ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Reproductive outcomes of familial oocyte donation

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Objective: Oocyte donation (OD) from a family member may be more available to patients. Our objective was to compare reproductive outcomes of familial OD with those of unrelated OD.
Design: Retrospective cohort study in a single university-affiliated center.
Setting: Not applicable.
Patient(s): Four hundred thirty OD cycles performed from 2010 to 2014: 124 from family members and 306 from unrelated donors.
Intervention(s): None.
Main Outcome Measure(s): Ovarian stimulation parameters and cycle outcomes (total gonadotropin dose, number of retrieved oocytes, number of embryos, number of vitrified embryos, blastocyst transfer rate, rate of fresh transfers); endometrial preparation parameters; implantation, clinical pregnancy, miscarriage, and live birth rates; perinatal outcomes (gestational age at birth, birth weight, delivery mode, cesarean delivery rates).
Result(s): Implantation, clinical pregnancy, miscarriage, and live birth rates were similar between familial OD cycles and unrelated OD cycles (32.9% vs. 39.7%, 41.9% vs. 44.4%, 30.7% vs. 30.9%, and 29% vs. 28.7%, respectively). Gestational age at birth and birth weight were similar (37.8 wk ± 2.2 d vs. 37.1 wk ± 3 d and 3,043 ± 722 g vs. 2,906 ± 788 g, respectively). Similar outcomes were also found in single-embryo transfer OD cycles (live birth rate 26.7% vs. 24.2%). Sister-to-sister OD cycles outcomes were similar to those of unrelated donors.
Conclusion(s): The reproductive outcomes of familial OD are similar to those of unrelated OD. These findings are in contrast to previous presumptions regarding the efficiency of familial OD and may help in the counseling of women who need OD. (Fertil Steril® 2016;■: ■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Oocyte donation, reproductive outcome, family members, siblings, premature ovarian insufficiency

Discuss: You can discuss this article with its authors and with other ASRM members at

Oocyte donation (OD) is a well known alternative to enable women with oocyte-related infertility to conceive (1). It is offered mostly to women with age-related infertility, but infertile women with premature ovarian insufficiency (POI) and those who have failed repeated in vitro fertilization (IVF) treatments may also benefit from OD. The increasing need for OD is partially due to the growing numbers of women deferring pregnancy (2). As a result, there was a substantial rise in the number of OD cycles performed both in Europe and in the United States. The annual number of OD cycles performed in the U.S. almost doubled from 2000 to 2010 (10,801 cycles in 2000 to 18,306 cycles in 2010) (3). In Europe, the number of OD cycles reported by 22 countries increased by 28% from 2010 to 2011 (23,625 cycles in 2010 and 30,298 cycles in 2011) (4).

The legal status and compensation models of OD vary significantly between countries. A predominantly commercial OD model, as in the U.S., tends to be associated with a relatively higher cost of OD cycles. These expenses are usually not covered by the various insurers and are thus "out of pocket" for patients, limiting the ability of infertile couples to further pursue this option. In other countries, including Canada, commercial OD is prohibited and OD is legal only if it is gratuitous. Consequently, oocyte recipients are required to find oocyte donors by themselves. These regulations, combined with increasing demand for donated oocytes, pose significant limitations for patients who need OD. In such situations, OD from a family member and especially from a sibling may be the most feasible option.

Both the American Society of Reproductive Medicine (ASRM) Ethics Committee and the European Society of Human Reproduction and Embryology (ESHRE) Task Force on Ethics and Law accept familial OD, as long as strict ethical principles are kept (1, 5). As stated by both societies,

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avoiding consanguinity and incest, respecting all parties' autonomy, and keeping the nonmaleficence principle are of paramount importance. However, there is still a paucity of data regarding the use of familial gamete donors, although a recent study found that a mean of 3.3% of all ODs in 11 European countries were between family members. The proportion also varies widely between countries. In Belgium, 26% of ODs were to a family member, whereas no familial OD were performed in Spain, Portugal, and Greece (6). To date, there have been only several publications evaluating familial OD. Most focused on the psychosocial aspect and not on the clinical reproductive outcome (7–14). The purpose of the present study was to compare the clinical reproductive outcome of familial OD cycles with that where the donated oocytes originated from unrelated donors. We also evaluated OD between sisters, because in these cycles the genetic resemblance between donor and recipient is relatively high.

MATERIALS AND METHODS

All OD cycles conducted at the reproductive unit of McGill University Health Center (MUHC) from 2010 to 2014 were included. We retrospectively collected demographic data and cycle characteristics of donors and recipients as well as cycle outcomes. We compared cycles where the donated oocytes originated from family members or from unrelated donors. Similar to the definitions applied by ASRM and ESHRE, we defined familial OD as donation from sisters, cousins, nieces, and sisters-in-law (1, 5, 7). All data were collected from our database and crosschecked with patients' electronic medical charts.

In agreement with Canadian legislation, the recipients themselves recruited all oocyte donors. All oocyte donors were counseled regarding the medical implications of the donation process. The reproductive center's psychologist evaluated both oocyte donors and recipients separately. Both recipients and donors signed informed consent forms before commencing treatment. The Institutional Research and Ethics Board of MUHC approved the study (MUHC study code 14-242 SDR).

Ovarian Stimulation (Donors)

Donors underwent treatment mainly with one of three controlled ovarian stimulation protocols: a microdose flare protocol, a fixed GnRH antagonist protocol, or a long GnRH agonist protocol. hCG triggering was performed when at least three follicles reached a diameter of 17–18 mm. Oocyte retrieval was performed 34–38 hours after hCG triggering, and 2–4 hours after retrieval the oocytes were inseminated with either conventional insemination or intracytoplasmic sperm injection based on semen quality on the day of oocyte retrieval.

Embryos

Embryos were cultured in the cleavage medium for the first 72 hours after fertilization, and subsequently in the blastocyst medium until day 5. The day of embryo transfer was determined based on the quantity and quality of embryos on either day 2 or 3 (cleavage stage) or day 5 (blastocyst stage). If there were more than two good-quality cleavage-stage embryos, they were further cultured to the blastocyst stage. A single-blastocyst transfer policy was applied generally, but exceptions were made in cases of repeated failures or poor-quality embryos. Cleavage-stage embryos were defined as good quality (grade 1–2) as previously described (15). Day 5 blastocysts were graded according to size, inner cell mass, and trophectoderm development. Good-quality (grade 1–2) embryos were defined as Gardner grade $\geq$3BB (16). Excess good-quality blastocysts were vitrified. All embryo transfers were performed under ultrasound guidance, and a serum β-hCG pregnancy test was performed 16 days after oocyte collection or 11–12 days after transfer of vitrified-warmed blastocysts.

Endometrium Preparation (Recipients)

Premenopausal women undergoing fresh-embryo transfer were suppressed by means of daily administration of GnRH agonist (Buserelin; Sanofi-Aventis Canada) for $\geq$10 days until a thin endometrium (<5 mm) was seen. Subsequently, estrogen supplements (6–12 mg daily Estrace; Shire Canada) were administered until a thick trilinear endometrium (preferably $\geq$8 mm) was achieved. In synchronization with oocyte retrieval from the donor, recipients commenced daily administration of progesterone supplementation with either vaginal Endometrin, 100 mg twice daily (Ferring Pharmaceuticals), or 8% Crinone gel once daily (EMD Serono).

For menopausal recipients, no pituitary down-regulation was needed in fresh-embryo transfer cycles. In these cycles and in all vitrified-warmed–embryo transfer cycles, endometrial preparation was performed with the use of estrogen and progesterone supplementation. Blastocyst transfer was performed on the 6th day of progesterone supplementation. In women with inadequate response to oral estrogen supplements, transdermal E_2 patches (0.1 mg Climara daily; Bayer Healthcare Pharmaceuticals) were added daily. In a few patients who were resistant to exogenous E_2 administration and were not menopausal, either natural cycle or gonadotropin administration was used.

Clinical Outcomes

Cycle outcomes were evaluated as biochemical or clinical pregnancies. Biochemical pregnancy was defined as positive β-hCG test 11–12 days after blastocyst transfer or 13–14 days after cleavage-stage embryo transfer. Clinical pregnancy was defined as intrauterine fetal heart activity seen by means of ultrasound scan at 6–7 weeks of pregnancy. Implantation rate was defined as the number of intrauterine gestational sacs divided by the number of transferred embryos. Clinical pregnancy outcomes were further categorized as miscarriage (spontaneous arrest of pregnancy before 20 weeks of gestation), stillbirth (intrauterine fetal death after 20 weeks of gestation), or live birth.