Journal of Assisted Reproduction and Genetics, Vol. 22, Nos. 9/10, October 2005 (© 2005)
DOI: 10.1007/s10815-005-5914-2

Assisted Reproduction

Endometrioma undergoing laparoscopic ovarian cystectomy: its influence on the outcome of in vitro fertilization and embryo transfer (IVF–ET)

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Submitted November 1, 2004; accepted May 11, 2005

***Purpose*:** To evaluate the effect of laparoscopic ovarian cystectomy for endometrioma on the clinical outcome of IVF treatment.
***Methods*:** Patients who received IVF treatment were retrospectively classified into two groups. Group 1 included 95 patients who received IVF due to tubal occlusion. Group 2 included 127 patients who had received laparoscopic ovarian cystectomy for endometrioma(s) followed by IVF treatment. Clinical outcomes of IVF treatment were compared between two groups.
***Results*:** More oocytes were harvested per retrieval in Group 1 than Group 2 ($p < 0.05$). The fertilization rate was higher in Group 1 than Group 2 ($p < 0.05$). Although the implantation rate was higher in Group 2 ($p < 0.05$), the clinical pregnancy rate revealed no statistically significant difference between the two groups.
***Conclusions*:** Women who received ovarian cystectomy for endometriomas have fewer oocytes harvested during IVF treatment. However, their chance of pregnancy was comparable to patients with tubal problems who underwent IVF treatment.

KEY WORDS: Endometrioma; infertility; in vitro fertilization; ovarian function.

INTRODUCTION

Endometriosis remained as a major etiology in women who suffered from infertility. Among them, ovarian endometrioma is a common co-existing finding in infertile women with endometriosis. For years, the impact of ovarian endometrioma on the outcome of assisted reproductive technology (ART) remains controversial and the optimal management of ovarian endometrioma before in vitro fertilization and embryo transfer (IVF–ET) treatment is still open for debate. Laparoscopic cystectomy for ovarian endometrioma has been proposed in several studies (1–3).Vaporization of the internal wall of endometrioma without cystectomy has also been suggested (4). Medical therapy alone seems to be ineffective in enhancing fertility (5–8). Conservative treatment, such as ultrasound-guided aspiration of endometrioma has also been shown to be inefficient because of the high recurrence rate (9,10).

Previous reports have suggested that the presence of ovarian endometrioma might impair the quality of oocyte as revealed by their fertilization and implantation ability (11–13). Although resection of endometrioma is usually recommended before IVF therapy, the improper use of electrocoagulation during ovarian tissue hemostasis might lead to a reduction in the ovarian reserve. In such cases, surgery might be more detrimental than endometriosis itself on the patient's reproductive potential. In fact, a reduced response to controlled ovarian hyperstimulation after ovarian cystectomy has been

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reported in several studies (14–17). This retrospective analysis was performed to test the above finding and their influence on the outcome of IVF therapy.

PATIENTS AND METHODS

From January 2000 to December 2002, patients who received IVF–ET treatment were retrospectively classified into two groups. Group 1 included 95 patients who received IVF treatment due to bilateral tubal occlusion. Group 2 included 127 patients who had received laparoscopic ovarian cystectomy for endometriomas followed by IVF treatment. Only patients who had at least one endometrioma larger than 3 cm were included. All patients had undergone a complete infertility evaluation and only women whose partners had normal semen analysis were included in the study.

In patients who underwent the laparoscopic ovarian cystectomy, the surgical technique consisted of drainage of the "chocolate content" within the endometriomas followed by removal of the capsule wall. No sutures were used and the remaining ovary was left open. All visible pelvic adhesions were lysed, and foci of endometriosis were desiccated or resected if present. In all cases, histopathological confirmation of endometriosis was obtained. No medical treatment was administered afterwards, and the IVF–ET cycle commenced within 6 months of surgery.

Ovulation induction was achieved as previously described (18). Briefly, daily 0.9 mg of buserelin (Suprecur, Hoechst, Frankfurt Am Main, Germany) was applied from the 21st day of the previous cycle until the next menstruation began. Then the dosage was decreased to 0.45 mg per day. Complete down-regulation of the pituitary gland was defined as an estradiol level less than 75 pg/mL and no follicle greater than 1 cm was measured, when the menstruation began. After a complete down-regulation, ovulation stimulation was initiated with fixed dosage of recombinant follicular stimulating hormone (Gonal-F, Serono, Geneva, Switzerland) and/or human menopausal gonadotropin (Pergonal, Serono, Aubonne, Switzerland) on cycle Day 3. The dose was then adjusted according to the ovarian response as measured by serum estradiol level, and follicular growth as monitored by vaginal ultrasound. Human chorionic gonadotropin (Pregnyl, Organon, Oss, Holland), 10,000 IU was injected intramuscularly when at least two leading follicles greater than 16 mm were measured. Transvaginal oocyte retrieval was scheduled 34–36 h after the injection of hCG. Insemination was routinely performed 6 h after oocyte retrieval, and all embryos were checked 24–26 h after insemination to see whether early cleavage stage had occurred. Embryos that had cleaved to two-cell stage or above were defined as early cleavage embryos. Early cleavage embryos were predominantly used for embryo transfer, if present. Routine embryos grading and transfer were performed 3 days after oocyte retrieval. The number of transferred embryos in each patient was individualized according to the quality of the embryos and the patient's age. For patients who were younger than 35 years old, 2–3 embryos were transferred according to the embryo's grading. For patients who were older than 35 years old, 3–5 embryos were transferred also according to the embryo's grading. The guideline for embryo grading was described as following. Embryos with even number of blastomeres without any fragmentation were scaled as Grade 1 embryo and had 4 points in score calculation. Embryos with uneven number of blastomeres and fragmentation less than 10% of the whole embryo were scaled as Grade 2 embryos and had 3 points in score calculation. Embryos with uneven number of blastomeres and fragmentation percentage between 10–50% of the whole embryo were scaled as Grade 3 embryos and had 2 points in score calculation. Embryos with uneven number of blastomeres and fragmentation greater than 50% of the whole embryo were scaled as Grade 4 embryos and had 1 point in score calculation. Each embryo was scored as its blastomere number multiplied its grading point. A cumulative embryo score was routinely calculated to represent the embryo quality in each transfer. Cryopreservation was not routinely performed unless we had extra Grade 1 or 2 embryos after fresh transfer.

The outcome was reported as implantation and pregnancy rate per cycle. The implantation rate was defined as the total number of gestational sacs over the total number of transfer embryos. Only clinical pregnancy, which was defined as a gestation sac with fetal heartbeat visualized on vaginal ultrasound was calculated. Results are reported as means ± SD and percentages. Two-sample *t*-tests and χ^2-tests were performed to compare the differences between the two groups. The values were considered significant when $p < 0.05$. Data analysis was calculated through SPSS software program for windows (SPSS Inc., Chicago, IL, USA).

Table I. Characteristics of Patient Distribution between Two Groups

	Tubal group[a] (Mean ± SD)	Endometrioma group[b] (Mean ± SD)	*p* value
Age	33.9 ± 4.1	32.9 ± 3.6	NS
Day 3 E2	43.6 ± 26.4	51.9 ± 33.8	NS
Day 3 FSH	6.6 ± 3.4	7.7 ± 4.4	NS
Day 3 LH	4.2 ± 2.1	4.3 ± 2.5	NS
Total unit of gonadotropin	2863 ± 1283	2741 ± 1667	NS
E2 on day of hCG (pg/mL)	1914 ± 1271	1285 ± 1089	0.0002
No. of oocytes	7.0 ± 4.4	5.0 ± 3.7	0.00043
No. of available embryos	5.8 ± 3.9	3.6 ± 2.9	<0.0001

Note. NS: Not significant.
[a]Tubal group ($n = 95$ cycles).
[b]Endometrioma group ($n = 127$ cycles).

RESULTS

There was no statistically significant difference in the mean age of patients and D3 ovarian function parameters between the two groups (Table I). Although the total gonadotropin units for ovulation induction was comparable between the two groups (2863 ± 1283 vs. 2741 ± 1667, $p > 0.05$), the level of estradiol on the day of hCG injection and the number of oocytes per retrieval were significantly higher in the Group 1 than in the Group 2 (1914 ± 1271 vs. 1285 ± 1089, $p < 0.001$; 7.0 ± 4.4 vs. 5.0 ± 3.7, respectively; $p < 0.001$). Also the total number of available embryos was 5.8 ± 3.9 in Group 1 as compared to 3.6 ± 2.9 in Group 2, $p < 0.0001$.

The treatment outcomes are shown in Table II. The fertilization rate in Group 1 was significantly higher than the Group 2 (84.7% vs. 77.8%, $p < 0.05$). Though the number of embryos per transfer revealed no difference between the two groups (3.5 ± 1.5 vs. 3.0 ± 1.5, $p > 0.05$), the cumulative embryo score was better in Group 1 as compared to Group 2 (63.6 ± 33.7 vs. 50.8 ± 33.1, $p < 0.05$). However, due to the higher implantation rate demonstrated in the Group 2 (11.0% vs. 18.7%, $p < 0.05$), the clinical pregnancy rate revealed no statistically significant difference between the two groups (29.6% vs. 31.8%, $p > 0.05$). Also, there was a higher multiple pregnancy rate in Group 2 than in Group 1 (23.8% vs. 59.3%, $p < 0.05$).

DISCUSSION

Endometriosis is one of the leading causes of female infertility. Combine finding of endometrioma in patients with endometriosis represents an even more serious gynaecological morbidity. Nonetheless, the optimal management of ovarian endometriomas in infertile patients remains controversial. Until now, there is still no concensus regarding the best possible treatment for patients with endometriomas for IVF therapy. Some authors have declared surgery might impair the ovarian function. For example, Nargund *et al.* have reported reduced number of follicles and oocytes in IVF cycles after ovarian cystectomy (14). Al-Azemi *et al.* also showed a reduced ovarian response and an increase of gonadotropin units used in IVF patients with previous ovarian surgery (15). On

Table II. Comparison of the Treatment Outcome Between the Two Groups

	Tubal group[a]	Endometrioma group[b]	*p* value
Fertilization rate (%)	84.7 (482/569)	77.8 (421/541)	0.0032
Implantation rate (%)	11.0 (27/246)	18.7 (47/252)	0.016
No. of embryos per ET	3.5 ± 1.5	3.0 ± 1.5	0.038
Cumulative embryo score	63.6 ± 33.7	50.8 ± 33.1	0.0032
Clinical pregnancy rate (%)	29.6 (21/71)	31.8 (27/85)	NS
Multiple pregnancy rate (%)	23.8 (5/21)	59.3 (16/27)	0.014

Note. NS: Not significant.
[a]Tubal group ($n = 95$ cycles).
[b]Endometrioma group ($n = 127$ cycles).

the other hand, several studies also reported that the number of oocytes and embryos were not decreased in women committed to IVF–ET treatment after laparoscopic cystectomy (19,20). These conflicting results stemmed from the same surgery have been interpreted to have occured due to the use of different method and technique in the surgery. Indeed, the evidence suggest that certain specific laparoscopic procedure will affect the subsequent ovarian response (21,22). With CO_2 laser vaporization of the internal cystic wall without cystectomy Donnez *et al.* have shown that the affected ovary operated as such had a response similar to ovulation induction as the non-involved ovary (23). In his series, 50% of pregnancy rate was obtained in IVF treatment after the surgery in a series of 814 cases (4). Due to the non-availability of laser equipment in our hospital, the method described by Donez (23) could not be replicated or justified. However, extreme care was taken during the process of endometrioma cystectomy. The cortex was preserved as much as possible and excessive electrocoagulation during hemostasis was avoided. Still the number of oocytes available for IVF treatment in our study was significantly lower in women who had received laparoscopic ovarian cystectomy. We therefore propose that even with experienced hands and extreme care, an unanticipated deleterious effect from cystectomy may remain unavoidable.

Another concern in our study regards the relationship between the endometriosis and the oocyte quality. Previous reports have demonstrated that ovarian endometrioma might produce substances that deem toxic to the oocytes and reduce oocyte quality (12–13). Donnez *et al.* suggested that the lower fertilization rate seen in patients with endometrioma could be corrected by surgery (23). However, we found that the quality of oocyte from endometriosis patients remains rather unsatisfactory at times even after surgery. In our study, patients with endometrioma after cystectomy for IVF treatment produced oocytes with lower fertilization rate and embryos with lower cumulative embryo scores.

Also noted in our study is that the endometriosis did not seem to jeopardize the implantation probability of the embryo. In fact, Diaz *et al.* reported that women with stage III–IV endometriosis had implantation rates similar to those of recipients without endometriosis who received oocytes from the same donor (24). Garcia–Velasco *et al.* also illustrated that severe endometriosis does not seem to affect the expression of pinopodes, a morphological marker of uterine receptivity (25). In our study, we found that embryos from endometriosis patients possessed even higher implantation ability than embryos from patients with tubal problem. Although not statistically significant, we attributed this not only to the younger mean age in the patient group of endometriosis but also possibly proving the fact that endometriosis does not compromise uterine receptivity.

In conclusion, we found women who receive ovarian cystectomy for endometriomas have fewer oocytes harvested when received IVF treatment. Endometriosis might have a negative effect on the quality of oocyte but without compromising the uterine receptivity for embryo. After laparoscopic cystectomy, patients with endometrioma have the same chance of getting pregnant when compared to patients with tube problems in IVF treatment.

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