Abstract title:
Evaluation of Time Interval Between Ovulation Trigger With Triptorelin Acetate and Oocyte Retrieval in IVF Cycles. A Randomized Controlled Trial

Study question:
What is the optimal time interval between GnRH agonist trigger and follicular aspiration to maximise the number of mature oocytes collected?

Summary answer:
The egg collection performed after 36 hours of triptorelin acetate administration allows obtaining a higher number of metaphase II (MII) oocytes.

What is known already:
Both GnRH agonists (GnRHa) and hCG have proven to be effective in achieving ultimate oocyte maturation. Nevertheless, their mechanism of action is different, and the hormonal dynamics of the ovulatory peak and the molecular profiles differ between them. GnRHa faithfully reproduces the physiological characteristics of natural cycles. Therefore, the accurate time to achieve oocyte maturation could be different between the two drugs. Consequently, the optimum moment to perform the follicular puncture after the GnRHa administration could be different from the 36 hours described for hCG. A study of the optimum time interval between ovulation triggering and follicular puncture is crucial.

Study design, size, duration:
Randomised, controlled, single-blind clinical trial carried out in a university-based IVF unit between September 2014 and December 2017. Patients undergoing ovarian stimulation with FSH in a short antagonist protocol were randomized to undergo egg collection after 30, 36 or 40 hours after ovulation trigger with 0.2 mg of triptorelin acetate. In patients undergoing fresh embryo transfer, luteal phase support was achieved by administering 1500 IU of hCG and 400 mg of vaginal micronized progesterone.

Participants/materials, setting, methods:
Women aged 18-37 years with a baseline FSH <10mIU/ml, AMH 5-45pmol/l, AFC 6-24 were included in the study. Patients with at least 5 follicles ≥16mm were randomized. Egg collections were done separating follicles measuring more and less than 16mm. Embryo transfer was performed according to...
usual clinical practice. The main outcome variable was the number of MII oocytes retrieved and the number of MII oocytes retrieved per follicle measuring > 16mm the day of trigger

**Main results and the role of chance:**
A total of 121 patients were randomized to undergo ovulation triggering and egg collection after 30h (n=41), 36h (n= 42) or 40 hours (n=38). The proportion of MII retrieved was significantly lower after 30h of Decapeptyl administration in comparison with 36h and 40h follicular aspiration times (30h: 6.63±4.14, 36h: 9.10±4.75 and 40h: 7.26±4.49; p=0.03698). In addition to that, the ratio MII/follicles >16mm was higher 36h after trigger, compared to the 30h group (0.98±0.56 vs 0.73±0.39; p=0.05277). MII rates were concordant with molecular analysis results: a significantly downregulation of genes related to oocyte maturation (AREG, BTC, CYP19A1, EFN2, EREG, PHLDA1, RGS2 and UGP2) were found in GCs of punctured follicles at 30h. No significant differences regarding pregnancy rates or live birth rates were found between groups

**Limitations, reasons for caution:**
The external validity of this study could be limited to patients undergoing the same type of ovarian stimulation. The present study was not designed to detect differences in pregnancy or live birth rates. Larger studies need to be performed in order to confirm the findings of the present study

**Wider implications of the findings:**
The results of this study contribute to improving IVF protocols in order to recover the maximum number of MII oocytes and therefore, enhancing pregnancy rates. In addition, the use of GnRHa for ovulation induction would decrease the risk of OHSS associated with hCG stimulation protocols

**Keywords:**
egg collection
ivf
oocyte maturation
gnRH analogue
triptorelin acetate