Improvements achieved in an oocyte donation program over a 10-year period: sequential increase in implantation and pregnancy rates and decrease in high-order multiple pregnancies

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Objective: To compare outcome parameters and cumulative pregnancy rates (PRs) in oocyte donation cycles over a period of 10 years.
Design: Retrospective study.
Setting: University-affiliated assisted reproductive technology program.
Patient(s): Women undergoing oocyte donation (10,537 cycles) between 1995 and 2005.
Intervention(s): Ovarian stimulation and oocyte retrieval in donors. Embryo transfer performed in recipients after endometrial preparation.
Main Outcome Measure(s): Outcome parameters and cumulative PRs were calculated and compared in relation to indication, age, and origin of sperm used.
Result(s): Overall PR, implantation rate, clinical PR, and miscarriage rate per embryo transfer performed were 54.9%, 27%, 50.3%, and 19%, respectively. Ongoing PR per transfer was 40.2%, and twin and high-order multiple PRs were 39% and 6%, respectively. Mean number of embryos transferred was reduced from 3.6 ± 0.8 to 1.9 ± 0.3, implantation rate improved from 16.7% to 38.3%, and ongoing PR improved from 31% to 44.3%. Cumulative PRs did not differ significantly among different indications for oocyte donation, age groups, or origin of sperm used for oocyte insemination. Overall cumulative PRs after three and five cycles were calculated as 87% and 96.8%, respectively.
Conclusion(s): Significant improvements in outcome parameters were achieved within 10 years. Similar cumulative PRs were observed regardless of recipient age, indication for oocyte donation, or sperm origin. (Fertil Steril® 2007;88:342–9. ©2007 by American Society for Reproductive Medicine.)

Key Words: Oocyte donation, implantation rate, pregnancy rate, cumulative pregnancy rate, indications

Nowadays more and more women are delaying their desire to achieve pregnancy to later years of their reproductive life, and the mean age of maternity is increasing in many developed countries (1). Advanced age and reduced ovarian reserve are the major reasons for difficulty to conceive in an increasing number of women. Presently, IVF using donor oocytes is an increasingly used infertility treatment option for women with irreversible ovarian function loss or primary ovarian failure (2–5).

In countries where oocyte donation is performed, it is now apparent that PRs and implantation rates in oocyte donation cycles are higher than in standard IVF/intracytoplasmic sperm injection (ICSI) cycles (4–6). In 2004, Assisted Reproductive Technology Registry published results from 99,989 cycles of assisted reproductive technology (ART) treatment (6). In fresh nondonor IVF (73,406 cycles), a delivery rate per retrieval of 29.9% was reported, whereas in fresh donor oocyte IVF (7,581 cycles), a delivery rate per transfer of 43.7% was achieved. The major reason for higher success rates in oocyte donation cycles is recruitment of selected young women as donors, significantly reducing problems related to poor oocyte quality as compared with a more heterogeneous group of women undergoing standard IVF/ICSI cycles. The Spanish Reproductive Law permits women between 18 and 35 years of age to be oocyte donors in an anonymous manner.

Our aim was to analyze the evolution of the effectiveness of our oocyte donation program in the past 10 years. For this purpose, we studied cumulative PRs rates per cycle, implantation, clinical and ongoing PRs, together with mean number of embryos transferred and multiple PRs.

MATERIALS AND METHODS

Data from oocyte donation cycles were searched in a computer database between September 1, 1995, and September 30, 2005. A total of 11,515 cycles were initiated during this period; however, 2,107 cycles (18.2%) were cancelled be-

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fore oocyte retrieval and donation. The high number of cancellation in cycles initiated was due to various factors, including inadequate endometrial thickness, endometrial bleeding during hormonal preparation, donor cancellation (for reasons including poor administration of medication, low response to gonadotropins, >30% drop in E_2 level during stimulation, high risk for ovarian hyperstimulation syndrome), and other reasons such as the patient's own desire to postpone the treatment or cancel the cycle for personal reasons such as unavailability to be present at the center at the time of the donation.

Oocyte donation was performed in 9,408 cycles. A total of 8,430 embryo transfer procedures were performed. Unfortunately, cycle outcome parameters up to 12–14 weeks of pregnancy were unavailable or incomplete in 978 cycles (11.6%) after the transfer procedure. After excluding these 978 cycles, the remaining 10,537 initiated cycles were taken into consideration for further evaluation. From the 10,537 cycles initiated, a total of 8,430 donations and 7,186 embryo transfer procedures were performed and included in the study. After donation, embryo transfer could not be performed in 1,244 (14.7%) cycles because of fertilization failure, poor embryo quality, or unavailability of euploid embryos for transfer.

To evaluate trends in cycle parameters, we divided years between 1995 and 2005 into four consecutive periods as follows: September 1995–December 1997 (group 1), January 1998–December 2000 (group 2), January 2001–December 2003 (group 3), and January 2004–September 2005 (group 4).

Donors

The Spanish Law for Assisted Conception requires anonymity for oocyte donation. The donors receive minimal economic compensation for all requirements and annoyances endured. However, it is unthinkable that these compensations can be considered as a salary or payment. By law, a donor's age is limited to between 18 and 35 years. All donors sign a consent form after adequate information is given to them regarding IVF treatment, complications, and legal aspects of oocyte donation. Inclusion in the oocyte donor pool is based on the patient's history, clinical evaluation, and laboratory tests. All donors undergo testing for HIV, cytomegalovirus, and hepatitis B and C (7). Recently, we have started to screen donors for chromosomal abnormalities, and women with abnormal karyotypes have been excluded. Women with important health problems or personal or familial history of hereditary diseases are not recruited as donors. The protocol for ovarian stimulation, oocyte retrieval, and gamete handling in the IVF laboratory has been described elsewhere (8). Physical characteristics and blood groups of donors and recipients are taken into consideration when matching is performed.

Recipients

Written consents were obtained from all patients and their partners before initiating a cycle. Indications for oocyte donation were advanced age (>40 years), low response during IVF (<40 years, fewer than five oocytes retrieved), premature ovarian failure (POF), recurrent IVF failure, endometriosis, poor oocyte quality (<40 years of age, more than five oocytes retrieved), natural menopause (at age ≥40 years), genetic (Turner's syndrome, etc.), unexplained recurrent miscarriage, surgical menopause (<40 years), and mixed causes (presence of more than one indication) (Fig. 1). To evaluate the effect of age on uterine receptivity and cumulative PRs, recipients were divided into five different age groups: ≤30 years (n = 385 cycles), 31–35 years (n = 1,501 cycles), 36–40 years (n = 2,360 cycles), 41–45 years (n = 2,243 cycles), and ≥46 years (n = 697 cycles).

The protocol of endometrial preparation for recipients has been described previously (3, 4, 9, 10). In brief, patients with ovarian function were desensitized with a single IM administration of triptorelin 3.75 mg depot (Decapeptyl 3.75 mg; Ipsen-Pharma, Barcelona, Spain) administered between days 18 and 21 of the previous cycle. Estrogen replacement was started on day 3–5 of the next menstruation after confirming ovarian quiescence and a thin endometrium with transvaginal ultrasound examination. Oral E_2 valerate administration of 2 mg per day (Progynova; Schering, Madrid, Spain) was initially given for 8 days, increased to 4 mg per day for the following 3 days, and then maintained at 6 mg per day until the pregnancy test.

After 2 weeks of E_2 valerate administration, recipients were ready to receive embryos, and they waited until a suitable donation became available, taking into account physical characteristics and blood types. The recipients were started with P in oil 100 mg per day IM or vaginal P 800 mg per day (Progeffik; Laboratorios Effik, Madrid, Spain, or Utrogestan; Laboratorio Seid, Barcelona, Spain) on oocyte retrieval day of the donor (day 0) or the following day on confirmation of fertilization (day 1). In case of vaginal spotting or bleeding in the recipient during E_2 valerate administration, the cycle was cancelled.

Embryo transfers were performed under ultrasound guidance at cleavage stage (day 2 or 3) or blastocyst stage (day 5 or 6). The regimen of 6 mg per day E_2 valerate and P_4 was maintained until day 16 after egg retrieval, after which a serum β-hCG analysis was performed. If pregnancy was achieved, E_2 valerate and P_4 were maintained with the same dose until 11 weeks of pregnancy, then reduced to half dose, and suspended at 12 weeks.

Data Collection and Statistical Analyses

Each embryo transfer or pregnancy (whether first or subsequent cycles in the same patient) was regarded as a single event in the analysis of cycle outcome parameters.