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Effect of exercise on lipid challenged insulin resistance and cardiovascular risk markers in PolyCystic Ovary Syndrome (PCOS)

Submission date
15/07/2013

Recruitment status
No longer recruiting

Registration date
31/07/2013

Overall study status
Completed

Last Edited
08/03/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Polycystic ovary syndrome (PCOS) is commonly associated with obesity, high levels of free fatty acids and insulin resistance (a condition in which the body produces insulin, but the cells in the body become resistant to it and are unable to use it effectively). Therefore, women with PCOS are at risk of diabetes and heart disease. Over 50 years ago, it was proposed that excessive fat (free fatty acids) interferes with skeletal muscle insulin resistance. Women with PCOS are found to have an insulin signalling defect.
This study aimed to examine the effect of lipid infusion (a mixture of soya oil, glycerol, purified egg phospholipids and phosphate supplement given through a vein) on insulin resistance in PCOS compared to controls. Secondly it aimed to investigate the effect of moderate intensity exercise, which promotes fat utilization, on basal and lipid-induced insulin resistance in PCOS. Then we examine the effect of exercise on cardiovascular risk in women with PCOS and healthy volunteers.

Who can participate?
We recruit healthy women and women with PCOS aged 19-40 years, both lean participants with body mass index (BMI) 18-25 kg/m2 and obese participants with BMI 26-40 kg/m2.

What does the study involve?
Participants will be randomly allocated to two day procedures of either saline or intralipid infusion for 5 hours. All participants receive an 8-week program of supervised moderate intensity exercise.

What are the possible benefits and risks of participating?
Participants would improve their physical fitness and insulin resistance and subsequent cardiovascular risk at the end of the exercise program. The exercise intervention should not harm the participants apart from possible aches and pain in muscles at the beginning. During the insulin sensitivity measurement, there is a slight chance of lowering of blood glucose level (hypoglycaemia) that will be closely monitored and corrected appropriately. Lipid infusion contains soya oil, glycerol, purified egg phospholipids and phosphate. It is licensed to use as

nutritional supplement given through the vein to have a quick effect. Possible adverse effects are occasional febrile (fits) episodes and rarely (i.e. less than 1 in 1000 patients reported) severe allergic reactions. Appropriate safety measures are in place in the department and the whole test will be supervised and monitored by the experienced study doctor and staff. Inserting the cannulas (tubes) 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 the experienced study doctor in accordance with the local guidelines.

Where is the study run from?
This study is conducted at a single unit, the research diabetes centre, Hull Royal Infirmary.

When is the study starting and how long is it expected to run for?
The study started in October 2010 and will run until October 2014.

Who is funding the study?
The funding is provided by diabetes endowment fund and Hull York Medical School.

Who is the main contact?
Prof Stephen Atkin
Stephen.atkin@hyms.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Stephen Atkin

Contact details
Professor of Diabetes, Endocrinology and Metabolism
Hull York Medical School
Michael White Diabetes Centre
Hull Royal Infirmary
Hull
United Kingdom
HU3 2RW
+44 (0)1482 675312
Stephen.atkin@hyms.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Testing the hypothesis of metabolic competence in polycystic ovary syndrome

Acronym
PCOS

Study objectives
Metabolic incompetence is a progressive condition with chronic elevation of free fatty acids secondary to progressive weight gain and increased central obesity ultimately leading to polycystic ovary syndrome in women with reproductive age. It may be reversible when fat metabolism is modulated by endurance exercise.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds (Central) Research Ethics Committee; Reference:10/H1313/44

Study design
Case control descriptive hypothesis generating study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Polycystic ovary syndrome

Interventions
The participants who fulfil the inclusion and exclusion criteria will be recruited for the study. All the participants will undergo two day procedures of either saline or intralipid infusion for 5 hours with the measurement of insulin sensitivity in the last two hours of infusion by a hyperinsulinaemic euglycaemic clamp. Briefly, following a 12 hour overnight fast, subjects will attend the research centre at 8am for the infusion test. A cannula will be inserted in the elbow for the test infusions as per protocol. Another cannula will be placed into the other forearm vein for blood sampling. This arm will be wrapped with a blanket (60 deg C) in a heating box to be

able to measure the reliable blood glucose. An infusion either saline or intralipid with heparin will be given for first three hours and it will be followed by two hours of glucose/ insulin infusions to measure the rate of glucose disposal by the muscles (insulin sensitivity). A drop of blood will be taken for plasma glucose measurements every 5 minutes throughout 120 minutes. Blood samples will be collected every hour for 5 hours.
The same procedures will be repeated at the end of the exercise program.
Participants will be asked to attend the Department of Sport, Health and Exercise Science at the University of Hull to complete the VO2max test and receive 8 week exercise prescription. The VO2max test is an exercise test that will be performed on a motorised treadmill. The exercise program is 3 sessions (aiming 60 minutes in each session) per week, moderate intensity for 8 weeks. The performance and attendance will be supervised by the sports specialists from University of Hull. At the end of the program, the repeat measurement of VO2max will be conducted on the treadmill.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
VO2 max, HOMA-IR, rate of glucose disposal before or after intralipid, before or after exercise.

Secondary outcome measures
1. Lipid profiles, Blood pressure. BMI, HsCRP, endothelial markers (microparticles)
2. Platelet activation before and after intralipid infusion
All parameters will be measured at baseline and at the end of the exercise program

Overall study start date
17/10/2010

Completion date
01/10/2014

Eligibility

Key inclusion criteria
1. Age 18-40 year premenopausal women
2. For lean participants BMI 18-25 kg/m2
3. For obese participants 26-40 kg/m2
4. The absence or presence of polycystic ovary syndrome (evidence of anovulation /oligomenorrhoea, clinical or biochemical hyperandrogenism, polycystic ovaries on ultrasound scanning which meets the PCOS diagnostic criteria of Rotterdam consensus statement) for controls and women with PCOS respectively

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
40 Years

Sex
Female

Target number of participants
48

Key exclusion criteria
1. Pregnancy/breastfeeding/trying to conceive
2. History of cardiovascular, renal, hepatic and thyroid disease
3. History of physical disability to exercise
4. History of diabetes mellitus
5. History of allergy to insulin/ soy oil, purified egg (intralipid)
6. Currently on oral anti-diabetic medication that improves insulin sensitivity such as metformin, weight reduction medication (orlistat, sibutramine)
7. Family history of sudden death
8. History of regular exercise three times a week for the last three months
9. Unwilling to be informed to their GP about their participation

Date of first enrolment
17/10/2010

Date of final enrolment
01/10/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Professor of Diabetes, Endocrinology and Metabolism
Hull
United Kingdom
HU3 2RW

Sponsor information

Organisation
Hull and East Yorkshire Hospitals NHS Trust (UK)

Sponsor details
c/o James Illingworth
R & D Manager
2nd Floor, Daisy Building
Castle Hill Hospital, Cottingham
Hull
United Kingdom
HU16 5 JQ
+44 (0)1482 461903
james.illingworth@hey.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.hey.nhs.uk/

ROR
https://ror.org/01b11x021

Funder(s)

Funder type
University/education

Funder Name
Diabetes Endowment Funds/ Hull York Medical School (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	28/02/2014		Yes	No
Results article	results	27/02/2019		Yes	No
Results article	results	01/08/2019	02/09/2020	Yes	No
Results article	results	30/09/2020	27/10/2020	Yes	No
Results article		17/02/2022	08/03/2022	Yes	No