ISRCTN02750360 https://doi.org/10.1186/ISRCTN02750360

An additional rescue dose of GnRH antagonist administered the day before hCG trigger is effective to prevent ovarian hyperstimulation syndrome (OHSS) in IVF/ICSI antagonist cycles at risk for OHSS without affecting the reproductive outcomes

Submission date
13/07/2014

Recruitment status
No longer recruiting

Registration date
13/08/2014

Overall study status
Completed

Last Edited
19/10/2017

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
Gonadotrophin releasing hormone (GnRH) antagonists are compunds that are similar to the natural hormone but have an opposite effect. Treatment with GnRH antagonists lowers but does not eliminate the risk of ovarian hyperstimulation syndrome (OHSS) in hyper-responding patients who are undergoing in vitro fertilisation (IVF/ICSI cycles). A double daily GnRH antagonist dose given for 1-3 days before a process called human chorionic gonadotrophin (hCG) triggering seems to eliminate the risk of OHSS in oocyte donation cycles. In addition, GnRH agonist triggering for final oocyte maturation reduces pregnancy rates. The aim of this study was to find out the prevalence of early and late OHSS as well as the pregnancy rate in patients at risk for OHSS, stimulated with the antagonist who received a double dose of the antagonist regiment (Ganirelix) for a single day, with a reducing daily dose of follicle stimulating hormone (FSH). These patients were compared with a control group of patients at a high risk for OHSS who did not receive the double dose of the antagonist regiment, with a reducing dose of FSH.

Who can participate?
The study included patients at high risk for OHSS who underwent ovarian stimulation for IVF using the 6th day fixed GnRH antagonist method. Patients were aged above 18 years but younger than 40 years, with polycystic ovaries.

What does the study involve?
Participants were randomly allocated to one of two groups: Intervention Group A and Control Group B. Group A received a double dose of GnRH antagonist the day before hCG while control group B did not. In both groups FSH dosage was reduced to 100IU on the day of the allocation.

What are the possible benefits and risks of participating?
Patients can benefit by avoiding cancellation of their IVF cycle and proceed to fresh embryo transfer with safety. A rescue double GnRH antagonist dose the day before hCG trigger may effectively be a safe alternative preventive strategy for early and late OHSS without affecting the pregnancy outcomes. The main risks for the patients is that since the intervention proposed is new with lack of robust references regarding the safety of approach, OHSS can still occur and cycle cancellation might still be suggested as a preventive measure after all.

Where is the study run from?
The study is run from a private fertility centre IAKENTRO in Thessaloniki, Greece

When is study starting and how long is it expected to run for?
November 2009 to February 2013

Who is funding the study?
IAKENTRO fertility centre (Greece)

Who is the main contact?
Professor Yannis Prapas, yannis@iakentro.gr
Konstantinos Ravanos MD, MSc, kdravanos@hotmail.com

Contact information

Type(s)
Scientific

Contact name
Prof Yannis Prapas

Contact details
Agiou Vasiliou 4
Thessaloniki
Greece
54250

Additional identifiers

Study information

Scientific Title
An additional rescue dose of GnRH antagonist administered the day before hCG trigger is effective to prevent OHSS in IVF/ICSI antagonist cycles at risk for OHSS without affecting the reproductive outcomes: a prospective randomized controlled trial

Study objectives
In GnRH antagonist IVF/ICSI cycles at risk for ovarian hyperstimulation syndrome (OHSS), is a double antagonist dose (0,25mg/12h) administered the day before hCG trigger, effective to prevent OHSS without affecting the reproductive outcomes?

Ethics approval required

Old ethics approval format

Ethics approval(s)
Institutional Review Board; ref. 11/2009

Primary study design
Interventional

Study design
Prospective randomized controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Ovarian hyperstimulation syndrome (OHSS), ovarian stimulation, GnRH antagonist, IVF

Interventions
Patients were randomised to:
1. Intervention group A (down-regulate FSH daily dose to 100 iu, up until hCG trigger and receive double GnRH antagonist dose the day before hCG trigger)
2. Control group B (down-regulate FSH daily dose to 100 iu, up to the hCG trigger)

Patients were considered at actual risk of developing moderate to severe OHSS when they had a high or rapidly rising serum estradiol (≥3500 pg/ml before oocyte maturation and projected to be >4500 pg/ml the day of hCG administration) and 18 or more follicles ≥11 mm but without any mature follicle >16 mm appearing at that time. A standard fixed 6th day antagonist protocol (Orgalutran 0.25 mg, Organon) with 225 IU/day recombinant FSH (rFSH, Puregon Organon) starting on day 2 of the cycle was used for the ovarian stimulation. In the 5th and 7th day of stimulation the rFSH daily dose, if needed, was adjusted according to ovarian response, accounting ultrasound control of growing follicles and oestradiol levels (blood sample). The criteria for the allocation of patients to the study groups were met from the 7th day of stimulation and onwards. Final oocyte maturation was achieved by administration of 10.000 IU of hCG (Pregnyl, NV Organon, the Netherlands) as soon as three or more follicles of ≥17mm were present on ultrasound control. Transvaginal oocyte aspiration was performed 36 hours after hCG administration by ultrasound-guided follicle puncture. All women were examined clinically and by ultrasound three and five days after oocyte retrieval or earlier if any discomfort appeared, for signs of moderate or severe OHSS using grading criteria (Golan et al., 1989; Grossman et al., 2010). If these symptoms of OHSS were present, the embryo transfer was cancelled, all embryos were cryo-preserved at the stage of blastocyst. Patients in both groups, without signs of OHSS had at least one embryo transferred on day 5 after OPU (blastocyst stage). A pregnancy test was performed 15 days after embryo transfer. The concurrency of a positive β-hCG test and a fetal heart beat (seen by ultrasound at 7 weeks of gestation) was defined as a clinical pregnancy, otherwise it was considered a biochemical pregnancy.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Early and late OHSS rates
2. Clinical pregnancy rate

Key secondary outcome(s)
1. Oestradiol (E2)
2. Luteizing hormone (LH)
3. Progesterone (PR) levels

Completion date
28/02/2013

Eligibility

Key inclusion criteria
1. Patients age 18-40 years, at high risk for OHSS who underwent ovarian stimulation for in vitro fertilization (IVF) using the 6th day fixed GnRH antagonist protocol. Patients were considered at actual risk of developing moderate to severe OHSS when they had a high or rapidly rising serum estradiol (≥3500 pg/ml before oocyte maturation and projected to be >4500 pg/ml the day of hCG administration) and 18 or more follicles ≥11 mm but without any mature follicle >16 mm appearing at that time.
2. With polycystic ovaries (The Rotterdam ESHRE/ASRM-sponsored PCOS consensus Workshop Group, 2004)
3. At high risk for OHSS
4. Not willing to cancel their IVF cycle

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
40 Years

Sex
Female

Key exclusion criteria
Polycystic ovarian syndrome (PCOS) patients

Date of first enrolment
01/11/2009

Date of final enrolment
28/02/2013

Locations

Countries of recruitment
Greece

Study participating centre
IAKENTRO
Thessaloniki
Greece
54250

Sponsor information

Organisation
IAKENTRO (Greece)

ROR
https://ror.org/05mnrce88

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
IAKENTRO fertility centre (Greece)

Results and Publications

Individual participant data (IPD) sharing plan

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	01/11/2017	Yes	No