The outcome of in-vitro fertilization treatment by egg donation and intracytoplasmatic sperm injection for severe male factor infertility: a preliminary report

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Due to a paucity of donated eggs, we have excluded, until recently, couples with severe male factor infertility from our egg donation programme, except for those who accepted insemination with donor spermatozoa. The purpose of this study was to assess the feasibility of a shared in-vitro fertilization (IVF)–embryo transfer treatment whenever the recipients have severe oligoasthenoteratozoospermia (OTA) and need intracytoplasmatic sperm injection (ICSI) for egg fertilization. The results from 163 consecutive couples with ovarian failure who underwent 273 cycles of IVF with donated eggs and augmented with ICSI were analysed. The rate of diploid fertilization was 54.7%; in 92.3% of the cycles, at least one embryo was available for transfer. Forty-seven clinical pregnancies were achieved, representing 18.6% conceptions per transfer. The highest pregnancy rate was achieved in menopausal patients aged 40–45 years (26.2% per cycle) and the lowest in patients >45 years old (10.8% per cycle, P = 0.03). Overall, 28.8% of the cycles achieved a clinical pregnancy. A total of 196 treatment cycles resulted in 46 clinical pregnancies (23.5%) among the donors. No statistical differences were found in pregnancy rate achieved by the donors when compared with the recipients. We conclude that ICSI with egg donation is a reliable treatment in patients with ovarian failure and severe OTA.

Key words: egg donation/ICSI/infertility/IVF/male factor

Introduction

Oocyte donation, originally performed in patients with premature ovarian failure or surgical castration, is now commonly used in menopausal patients, despite their advanced age (Jansen, 1997). In countries like Israel, where a paid donor is prohibited by law, the paucity of available eggs is a major problem. It is a ‘shared’ egg donation programme; therefore, only a limited number of eggs is available for donation. As a result, between three and five eggs are available for recipients. Until recently, this limitation excluded couples with severe male factor from our egg donation programme, except for those who accepted insemination with donor spermatozoa. Since the introduction of the intracytoplasmatic sperm injection (ICSI) programme, we have offered egg donation to patients with severe male factor infertility according to sperm parameters and/or to previous attempts with failure of fertilization. The practice of ICSI has become widespread, and high success rates have been reported throughout the world in cases of severe male factor infertility. In this study, we analysed the cycle outcomes for a ‘shared’ egg donation programme in couples with severe male factor and ovarian failure.

Materials and methods

We analysed only those cycles of egg donation performed between 1 January 1995 and 31 December 1996 in whom the male partner of the recipient was diagnosed with severe oligoasthenoteratozoospermia (OTA). Each recipient received oocytes donated by only one individual, although donors supplied oocytes to one or more recipients.

According to the regulations of the Israeli Ministry of Health, oocytes may be donated anonymously only by patients undergoing IVF themselves. Therefore our egg source was young (age <35 years), healthy women undergoing IVF, who willingly consented to donate excess oocytes. Our own policy is to encourage them to donate a limited number of eggs if over 15 eggs were retrieved.

Donors

Oocyte donors were 146 patients undergoing assisted reproductive treatment cycles who agreed to anonymously donate their excess oocytes. Their mean age was 29 ± 3.94 years. Following initial pituitary suppression with a gonadotrophin-releasing hormone agonist, ovarian stimulation was achieved by administration of human menopausal gonadotrophins (HMG) (Pergonal; Teva Pharmaceutical Industries Ltd., Kuar Sava, Israel). According to sonographic data (leading follicle size >18 mm) and hormonal criteria (oestradiol concentration), oocyte maturation was induced by administration of human chorionic gonadotrophin (HCG) (10 000 IU) (Chorigon; Teva Pharmaceutical Industries Ltd.), and oocytes were collected under vaginal ultrasound-guided puncture 36 h later.

Recipients

A total of 163 couples with ovarian failure was treated. All patients had a preliminary workup to evaluate their general health status. A hysterosalpingography and/or hysteroscopy was performed before the treatment to confirm the presence of an adequate uterine cavity. During the transfer cycle, women first received oestradiol valerate (Progyluton; Schering AG, Berlin, Germany) in a fixed dose of 6 mg over a period varying between 12 and 30 days depending on the patient. Natural micronized progesterone (via the vaginal route) 300 mg divided three times a day was started once oocytes were available.

Twelve days after the embryo transfer, a blood test for β-HCG assessment was performed and clinical pregnancy was considered only when a gestational sac was visualized by ultrasonography. Once the β-HCG test was found to be positive, the replacement therapy was continued for the next 5–7 weeks.
Clinical pregnancies, 15 (88.2%) were delivered and two for those recipients up to 40 years old and those older; of 17 pregnancy. The following pregnancy outcomes were obtained pregnancy rates 10.8% (P).

A mean of 2.6 embryos was transferred in each patient. After 2 years, 28.8% of the recipients achieved a clinical conception. Forty-seven clinical conceptions were achieved by the recipients.

Cycle outcomes: comparative data between donors and recipients (Table II). Furthermore, the pregnancy rate for donors who donated to patients 45 years was 22%.

**Laboratory procedure**

Oocytes were denuded from cumulus and corona radiata using an enzymatic hyaluronidase step followed by mechanical denudation (Van Steirteghem et al., 1995). The oocytes were then observed under an inverted microscope at ×100 in order to assess the maturation stage by observing the presence of the first polar body. The microinjection was performed on metaphase II oocytes.

After evaluation of sperm count, motility and morphology, sperm selection was carried out using the mini-Percoll technique (Ord et al., 1990). We followed the injection techniques described by Van Steirteghem et al. (1993). Two to 3 days after ICSI, all the available embryos were transferred into the patient’s uterus.

**Results**

A total of 273 cycles of egg donation and ICSI was performed in 163 couples during this period. In 252 (92.3%) cycles, at least one egg was fertilized, and embryo transfer was performed. A total of 1239 eggs was donated (4.6 ± 0.7 per patient) and 678 (54.7%) of these were fertilized (2.5 ± 1.3 per patient). A mean of 2.6 ± 1.4 embryos was transferred in each patient.

Forty-seven clinical conceptions were achieved by the recipients, with a mean of 17.2% pregnancies per cycle and 18.7% per transfer. No statistical difference was found between the number of received eggs, fertilized and transferred embryos according to different age groups of the recipients (Table I); however, the pregnancy rates differed. The highest pregnancy rate was achieved for recipients aged between 40 and 45 years with 26.2% pregnancy rate per cycle, and the lowest for patients >50 years old with only 10% pregnancy rate per cycle. Patients >45 years old shared significantly lower pregnancy rates 10.8% (P = 0.02).

After 2 years, 28.8% of the recipients achieved a clinical pregnancy. The following pregnancy outcomes were obtained for those recipients up to 40 years old and those older; of 17 clinical pregnancies, 15 (88.2%) were delivered and two (11.8%) were miscarriages. Ten (66.7%) of the deliveries in patients <40 years were singleton deliveries, four (26.7%) were twin deliveries and one (6.7%) was a triplet delivery. For the older group of patients (>40 years), 12 (40%) deliveries resulted in miscarriages, 15 (83.3%) were singleton deliveries and only three (16.7%) were twin deliveries. Triplets or more were not obtained in this group of patients.

In all, 196 treatment cycles resulted in 46 clinical pregnancies (23.5%) among the donors. No statistical differences were noted in pregnancy rates among the donors when classified according to the recipient’s age (Table II). Furthermore, the pregnancy rate for donors who donated to patients >45 years was 22%.

**Discussion**

IVF therapy, augmented with ICSI, offers a new and efficient therapeutic option to treat couples with severe male infertility irrespective of the type of sperm abnormality present in the ejaculate. With the introduction of ICSI, a new era of successful fertilization in cases of extremely impaired semen parameters has dawned. Paradoxically, couples once considered to be suffering from infertility due to intratable male factor infertility can now be successfully treated by this new technique, but are confronted with a new and serious problem, the ageing female partner. In a recent paper, Tucker et al. (1996) suggested that donor oocyte cryopreservation might improve the efficiency of the oocyte donation programme. Cryopreserved donated oocytes were thawed and inseminated by ICSI. Although high fertilization rates and embryo development were obtained, the clinical use of this technique is still unacceptable due to the very low cryosurvival rate of fresh donated oocytes (24.7%).

In the present study, we evaluated the feasibility of ICSI when applied to a very limited number of eggs. Our results
show that infertile couples in whom the female partner requires donated oocytes and the male partner suffers from severe male factor infertility can achieve pregnancy by undergoing oocyte donation combined with the ICSI technique. The fertilization, embryo development and pregnancy rates approach the results of ICSI when used in couples with OTA and normal female partner (Hourvitz et al., 1998).

In countries like Israel, paid donors are forbidden, and so the only source of eggs is infertile patients undergoing assisted reproductive treatment cycles (Ahuja et al., 1997). Obviously, only a few oocytes are donated; thus an accurate ICSI technique is imperative for success in these cases. Recently Borini et al. (1996) reported on their experience with ICSI in donated eggs. However, this is a small group of only 15 cycles and therefore the conclusions are limited.

Like Borini et al. (1996) and Tucker et al. (1996), we obtained high fertilization and cleavage rates. In contrast with other findings in egg donated cycles in regular IVF (Navot et al., 1994), we found a decrease in pregnancy rates and an increased abortion rate in the older group (>45 years old) of recipients. In contrast, the multiple pregnancy rate for the younger population (those who delivered) was as high as 28.6%, with 7.14% of these triplets. We believe that this difference is due to a more accurate dichotomization of the results into more structured age levels, which was possible in our study because of a larger sample population.

Although the endometrium of those patients >40 years could be induced successfully (and a 19.6% pregnancy rate achieved), the high abortion rate needs further clarification. This observation can possibly be explained either by the limited ability of the ageing uterus to cope with advanced pregnancies or simply due, unfortunately, to embryos of lower quality. Another possible explanation can be provided by a missed, associated fertility problem in this older group of patients who previously failed to conceive before the introduction of ICSI, despite normo-ovulatory and normomechanical profiles. Although the figures are limited, we cannot ignore the decline in pregnancy rates and pregnancy outcome for patients >45 years old.

In conclusion, we present the largest series published to date of IVF treatment by egg donation (from a shared program) and ICSI for couples with severe male factor and ovarian failure. Our data suggest a decreased pregnancy rate and increased pregnancy loss in patients >45 years old, but nevertheless support the concept of ICSI treatment in egg donation cycles even when only a few eggs are available.

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References


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