tube using a plastic straw. Total amount of blood taken will be about 40-50ml. The meal test will take 6 hours.
Visit 3: Acipimox tablet is known to lower the fat level in the blood. You will be advised to take acipimox 250mg at 2000 hour, 2300 hour and 0600 hour with water only. You will be asked to fast since 1900 hour except water on the day before the meal test. The meal test will be done at 0800 hour in the next morning. The procedure for the meal test is same as that for visit 2.
Then you will be asked to take a weeks course of acipimox 250mg three times a day to be taken with food starting from next day before the third meal test.
Visit 4 (a week after visit 3): The visit is for the third meal test following a weeks course of one acipimox tablet three times per day. Then the meal test will be performed following overnight fasting using the same meal protocol.

What are the possible benefits and risks of participating?
There is no immediate benefit to the participants but the findings would be very useful to find a way to improve insulin resistance and cardiovascular risk. Possible adverse effects are hot flushes and skin rash which are common side effects of acipimox. The study doctor will look after the study participants throughout the study. Detailed information will be provided in the participant information sheet. Inserting the cannulas and taking blood samples may well cause discomfort and risks of inflammation/ infection/ bruising at the needle site. The risk will be minimised as the cannulation will be performed by experienced study doctors in accordance with the local guidelines.

Where is the study run from?
The study will be run at the Diabetes Centre, Hull Royal Infirmary

When is the study starting and how long is it expected to run for?
December 2009 to December 2013

Who is funding the study?
The study is funded by the diabetes charitable fund, Hull and East Yorkshire Hospital NHS Trust and the University of Hull (UK).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Study information

Scientific Title
To determine if acute lowering of circulating non-esterified fatty acids (NEFAs) with acipimox improves postprandial hypertriglyceridaemia and insulin resistance in women with polycystic ovary syndrome (PCOS) and with type 2 diabetes mellitus (DM)

Study objectives
High non-esterified fatty acids (NEFA) are associated with insulin resistance and obesity. Therefore we hypothesize that lowering NEFA would improve insulin resistance in obese PCOS and diabetes.

Postprandial hypertriglyceridaemia and hyperglycaemia are independent cardiovascular risk. Increased NEFA release from adipose tissue to the liver could increase very low density lipoprotein-triglyceride-triglyceride (VLDL-TG) synthesis. This could interfere with chylomicron clearance. We therefore aim to examine the beneficial metabolic effects of acute lowering of endogenous NEFA influx on postprandial hypertriglyceridaemia and hyperglycaemia in women with PCOS and with Type 2 DM.

The study also aims to determine the extent to which the suppression of VLDL-TG synthesis improves effective clearance of postprandial chylomicrons and improves postprandial hypertriglyceridaemia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hull and East Riding Research Ethics Committee, 19 November 2009, Reference Number: 09 /H1304/72

Primary study design
Interventional

Study design

Single centre non-randomised trial

Study type(s)
Screening

Health condition(s) or problem(s) studied
Type 2 diabetes mellitus, polycystic ovary syndrome

Interventions
An oral glucose tolerance test will be performed in women with PCOS and control subjects to exclude diabetes at screening. All the participants who fulfil the inclusion and exclusion criteria will enter into the study and attend three visits for meal tests.

Interventions: meal tests with overnight and a 1-week course of acipimox treatment.
All the eligible participants (control, PCOS, and Diabetes) will have same three meal tests using the same protocol.
Each participant will have a 900 Kcal standardised meal test, at baseline, following overnight acipimox treatment (250mg at 8pm, 11pm and 6am), and following a week course of acipimox 250mg three times a day with an interval of a week between the meal tests. Participants will be asked to fast overnight from 8pm except water and attend the research centre at 8am. After taking the baseline blood samples and breath samples, a meal made of milk, cereals, cream, cheese and bread, and an emulsion with a small amount of carbon labelled fat (13C tripalmitic acid 10mg /kg body weight) will be provided. Blood samples and breath samples will be taken ½ hourly for first 3 hours and hourly for 3 hours through the inserted cannula at the forearm. Subjects will be asked to collect 4 more breath samples at home after the meal test. The breath test is simple and it is basically exhaling breath for a few seconds into a test tube using a plastic straw. The meal test will take 6 hours.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
1. Changes in HOMA-IR
2. Changes in fasting lipid profiles
3. Changes in fasting postprandial triglycerides, insulin secretion and glucose

Measured at baseline and post acipimox treatment

Key secondary outcome(s)
Changes in lipid oxidation, exhaled 13CO2 AUC at 24 hour

Completion date
31/12/2013

Eligibility

Key inclusion criteria
PCOS Arm:
1. Female
2. Age 18-45 year premenopausal
3. No history of diabetes
4. BMI 28-45 kg/m2

Diabetes arm:
1. Female
2. Age 18-45 year premenopausal
3. BMI 28-45 kg/m2
4. Type 2 Diabetes mellitus

Healthy controls:
1. Female
2. Age 18-45 year premenopausal
3. BMI 28-45 kg/m2
4. No history of Diabetes or PCOS

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Key exclusion criteria
1. Pregnancy/breastfeeding
2. History of cardiovascular, renal, hepatic and thyroid disease
3. History of PCOS
4. History of allergy to acipimox
5. History of dyspepsia or peptic ulcers
6. History of food allergy
7. Patient on any hormonal replacement or oral contraceptive pills or cholesterol lowering agents
8. Unwilling for GP to be informed

Date of first enrolment
21/12/2009

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Diabetes Centre
Hull
United Kingdom
HU3 2JZ

Sponsor information

Organisation
Hull and East Yorkshire Hospitals NHS Trust (UK)

ROR
https://ror.org/01b11x021

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Diabetes charitable fund, The Hull and East Yorkshire Hospital NHS Trust and the University of Hull (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration