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Hormonal and metabolic effects of diet and physical activity in women with polycystic ovary syndrome (PCOS)

Submission date
29/01/2018

Recruitment status
No longer recruiting

Registration date
05/02/2018

Overall study status
Completed

Last Edited
09/08/2019

Condition category
Pregnancy and Childbirth

[_] 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 the most condition that affects the ovaries. Its main characteristics are hyperandrogenism (high levels of male horomones), chronic anovulation (not ovulating) and polycystic ovaries (ovaries covered with cysts). Obesity and hyperinsulinemia (high levels of insulin) are also highly prevalent among women with PCOS. These issues can negatively affect endometrial function (the lining of the uterus). Impaired endometrial function is leading to implantation failure and endometrial abnormalities, such as hyperplasia (the enlargement of organs) and cancer. The aim of this study is to investigate whether weight loss and improved menstrual function can affect the expression of hormonal receptors that are of important for endometrial function in women with PCOS.

Who can participate?
Women aged 18-40 years old who have PCOS.

What does the study involve?
Participants are allocated to groups based on their weight. Participants are provided with individualized diet plans that are high in protein and low in carbohydrates. It is dietician supervised. Participants who are overweight are provided with a membership to a local exercise facility. Recommendations regarding the type, duration and frequency of training were individualized on the basis of interest, experience and present condition, with a weekly average of 2 or 3 45-min sessions of aerobic activity and verification by the staff of the gym. Participants are assessed before the intervention and on days 6-8, 21-24 of their menstruation cycle. Blood samples are taken from participants and analyzed. Endometrial biopsies are taken and transvaginal ultrasounds are done. Participants record their menstrual bleedin in a diary.

What are the possible benefits and risks of participating?
All patients participating in the study undergo general health check as well as gynecological examination. Taking part in the lifestyle intevention can result in improvement of general health. The risks of participating in the study are judged to be small. Endometrial biopsy and blood sampling are clinical routine examinations and rarely cause greater discomfort or

complications. The overall risk is judged to be small in relation to the benefit of participating in the study.

Where is the study run from?
1. Swedish Research Council (Sweden)
2. Swedish Cancer Society (Sweden)
3. Karolinska Institutet (Sweden)

When is the study starting and how long is it expected to run for?
January 2008 to December 2012

Who is funding the study?
1. Swedish Research Council (Sweden)
2. The Swedish Cancer Society (Sweden)
3. Karolinska Institutet (Sweden)
4. Regional agreement on medical training and clinical research (ALF) between Stockholm County Council and Karolinska Institutet (ALH, LS) (Sweden)

Who is the main contact?
Prof Angelica Lindén Hirschberg (Scientific)
angelica.linden-hirschberg@sll.se

Contact information

Type(s)
Scientific

Contact name
Prof Angelica Lindén Hirschberg

Contact details
Department of Women's and Children's Health
Karolinska Institutet
Stockholm
Sweden
17176

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Dnr 2008/865-32

Study information

Scientific Title
Hormonal and metabolic effects of diet and physical activity in women with polycystic ovary syndrome (PCOS) - a lifestyle intervention study

Study objectives
Lifestyle intervention aiming at weight loss could improve reproductive and metabolic health including endometrial function in overweight/obese women with PCOS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Regional Ethics Committee Stockholm, 2008/06/18, ref: Dnr 2008/865-32

Study design
Prospective lifestyle intervention study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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 (PCOS)

Interventions
The three-month individualized intervention involved changes in lifestyle designed to achieve weight loss. The diet was high in protein with little carbohydrate (40E% carbohydrates, 30E% fat and 30E% proteins). The dietician supervised and recommended the participants to intake three major meals and two or three snacks daily. Each participant reported her food intake, which was adjusted if necessary. In order to increase physical activity, all overweight women with PCOS are provided with membership in a local exercise facility (Friskis & Svettis). Recommendations regarding the type, duration and frequency of training were individualized on the basis of interest, experience and present condition, with a weekly average of 2 or 3 45-min sessions of aerobic activity and verification by the staff of the gym.

The group of overweight/obese women with PCOS are examined before and immediately after the intervention, on days 6-8 and 21-23 of the menstrual cycle (assessed on the basis of

spontaneous menstruation or bleeding induced by administration of 10 mg medroxyprogesterone acetate daily for 7 days). The women of normal weight with PCOS and all controls are examined once on days 6-8 and 21-23 of the same menstrual cycle.

While still fasting, a blood sample was taken from a peripheral vein at the same time each morning. Serum collected by centrifugation was stored at -70° C for later analyses. All gynecological examinations, including transvaginal ultrasound, are performed with the Sonoline SL-250 apparatus (Siemens Healthcare Diagnostics) by a single investigator. Under local anesthesia, endometrial biopsies were taken with a suction curette (Pipet Curet, CooperSurgical, USA).

During the intervention, the women in the OB-PCOS group recorded their menstrual bleedings in a diary and their ovulation are monitored (serum progesterone > 17 nmol/l). Alteration from amenorrhea to oligomenorrhea/regular menstruation or from oligomenorrhea to regular menstruation was defined as improvement.

Intervention Type
Behavioural

Primary outcome measure
Weight change is measured using the body weight at baseline and 12 weeks.

Secondary outcome measures
1. Menstrual function is evaluated using recordings of menstrual pattern and blood sampling of hormones during the intervention. The menstrual function is considered to be improved from baseline to 12 weeks when there is a shift from amenorrhea to oligomenorrhea/regular menstruation or from oligomenorrhea to regular menstruation and/or ovulation is confirmed by increased serum progesterone >17 nmol/L
2. Insulin sensitivity of the endometrium is measured using determination of gene and protein levels of molecules involved in insulin signaling at baseline and 12 weeks
3. Endometrial hormone receptor expression is measured using determination of gene and protein levels of hormone receptors at baseline and 12 weeks

Overall study start date
01/01/2008

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. All Rotterdam criteria for the diagnosis of PCOS should be met (anovulation, hyperandrogenism, polycystic ovaries)
2. 18-40 years
3. BMI >27
4. No medication or hormone-containing contraceptives for 3 months before beginning the study
5. Willing to sign informed consent

Healthy controls:
Women with normal weight with PCOS

Participant type(s)
Mixed

Age group
Adult

Lower age limit
18 Years

Upper age limit
40 Years

Sex
Female

Target number of participants
50 women with complete investigations

Key exclusion criteria
1. Pregnancy or lactation during preceding 12 months
2. Smoking
3. Use of hormone-containing contraceptives
4. Current disease
5. Regular medication including insulin-sentizing drugs
6. Eating disorder

Date of first enrolment
01/07/2008

Date of final enrolment
31/12/2011

Locations

Countries of recruitment
Sweden

Study participating centre
Karolinska University Hospital
Stockholm
Sweden
171 76

Sponsor information

Organisation
Karolinska Institutet

Sponsor details
Solnavägen 1
Stockholm
Sweden
17176
+46 08 524 800 00
registrator@ki.se

Sponsor type
University/education

Website
http://ki.se

ROR
https://ror.org/04hmgwg30

Funder(s)

Funder type
Not defined

Funder Name
Swedish Research Council

Funder Name
Cancerfonden

Alternative Name(s)
Swedish Cancer Society

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Funder Name
Karolinska Institutet

Results and Publications

Publication and dissemination plan
Three papers from the study have been published. There are plans to publish three more papers in high-impact peer reviewed journals.

Intention to publish date
05/02/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Angelica Lindén Hirschberg: angelica.linden-hirschberg@sll.se

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2014		Yes	No
Results article	results	01/02/2016		Yes	No
Results article	results	01/04/2017		Yes	No
Results article	results	01/03/2020	09/08/2019	Yes	No