The administration of the GnRH antagonist, cetrorelix, to oocyte donors simplifies oocyte donation

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BACKGROUND: We report our experience on the efficacy of a new regimen of the GnRH antagonist, cetrorelix, and recombinant FSH, Gonal-F, for controlled ovarian stimulation in a donor oocyte programme. METHODS AND RESULTS: Six oocyte donors were commenced on Gonal-F (150 IU) and two on Gonal-F 225 IU daily on day 4 together with cetrorelix 0.25 mg daily on day 8 until the day of administration of hCG. Six premenopausal recipients were down-regulated with intranasal Nafarelin 400 µg twice daily; two women with premature menopause did not require down-regulation for synchronization between donor and recipient cycles. The median (range) of oocytes retrieved and the median (range) fertilization rates were 7 (3–13) and 50% (0–71%) respectively. With the exception of a recipient who had failed fertilization, seven recipients had two embryos transferred. The median (range) number of days of ovarian stimulation, cetrorelix administration and number of Gonal-F ampoules administered for ovarian stimulation were 9 (7–12) days, 5 (3–8) and 18 (14–24) respectively. The clinical pregnancy rate per cycle was 50% (4/8) and one of the latter women miscarried at eight weeks gestation. Three women (37.3%) had full term deliveries. CONCLUSION: This preliminary study has shown that using a combination of cetrorelix and Gonal-F resulted in a high pregnancy rate, reduced the duration of treatment for the donor and simplified oocyte donation.

Key words: cetrorelix/donor/FSH/oocyte/recombinant

Introduction

It is well established that successful outcome from treatment using donor oocytes require synchronization of the donor and recipient. In order to allow synchronization between the donor and recipient, a GnRH agonist is used to down-regulate the pituitary (Marcus et al., 1999). While the safety of GnRH agonist for oocyte donation is established (Sauer et al., 1996), the latter may result in donors experiencing symptoms due to the GnRH agonist-induced hypo-estrogenic status. In addition, to achieve pituitary down-regulation using a GnRH agonist takes at least 2 weeks using the long protocol and prolongs the treatment period for the donor.

The earlier GnRH antagonists induced histamine release together with allergic side effects (Hahn et al., 1985; Reissmann et al., 1995). The newer GnRH antagonists have overcome the latter problems (Felberbaum et al., 1999). In contrast with GnRH agonists, the GnRH antagonist, cetrorelix, can suppress gonadotrophins within a few hours and has potential advantages over GnRH agonists during ovarian stimulation for assisted conception treatment. The rapid suppression of gonadotrophins allows clinicians to restrict administration of the GnRH antagonist to part of the ovarian stimulation treatment where it is necessary to suppress a premature LH surge. GnRH antagonist suppresses gonadotrophins by dose-dependent effect and through competitive inhibition of the pituitary GnRH receptors.

The efficacy of GnRH antagonist cetrorelix for assisted conception treatment has been reported (Albano et al., 1996; 1997; Wikland et al., 2001). Albano et al. (1996; 1997) reported that a single daily dose of 0.25 mg cetrorelix administered from day 6 of ovarian stimulation with gonadotrophins to the day of administration of hCG was effective in suppressing the premature LH surge. In a randomized study comparing the administration of a single daily dose of 0.25 mg cetrorelix to the day of administration of hCG compared with daily administration of buserelin 600 µg, the incidence of ovarian hyperstimulation syndrome (OHSS) was lower in the cetrorelix group (Felberbaum et al., 1999).

We report our experience on the administration of cetrorelix to oocyte donors to evaluate the efficacy of this new method of synchronization of the donor and recipient treatment.

Materials and methods

All eight consecutively-treated oocyte donors were evaluated. The oocyte donors were <35 years old, had regular menstrual cycles of 25–35 days, two normal ovaries based on transvaginal scan findings, body mass index (BMI) <32 kg/m² and agreed to donate their oocytes.
all donors were given a single i.v. dose of 1.2 g Augmentin after hCG injection followed by IVF. An hour prior to oocyte retrieval, hCG (Profasi; Serono). Oocyte recovery was carried out 34±36 h triggered by the administration of a single s.c. injection of 10 000 U hCG (Profasi; Serono). Cetrorelix 0.25 mg was administered s.c. daily on day 8 until the day of administration hCG (Profasi; Serono). Cetrorelix administration for oocyte donation (SmithKlineBeecham). Following oocyte retrieval, all donors were given a single dose (1 g) of azithromycin (Zithromax, Pfizer) and were given a follow-up consultation at the clinic.

For all recipients who were still cycling, down-regulation was carried out using the intranasal GnRH agonist (Nafarelin; Searle) 400 µg twice daily for 2 to 4 weeks. A baseline transvaginal scan was carried out prior to down-regulation to ensure that the uterus and adnexa were normal. On the day that the donor telephoned the Unit with the onset of her period, a member of staff in the Unit telephoned the recipient immediately and advised the latter to start oral estradiol valerate (Climaval; Novartis tablets). All recipients took estradiol valerate 2 mg from day 1 to 5, 4 mg from day 6–10 and 6 mg from day 11 to day of donor’s oocyte retrieval. Estradiol valerate 4 mg was continued until a pregnancy test 14 days later. The endometrial thickness of the recipient was measured prior to administration of i.m. progesterone. An i.m. injection of 50 mg progesterone (gestone; Ferring) was administered to the recipient on the day of the donor’s oocyte retrieval and again the following day. Following this, i.m. gestone 100 mg daily or progesterone vaginal suppositories, Cyclogest (Shire) 200 mg twice daily were administered until pregnancy test. A maximum of two embryos were replaced 48 h after commencing on i.m. progesterone.

If pregnancy was confirmed, women were advised to continue with estradiol valerate 8 mg daily and progesterone vaginal suppositories 200 mg twice daily until 9 weeks gestation. Women who failed to conceive were advised to stop the medications and to go back on hormone replacement therapy, if they had premature ovarian failure.

Assessments
Follicular number and size were measured by transvaginal ultrasonography. Blood samples were taken from the donors for measurement of serum LH carried out on day 4 of stimulation and on subsequent visits. Measurements of serum estradiol were carried out if clinically indicated to assess ovarian response.

The hormonal LH and estradiol assays were carried out using the standard protocols in our laboratory (Vankrieken et al., 1999).

Statistical analyses
Values were expressed in median (range) as the data were non-parametric.

Results
In this study of eight patients, the median (range) age of the donors and recipients was 33 years (range 29–35) and 40 years (range 31–49) respectively. Seven out of the eight donors (87.5%) were parous. All of the recipients were nulliparous. All donors had three follicles ≥17 mm diameter following ovarian stimulation and underwent oocyte retrieval. None of the donors had a premature LH surge or complications post operatively. The mean (range) number of days of cetrorelix and number of Gonal-F ampoules for ovarian stimulation were 5 (3–8) and 18 (14–24) respectively. The median (range) of oocytes retrieved and the median (range) fertilization rate were 7 (3–13) and 50% (0–71%). A solitary parous donor who was 29 years old had four oocytes retrieved and there was no fertilization. With the exception of the recipient who had failed fertilization, all of the remaining seven recipients had two embryos transferred [median 2 (range 0–2)].

The clinical pregnancy rate per cycle commenced based on transvaginal scan findings at seven weeks gestation was 50%
number of patients have to be carried out using this regimen to confirm our findings.

In conclusion, the reported regimen is safe, cost-effective and simplifies the management of the donor in the oocyte donation programme. By restricting the injection of GnRH antagonist to a few days to suppress LH surge, this treatment regimen reduces the exposure of the donors to medication. A starting dose of 150 IU of rFSH for controlled ovarian stimulation should be considered to reduce the cost of treatment and the risk of OHSS.

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References


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