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Homocysteine levels in polycystic ovary syndrome (PCOS) patients

Submission date
23/11/2022

Recruitment status
No longer recruiting

Registration date
09/12/2022

Overall study status
Completed

Last Edited
12/06/2023

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Polycystic ovary syndrome (PCOS) is a metabolic and endocrine disorder. Among the metabolic disturbances in PCOS, it is common to find and increased blood fating homocysteine (hcy). This is a metabolic reporter of the one carbon metabolism, which is of paramount importance for a healthy pregnancy, that can be modified with the dietary assumption of specific micronutrients. Previous studies have shown that hcy can be increased in follicular fluid of PCOS ladies undergoing ovarian hyperstimulation and that this increase could be a sign of defective quality of the follicle. This opens the possibility to evaluate the quality of a follicle at time of oocyte pick-up by measuring its hcy content and to select in this way the best embryos to be transferred.
The present study is intended to test the hypothesis that follicular hcy can be predictive of the clinical outcome from the respective oocyte. Moreover, the study will investigate whether a nutritional supplementation already shown to correct hcy in PCOS lady, may exert the same effect also on follicular hcy.

Who can participate?
The study will enrol women aged 18 years or older needing to undergo ovarian hyperstimulation due to infertility treatments and with a diagnosis of Poli Cystic Ovary Syndrome (PCOS) diagnosed according to the official criteria (so called Rottherdam criteria). To be eligible for the study the PCOS affected women should also be not pregnant, not affected by systemic diseases and not under any type of pharmacologic treatment. Participation to the study is conditioned by the signature of an informed consent to participate. However, this consent can be withdrawn by the patient at any time during the study without any consequences and any changes in the level of medical assistance delivered to the patient.

What does the study involve?
Women enrolled in the study will not undergo any added procedure that was not already scheduled based on their condition and on the necessary treatment. The only difference is that an added analysis will be performed on the follicular fluid that will be extracted at time of the planned oocyte pick-up. Moreover, those women randomized to (i.e. assigned by chance to) the intervention group will also assume a dietary supplement, one tablet per day, during the following 3 months.

What are the possible benefits and risks of participating?
The study aims to validate a new diagnostic procedure allowing a better selection of the embryos in assisted reproduction treatments. If successful, this procedure may result in increased efficacy in the single treatment cycle and reduced risk to repeat the treatment in case of failure. The patients accepting to contribute to this aim by participating in the study will therefore produce benefits for all future patients needing the same treatment and for themselves, should they need again the same treatment.
The risk assumed by the patients from the participation in the study is negligible. Those attributed to the control group will not at all modify their exposure. Those assigned to the active treatment will assume a dietary supplement already approved and regularly assumed by women carrying the same condition and that has never raised any concern so far. Indeed the supplement contains only micronutrients that are part of a normal diet and in amounts within the daily need for said micronutrients. These micronutrients include B vitamins (B2, B3, B6 and B12 in the activated form of methylcobalamin), folates (in the activated form of methylfolate) betaine, cystine and zinc. None of these micronutrients are known to cause allergies, furthermore the product is certified as lactose free and gluten free.

Where is the study run from?
Acibadem Fulya Hospital IVF Center (Turkey)

When is the study starting and how long is it expected to run for?
January 2017 to May 2022

Who is funding the study?
Partogen Pharmaceuticals (Turkey)
Parthenogen SAGL (Switzerland)

Who is the main contact?
Prof Tansu Kucuk, tansukucuk@hotmail.com

Contact information

Type(s)
Principal investigator

Contact name
Prof Tansu Küçük

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
2017-3/42

Study information

Scientific Title
Investigation on the role of follicular homocysteine in assisted reproduction cycles of polycystic ovary syndrome (PCOS) patients

Acronym
HOMO PCOS

Study objectives
Oocytes with proper metabolic activity can turn to competent embryos good to implant

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/02/2017, Acibadem University Research Ethics Committee (ATADEK, Kerem Aydinlar Kampusu, Kayisdagi Caddesi, No 32, Atasehir, Istanbul, Türkiye; +90216 5004444; atadek@acibadem.edu.tr), ref: 2017/3

Study design
Single center interventional blinded randomized controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Improving the metabolic competence in oocytes of PCOS patients undergoing IVF treatment.

Interventions
Patients providing informed consent are randomized for treatment or no treatment. Randomization is based on a computer-generated randomization list comprising 12 blocks of 4 positions each, total 48 positions. The positions are assigned on a strict chronological order.

PCOS patients randomized to the study group were given two cycles of 200 mg Betaine, 200 mg L-cystine, 16mg Niacin, 10 mg Zinc, 1.4 mg Vitamin B6, 1.4 mg Riboflavin, 400 mcg Folic acid (5MTHF – glucosamine), 2.5 mcg Vitamin B12 (methylcobalamin) preceding IVF cycle. The treatment, at the dose of one tab per day, is to be taken during 2 months before the planned follicular stimulation and thereafter during the stimulation.

Intervention Type

Supplement

Primary outcome(s)
Clinical pregnancy, calculated as number of fetuses with heart activity beyond 20 weeks of gestation per transferred embryo

Key secondary outcome(s))
1. FSH consumption during stimulation, calculated as cumulative number if FSH units injected
2. Fertilization rate, calculated as the rate of fertilized oocytes (2 PN) out of the total number of inseminated oocytes
3. Blastocyst rate, calculated as the rate of fertilized oocytes reaching the blastocyst stage at 5-6 days
4. Biochemical pregnancy, calculated as the rate of positive hCG at 7 days post embryo transfer out of the number of patients receiving an embryo transfer

Completion date
05/05/2022

Eligibility

Key inclusion criteria
1. PCOS patients diagnosed using Rotterdam's Criteria
2. Primary infertility for at least 1 year
3. No other condition leading to infertility

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
43

Key exclusion criteria
Patients who requested two embryos but implanted only one.

Date of first enrolment
01/11/2017

Date of final enrolment
02/02/2022

Locations

Countries of recruitment
Türkiye

Study participating centre
Acibadem Fulya Hospital IVF Center
Hakki Yeten Cad Y Cimen Sokak 23
Fulya
Besiktas
Istanbul
Türkiye
34349

Sponsor information

Organisation
Acibadem Healthcare

Funder(s)

Funder type
Industry

Funder Name
Partogen Pharmaceuticals

Funder Name
Parthenogen SAGL

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Prof Tansu Kucuk (tansukucuk@hotmail.com)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		10/06/2023	12/06/2023	Yes	No
Participant information sheet		01/02/2017	09/12/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file		01/02/2017	09/12/2022	No	No