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SHORT COMMUNICATION

Triggering with GnRH agonist in oocyte-donation cycles: oestradiol monitoring is not necessary during ovarian stimulation

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Abstract This prospective observational study evaluated the efficacy and safety of oocyte-donation cycles triggered with a gonadotrophin-releasing hormone (GnRH) agonist without monitoring oestradiol concentrations during ovarian stimulation. A total of 97 oocyte donors received recombinant FSH (150–225/day) and GnRH antagonists (0.25 mg/day). Oocyte maturation was triggered with 0.2 mg triptorelin s.c. Donors aged 25.4 ± 4.1 years were stimulated for 8.8 ± 0.9 days and underwent 2.9 ± 0.5 (2–4) ultrasound assessments. Total FSH dose was 1703.4 ± 304.7 IU, antagonists were administered for 4.3 ± 1.0 days, 14.7 ± 8.8 oocytes were retrieved and there were no cases of ovarian hyperstimulation syndrome. Recipients (n = 123) aged 40.3 ± 3.4 years received 10.9 ± 4.3 oocytes, 88.7% of which were metaphase II. Intracytoplasmic sperm injection fertilization rate was 79% and 2.18 ± 0.6 (1–3) embryos were transferred. The pregnancy, clinical pregnancy and twin pregnancy rates were 64.2%, 57.7% and 19.7%, respectively. In conclusion, given the high efficacy and safety of the GnRH-antagonist protocol triggered with a GnRH agonist, the monitoring of oestradiol concentrations is not necessary. Ultrasound monitoring is enough for an adequate follow up of the stimulation cycle in oocyte donors.

KEYWORDS: GnRH-agonist triggering, GnRH antagonist, oestradiol, oocyte donation

Introduction

Traditional monitoring of an IVF cycle includes regular oestradiol measurements and ultrasound scans in an attempt to reduce the risk of ovarian hyperstimulation syndrome (OHSS). The same principle is extended to oocyte-donation cycles. However, the need for oestradiol monitoring remains controversial. A recent Cochrane Review (Kwan

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et al., 2008) found that cycle monitoring by ultrasound plus serum oestradiol was not more efficacious than cycle monitoring by ultrasound only on the outcomes of live births and pregnancy rates. However, regarding OHSS, which is a potential complication for oocyte donors, the same review states: 'cycle monitoring by transvaginal ultrasound plus serum oestradiol may need to be retained as a precautionary good practice point'. This conclusion is based not on a consistent trial favouring it, but just the opposite: a lack of solid evidence against the dual monitoring in preventing OHSS (Kwan et al., 2008). Alternatively, several retrospective and randomized trials (Bodri et al., 2009; Galindo et al., 2009; Hernández et al., 2009) have demonstrated that triggering ovulation using a gonadotrophin-releasing hormone (GnRH) agonist in oocyte-donation cycles completely eliminates OHSS (Bodri et al., 2010; Humaidan et al., 2011; Melo et al., 2009) without compromising embryo development or reproductive outcome (Acevedo et al., 2006; Erb et al., 2010; Sismanoglu et al., 2009).

Although some forms of compensation are allowed among countries, oocyte donation is basically an altruistic act made by otherwise healthy, young women. Hence, protocols offered to donors must be as friendly as possible and free of risks. Furthermore, some studies have shown that simpler protocols are associated with reduced treatment burden and psychological distress, optimizing the patient's experience towards ovarian-stimulation protocols (Devroey et al., 2009).

The purpose of this study was to evaluate the efficacy (number and quality of oocytes collected and fertilization rate), safety (OHSS rate) and reproductive outcome (recipient pregnancy rate) of oocyte-donation cycles triggered with a GnRH agonist without monitoring serum oestradiol concentration during the stimulation cycle.

Materials and methods

This is a prospective, observational, non-controlled study performed within the oocyte-donation programme in a private setting. A total of 97 consecutive oocyte-donation cycles (September 2010 to January 2011) were included. Individual donors were permitted to donate their oocytes to a maximum of two recipients.

The stimulation protocol was started on day 2–3 of the menstrual cycle. An ultrasound was made to exclude ovarian pathologies in the present cycle. Ovarian stimulation was started with 150–225 IU s.c. recombinant FSH (Puregon, Organon, Barcelona Spain; Gonal F, Serono, Madrid, Spain). After 5–6 days, an ultrasound was scheduled to verify follicular development and modify gonadotrophin dose if necessary. A daily 0.25 mg GnRH antagonist s.c. (Cetrotide, Serono, Geneva, Switzerland; or Orgalutran, Organon) was added when a 14-mm follicle was seen on ultrasound. The following controls were set every 2 or 3 days according to individual response. Final follicular maturation was performed with 0.2 mg triptorelin s.c. (Decapeptyl, IPSEN Laboratories, Barcelona, Spain) when at least two follicles of 17 mm in diameter were seen on ultrasound. Oocyte retrieval was scheduled 36 h later. The recovered oocytes were fertilized with intracytoplasmic sperm injection. No blood samples were taken during the stimulation cycle. Recipients with ovarian function were desensitized with a single i.m. administration of 3.75 mg leuproreline acetate (Ginecrin depot; Abbott, Madrid, Spain) in the secretory phase of the previous cycle. Hormonal replacement started on day 3 of the cycle with administration of oestradiol valerate (Progynova; Schering, Madrid, Spain) using increasing doses of oestradiol valerate (2–6 mg) as described elsewhere (Remohí et al., 1997). On the day of recovery of donated oocytes, 800 mg/day of natural micronized progesterone (Progeffik; Laboratorios Effik, Madrid, Spain) was vaginally administered to the recipient. Embryo transfer was performed 48–72 h after oocyte recovery. Surplus embryos were cryopreserved using vitrification protocols 48–72 h after oocyte recovery. Pregnancy was defined as a positive β-human chorionic gonadotrophin test in urine 14 days after embryo transfer, while clinical pregnancy was defined as the visualization of a heartbeat 2–3 weeks after the pregnancy test. Implantation rate was defined as the number of gestational sacs divided by the number of embryos transferred. Once clinical pregnancy was confirmed by transvaginal ultrasound, recipients were referred to their obstetrician in charge.

Results

As shown in **Table 1**, oocyte donors (n = 97) had a mean age of 25.4 ± 4.1 and received ovarian stimulation over a regular number of days (8.8 ± 0.9). No more than four ultrasound assessments were performed during the stimulation protocol (2.9 ± 0.5), donors received regular doses of recombinant FSH (1703.4 ± 304.7 IU) and the mean number of days of GnRH-antagonist application was 4.3 ± 1.0. As expected, a high number of oocytes were retrieved (14.7 ± 8.8). Importantly, none of them developed OHSS.

As shown in **Table 2**, recipients (n = 123) had a mean age of 40.3 ± 3.4. They received 10.9 ± 4.3 oocytes; 88.7% of them were in metaphase II. The fertilization rate was 79%. The mean number of embryos transferred was 2.18 ± 0.6 (1–3). The pregnancy rate was 64.2% (79/123), the clinical pregnancy rate was 57.7% (71/123) and the implantation rate was 31.0% (85/274). Finally, the multiple pregnancy rate was 19.7% (14/71), all of which were twin pregnancies.

Discussion

Triggering ovulation with GnRH agonists has been shown to be an efficient surrogate for human chorionic gonadotrophin. This finding is especially relevant for oocyte donors,

Table 1 Characteristics of oocyte donors.

Characteristic	*Oocyte donors (n = 97)*
Age (years)	25.4 ± 4.1 (18–32)
Stimulation (days)	8.8 ± 0.9 (7–11)
Ultrasound assessments	2.9 ± 0.5 (2–4)
Total FSH dose (IU)	1703.4 ± 304.7 (1050–2325)
Oocytes retrieved	14.7 ± 8.8 (8–46)
Days of antagonist	4.3 ± 1.0 (2–6)
OHSS	0

Values are mean ± SD (range).