

Treatment outcome of women with a single ovary undergoing *in vitro* fertilisation cycles

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ABSTRACT

Introduction: Women with a single ovary present a unique problem in assisted reproductive techniques. The aim of our study was to compare the ovarian response and pregnancy rates of women with one ovary and those with two ovaries in assisted reproduction.

Methods: A total of 18 consecutive women with a single ovary (n is 22 cycles) were identified. The control group included 44 women with two ovaries and mechanical infertility, who were selected as frequency-matched samples (2:1) to meet the distribution of age at treatment and race in the single ovary group. All patients underwent controlled ovarian hyperstimulation treatment via the long down-regulation protocol using a gonadotropin-releasing hormone agonist. Standard procedures were carried out for gamete-embryo handling, and embryo transfer was performed using a soft catheter on day two in all cases. The luteal phase was supported by progesterone or Pregnyl after oocyte pick-up.

Results: The duration of stimulation (11.3 +/- 1.7 versus 10.1 +/- 1.4 days) and the total follicle stimulating hormone (FSH) consumption (3906.8 +/- 1860.6 mIU/ml versus 2900.0 +/- 1440.0 mIU/ml) were significantly higher, and the mean number of oocytes (10.8 +/- 4.5 versus 16.8 +/- 10.9) and metaphase II oocytes collected (9.5 +/- 4.5 versus 13.3 +/- 7.7) were significantly lower in the single ovary group (p is less than 0.05). The clinical pregnancy rates (31.8 percent versus 43.2 percent) were comparable between the two groups.

Conclusion: Although women with a single ovary required significantly higher doses of FSH and a longer duration of stimulation, as well as produced less oocytes, their clinical pregnancy rates were comparable to those of women with two ovaries in assisted reproduction.

Keywords: gonadotrophin-releasing hormone agonist, *in vitro* fertilisation, outcome, single ovary

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INTRODUCTION

Women undergoing assisted reproduction technologies (ART) are naturally concerned about their success rates. The worries of women with a single ovary may be particularly heightened. Hence, it is important to know what information to provide to these patients before they embark on ART for fertility purposes and how to address their concerns. A proportion of women who undergo *in vitro* fertilisation (IVF) have had a previous oophorectomy for various reasons such as benign ovarian cysts, pelvic inflammatory disease or ectopic pregnancy. IVF patients with one ovary may be deemed to be at a disadvantage in terms of the IVF success rate, compared to women with two ovaries. This retrospective study was designed to evaluate the outcome of women with a single ovary compared to those with two ovaries who undergo IVF, and to determine whether the loss of an ovary reduces the chances of pregnancy.

METHODS

The study included women undergoing IVF cycles at the IVF Centre of KK Women's and Children's Hospital between January 2005 and May 2006. 18 consecutive women with a single ovary (n = 22 cycles) were identified. The control group consisted of 44 women with two ovaries and mechanical infertility, who were selected as frequency-matched samples (2:1) to meet the distribution for age at treatment and race in the single ovary group.

All the patients underwent controlled ovarian hyperstimulation via the standard long down-regulation protocol with gonadotropin-releasing hormone (GnRH) agonist. The pituitary gland was desensitised using 0.5 mg subcutaneous leuprolide acetate (Lucrin, Abbott, Cedex, Istanbul, Turkey) daily, starting on day 21 of the menstrual cycle and continuing until and including the day of human chorionic gonadotropin (hCG) administration. After 10–14 days of GnRH

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Table I. Ratio of the various blood components utilised.

	Single ovary	Two ovaries
No. of women	18	44
No. of treatment cycles	22	44
Mean age \pm SD (yrs)*	33.6 \pm 2.4	33.7 \pm 2.3
D3 FSH (mIU/ml)*	7.4 \pm 2.7	6.7 \pm 2.3

*Values were not statistically different.

FSH: follicle stimulating hormone; SD: standard deviation

agonist administration, pituitary down-regulation was confirmed by transvaginal ultrasonography (thin endometrium < 8 mm and ovarian inactivity, i.e. all follicles < 10 mm and plasma estradiol < 50 pg/ml). Once ovarian suppression was achieved and the patient reported menstrual bleeding, the stimulation phase was started. The dosage of follicle-stimulating hormone (FSH) (Puregon, NV Organon, Oss, The Netherlands) was adjusted according to the ovarian response and was continued until follicular development was considered adequate (at least three follicles > 17 mm in diameter). The standard ovulating dose of 10,000 IU hCG (Pregnyl, NV Organon, Oss, The Netherlands) was then administered intra-muscularly. Oocyte pick-up (OPU) was performed 36–38 hours later, with the patients under sedation. Following oocyte collection, IVF was commenced, and embryo transfer was carried out 2–3 days after oocyte retrieval. In the majority of the patients, 2–3 embryos were routinely transferred. When < 15 oocytes were obtained, luteal support was provided with four doses of 1,000 IU Pregnyl on Day 2, 5, 8 and 11 after OPU. When \geq 15 oocytes were obtained, intramuscular injections of 25 mg progesterone on the day of embryo transfer and 50 mg daily for the subsequent 16 days were administered. Serum β hCG was measured 19 days after OPU to confirm pregnancy. Clinical pregnancy was defined as the presence of a viable foetus on ultrasonography at six weeks of gestation. Biochemical pregnancy (i.e. evidence of conception based only on temporarily elevated serum β hCG levels, in the absence of a gestational sac detected at ultrasonography) was recorded as non-pregnant.

The total amount of FSH used, the duration of stimulation, the number of oocytes retrieved, the number of oocytes fertilised and the clinical pregnancy rates were then compared between the groups. The data was analysed using the Statistical Package for the Social Sciences version 9.0 (SPSS Inc, Chicago, IL, USA). Normally distributed (Kolmogorov-Smirnov test) parametric variables

were tested by an independent sample *t*-test. The chi-square and Fisher's exact test were used to analyse nominal variables in the form of frequency tables. Non-normally distributed metric variables were analysed using the Mann-Whitney U test. Values are expressed as mean \pm standard deviation (SD), unless otherwise stated.

RESULTS

A total of 18 women with a single ovary underwent 22 cycles of IVF, without any cycle cancellation prior to oocyte retrieval (Table I). The control group consisted of 44 women with two ovaries. These women had mechanical infertility and were selected as frequency-matched samples (2:1) to meet the distribution for age at treatment and race in the single ovary group.

Women with a single ovary showed significantly poorer responses to ovulation induction. They required longer periods of stimulation and approximately 35% more of total recombinant FSH to achieve the criteria for oocyte retrieval. They also yielded fewer follicles, and fewer oocytes were retrieved from this group of patients. However, in both groups, the fertilisation rate was similar even though more oocytes were retrieved and more embryos were available for transfer in women with two ovaries; also, the clinical pregnancy rates per embryo transfer did not differ significantly between the two groups. The IVF cycle outcomes are summarised in Table II. None of the women in the control or study group developed ovarian hyperstimulation syndrome.

DISCUSSION

This study evaluated the responses of women with one ovary who underwent IVF. These women did not respond as well to the treatment as women with two ovaries, requiring 35% more recombinant FSH for controlled ovarian hyperstimulation and a longer duration of stimulation. In addition, they had fewer follicles recruited and fewer oocytes retrieved. However, the pregnancy rate was comparable in both groups.

These results support the observations that have been advanced by several authors.^(1,2) Neither Dodds et al nor Boutteville et al found any difference in the pregnancy rates of women with one vs. two ovaries.^(3,4) However, while Boutteville et al found that women with a single ovary required the same amount and duration of gonadotropins but had less oocytes retrieved when compared to those with two ovaries, Dodds et al found that women with a single ovary required a longer period of ovarian stimulation but had the same number of oocytes retrieved and used the same amount

Table II. IVF cycle outcomes between women with a single ovary and those with two ovaries.

	Mean value \pm SD	
	Single ovary (patients: n = 18; cycles: n = 22)	Two ovaries (patients: n = 44; cycles: n = 44)
Duration of ovarian stimulation (days)*	11.3 \pm 1.7	10.1 \pm 1.0
No. of oocytes/ cycle*	10.8 \pm 4.5	16.8 \pm 10.94
Total rFSH consumption*	3906.8 \pm 1860.6	2900 \pm 1440
No. of metaphase II oocytes/ cycle*	9.5 \pm 4.5	13.3 \pm 7.7
Fertilisation rate (%)	72.3	71.6
No. of embryos/ transfer	2.6 \pm 0.7	2.8 \pm 1.8
Clinical pregnancy rate (%)	31.8	43.2

*Values are significantly different at $p < 0.05$.

IVF: *in vitro* fertilisation; SD: standard deviation; rFSH: recombinant follicle stimulating hormone

of gonadotropin as those with two ovaries. Some other studies have pointed out different findings, such as a decreased response to external ovarian stimulation in the single ovary group,^(5,6) but in no case has it been found that women with a single ovary who undergo IVF have poorer outcomes when compared to their counterparts with two ovaries. In fact, Safaa Al-Hasani et al showed a higher but not statistically significant pregnancy rate,⁽⁶⁾ and Levitas et al observed a significantly higher pregnancy rate in the single ovary group.⁽⁷⁾ Overall, slight variations in the outcomes of IVF treatment have been reported in various centres, but the trend is that women with one ovary are not at a disadvantage in terms of the rate of pregnancy using IVF.

Women with a single ovary do not exhibit any clinical symptoms. The majority of these cases are iatrogenic, with these women undergoing surgical unilateral oophorectomy for various reasons, the commonest of which are the presence of an ovarian cyst (benign or malignant), a tubo-ovarian abscess in pelvic inflammatory disease, ovarian torsion and a ruptured ectopic pregnancy. Khalifa et al studied more than 150 patients who had unilateral oophorectomy before IVF treatment with the aetiological distributions of ovarian endometriosis, pelvic inflammatory disease, benign ovarian cyst and ectopic pregnancy at 47%, 22.2%, 15.7% and 15%, respectively.⁽⁸⁾ Our study concurred with the abovementioned causes with one exception, where the patient had unilateral oophorectomy simultaneously when she underwent an appendicectomy in China.

The success rates of IVF vary, and are dependent on many factors, including the cause of infertility, the adequacy of ovarian reserve and the number, maturity and quality of eggs retrieved. Evidence from previous studies seems to point toward the fact that women with a single ovary have reduced ovarian reserve, basically as a result of a reduction in the total available primordial follicles in their single ovary, rather than a reduction

in the quality of the oocytes.⁽¹⁻⁸⁾ Congenital absence of one or both fallopian tubes and ovaries is a finding that has been rarely described.⁽⁹⁾ There are two postulated pathways, the first of which is a defect in the development of the entire Müllerian and mesonephric system on one side, or a defect localised at the region of the genital ridge and the caudal part of the Müllerian duct.⁽¹⁰⁾ The second postulation is the occurrence of asymptomatic torsion of the ovarian pedicle in childhood or before birth.^(11,12)

The incidence of true congenital and unexplained unilateral absence of the ovary and fallopian tube is only one in 11,240 women.⁽¹³⁾ The actual prevalence of women with a single ovary in the normal population, or even in the sub-fertile group, is unknown. The incidence of a single ovary, however, can occur in up to 17% of women with severe tubal disease who require IVF treatment for conception.⁽¹⁴⁾

In conclusion, women with a single ovary do not seem to have a reduced potential to conceive via IVF treatment, even though they are considered to have a lower ovarian reserve. As the number of follicles grows directly in proportion to the ovarian reserve upon hormonal stimulation, this probably explains the poorer response to ovulation induction in women with a single ovary compared to those with two ovaries.

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