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EFFECT OF PELVIC ENDOMETRIOSIS, ENDOMETRIOMAS AND RECURRENT ENDOMETRIOMAS ON IVF-ET/ICSI OUTCOMES

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ABSTRACT

Introduction: Endometriosis, the most common gynecological disorder, is a challenging disease observed in 20% - 40% of subfertile women. **Material and Methods:** 380 women were divided into four groups. Group A consisted of 176 women with pelvic endometriosis. Group B consisted of 125 women who had previously undergone a laparoscopic endometrioma cystectomy. Group C consisted of 38 women with recurrent endometriomas without aspiration before IVF-ET/ICSI. Group D consisted of 41 women with recurrent endometriomas undergone aspiration before IVF-ET/ICSI. **Results:** Baseline FSH level (8.61 ± 3.42 mIU/mL) and total dose of Gn (2337.15 ± 853.00 IU) in Group A were the lowest ($p < 0.05$). The number of retrieved oocytes in Group B (7.98 ± 5.05) was significantly fewer than those in Group A and D ($p < 0.05$). The numbers of MII oocytes in Groups A, C and D were significantly larger than that in Group B. The number of retrieved oocytes, high-quality embryos, implantation and pregnancy rates were similar in Groups C and D. **Conclusions:** Pelvic endometriosis had a less adverse effect on ovarian reserve than endometrioma. No advantage was found in transvaginal aspiration for recurrent endometriomas before IVF-ET/ICSI.
Key words: pelvic endometriosis, recurrent endometriomas, transvaginal aspiration, IVF-ET.

1. INTRODUCTION

Endometriosis, the most common gynecological disorder, is a challenging disease observed in 20% - 40% of subfertile women (1). Endometriomas affect 17 - 44% of women with endometriosis (2, 3, 4). Cystectomy is usually used for endometriomas with diameters larger than 3 cm before assisted reproductive technology (ART) (5). Decreased ovarian reserve might result from surgical procedures (6, 7, 8) or endometriosis itself (9, 10). A reduced response to controlled ovarian hyper stimulation (COH) after cystectomy has been reported in other studies (11, 12).

There is no consensus regarding which treatment is most favorable in terms of preservation of ovarian reserve and subsequent ART outcome (13). Especially for the recurrent endometriomas after surgical resection, there is also no better approach. Transvaginal aspiration may be a choice in these conditions, but a minimal number of reports have been published regarding the management of recurrent endometriomas during in vitro fertilization - embryo transfer/intracytoplasmic sperm injection (IVF-ET/ICSI) cycles. Whether aspiration can improve the outcome of ART before COH remains unknown.

The first aim of this study was to evaluate the ovarian response to COH for IVF-ET/ICSI and the outcome of ART in patients with a history of endometriosis that have been treated once with laparoscopy with or without cystectomy. The secondary aim was to investigate whether aspiration of recurrent ovarian endometriomas before COH improved the prognosis of IVF-ET/ICSI cycles.

2. MATERIALS AND METHODS

2.1. Patients

This retrospective study was obtained ethical preapproval by the Third Affiliated Hospital of Sun Yat-Sen University Reproductive Medicine Ethic Committee. A total of 380 women with endometriosis who had previously undergone laparoscopic surgery before IVF-ET/ICSI cycles during 2012-2013 were retrospectively identified. Group A consisted of 176 women with pelvic endometriosis but without ovarian endometriomas diagnosed by laparoscopy. Group B consisted of 125 women who had previously undergone laparoscopic endometrioma cystectomy; the endome-

Variable	Group A N=176	Group B N=125	Group C N=38	Group D N=41	P-value
Duration of infertility, (means ± SD)	5.18 ± 3.02	4.36 ± 2.82	5.18 ± 3.81	4.32± 2.99	NS
Age, years (mean ±SD)	33.02 ± 4.62	32.78 ± 4.21	32.26± 5.26	31.73±4.21	NS
BMI, kg/m2 (mean ±SD)	20.68 ± 2.34	20.65 ± 2.65	20.27± 2.36	20.21±2.28	NS
Baseline FSH level (mIU/mL), mean ±SD	8.61 ± 3.42	9.52 ± 3.76	8.58 ± 2.26	11.00±6.08	<0.05
Total dose of Gn (IU), mean ±SD	2337.15 ± 853.00	2983.89 ± 1012.52	2785.53 ± 781.64	2957.32 ± 1007.10	<0.05
Duration of ovulation induction (day), mean ±SD	10.94 ± 2.44	11.83 ± 2.55	11.74± 2.04	12.27±2.46	<0.05
Plasma E2 level on hCG day (pg/mL), mean ±SD	2975.97 ± 1437.56	2362.99 ± 1475.35	2896.53 ± 1507.95	2649.32 ± 1564.85	<0.05
Endometrial thickness on hCG day (mm), mean ±SD	11.18 ± 2.73	11.57 ± 3.52	11.24± 2.07	11.37±2.57	NS

Table 1. Epidemiologic and stimulation characteristics. Note: NS =not statistically significant.

Variable	Group A N=176	Group B N=125	Group C N=38	Group D N=41	P-value
No. of oocytes retrieved (means ± SD)	10.11 ± 5.49	7.98 ± 5.05	9.79 ± 5.05	9.90 ± 6.06	<0.05
No. of MII oocytes (means ± SD)	8.28 ± 4.75	6.71 ± 4.27	8.55 ± 4.95	8.61 ± 5.61	<0.05
No. of high-quality embryos(means ± SD)	1.57 ± 2.01	1.18 ± 1.57	1.84 ± 2.39	1.46 ± 1.83	NS
No. of transferred embryos(means ± SD)	2.11 ± 0.54	2.06 ± 0.60	2.24 ± 0.54	2.05 ± 0.55	NS
Implantation rate (N, %)	117/372 (31.45%)	81/257 (31.52%)	30/85 (35.29%)	34/84 (40.48%)	NS
Pregnancy rate (N, %)	89/176 (50.57%)	62/125 (49.60%)	22/38 (57.89%)	22/41 (53.66%)	NS

Table 2. IVF/ICSI Outcomes. Note: NS =not statistically significant.

triomas were not recurrent before IVF-ET/ICSI cycles. Group C consisted of 38 women with recurrent endometriomas after a previous cystectomy; the endometriomas were not aspirated transvaginally before IVF-ET/ICSI cycles. Group D consisted of 41 women with recurrent endometriomas after a previous cystectomy; they underwent aspiration before IVF-ET/ICSI cycles.

2.2. COH protocols

Patients underwent COH with a GnRH-a prolonged protocol or a GnRH-a long protocol. Briefly, the patients who underwent prolonged down-regulation received 1.87 mg or 3.75 mg of Triptorelin (Diphereline, IPSEN, Pharma, France) every 28 days for 1-3 months before COH. As for patients taking long protocols, an injection of 1.0-1.3 mg of GnRH-a (Triptorelin) was administered from the mid-luteal phase of the preceding cycle. Complete pituitary suppression was confirmed by serum E_2 level <50 pg/mL and serum LH level <5 mIU/mL.

Recombinant FSH (Gonal-F, Serono, Switzerland) and/or hMG (LiZHu, China) were used at doses ranging between 225 and 450 IU/day. The dosage of FSH and hMG was adjusted according to the ovarian response. Recombinant hCG (Serono, Switzerland) was given to trigger follicle maturation when at least two follicles reached a mean diameter of 18 mm. Oocytes retrieval was performed 34-36 hours after hCG injection. Embryo transfers were performed 3 -5 days later. Pregnancy was diagnosed by a rising concentration of serum β-hCG, which was tested 14 days after ET. Clinical pregnancy was defined as presence of a gestational sac.

2.3. Statistical Analysis

The SPSS statistical software package (version 11.0) was used for statistical analysis. Values are expressed as the mean ± SD. One-way analysis of variance (ANOVA) with a post hoc test using Fisher's Protected Least Significant Difference (PLSD) was used to compare multiple means from different groups. A χ^2-test was used to compare categorical variables. *P* values <.05 were considered to be statistically significant.

3. RESULTS

3.1. Patient Characteristics and Stimulation Outcomes

A total of 380 women with endometriosis were retrospectively studied. The patient demographic variables were compared in Table 1. The four groups were similar regarding duration of infertility, age, body mass index and endometrial thickness on hCG day. There were significant differences among the four groups for baseline FSH, total dose of Gn, duration of ovulation induction and plasma E_2 level on hCG day.

When multiple comparisons were performed by a post hoc test, we obtained the following results: a) the baseline FSH level in Group D was 11.00 ± 6.08 mIU/mL, which was significantly higher than in other groups ($P < 0.05$); b) the total dose of Gn was significantly lower in Group A (2337.15 ± 853.00 IU) compared to the other three groups ($P < 0.05$) and c) the duration of ovulation induction for Group A (10.94 ± 2.44 days) was slightly shorter than that of Group C (11.74 ± 2.04 days) and was significantly shorter than those of Group B (11.83 ± 2.55 days) and Group D (12.27 ± 2.46 days). d) in Group A, the E2 level on hCG day was 2975.97 ± 1437.56 pg/mL, which was significantly higher than those of other groups ($P < 0.05$).

The average diameters of recurrent endometriomas in

Groups C and D were both less than 3 cm (12.98 ± 0.60 cm and 19.62 ± 0.93 cm).

3.2. IVF/ICSI Outcomes

As shown in Table 2, the numbers of high-quality embryos and transferred embryos were similar in the four groups. There were significant differences in the numbers of oocytes retrieved and MII oocytes among the four groups. From multiple comparisons with the post hoc test, we found that the number of retrieved oocytes in Group B was 7.98 ± 5.05, which was significantly smaller than those in Groups A and D ($P < 0.05$). The numbers of MII oocytes in Groups A, C and D were 8.28 ± 4.75, 8.55 ± 4.95 and 8.61 ± 5.61, respectively, which were significantly more than that in Group B. There were no significant differences in implantation rate or pregnancy rate among the four groups.

4. DISCUSSION

The increased prevalence of endometriosis among infertile women indicates that endometriosis impairs women's reproduction (14). Several mechanisms have been proposed, including distorted pelvic anatomy (15), impaired ovary function (16), altered micro environment (17, 18), affected endometrial receptivity (19-21) and reduced oocyte/embryo quality (22, 23). In our study, the baseline FSH level in Group D was 11.00±6.08 mIU/mL, which was significantly higher than those in other groups ($P < 0.05$). This finding showed that endometriomas, especially the recurrent endometriomas after surgical treatment, have a negative effect on the ovarian reserve.

According to the ESHRE guidelines, ovarian endometrioma (≥3 cm in diameter) removal and histologic diagnosis are recommended to identify endometriosis and to exclude rare instances of malignancy (24). But, the surgical intervention may have a negative effect on the ovarian reserve. Our study showed that after surgical treatment, the baseline FSH level in Group A was the lowest (8.61 ± 3.42 mIU/mL), which indicated that pelvic endometriosis had a less adverse effect on the ovarian reserve than endometrioma. Both the endometriotic ovarian cyst itself and surgical procedures could do harm to the ovaries. Maneschi et al. found a reduced number of follicles antecedent to surgery, suggesting that cysts may damage the ovary by pressing the ovarian cortex. Potential deleterious mechanisms in surgical procedures are the removal of a consistent amount of ovarian tissue during a cystectomy and the adverse changes in ovarian artery blood flow.

There is still controversy regarding the impact of endometriosis on IVF outcome (25, 26). A recent meta-analysis demonstrates that patients with endometriosis-associated infertility undergoing IVF-ET have a 36% reduction of pregnancy rate compared to women with other indications for IVF-ET (27). In our study, the data showed that there were no significant differences in the numbers of high-quality embryos, implantation rate or pregnancy rate among the four groups.

Koga K et al. showed that the recurrence rates of endometrioma after surgical excision were quite variable, ranging from 6 to 30% (28). There is still controversy on how to effectively treat recurrent endometriomas. A matched case-control study from Juan A. Garcia-Velasco et al. showed that a laparoscopic cystectomy for endometriomas before commencing an IVF cycle does not improve fertility outcomes. In our study, 41 women were treated by transvaginal aspiration before IVF-ET/ICSI cycles (Group D), while the others were not treated (Group C). We found that the number of retrieved oocytes, the numbers of high-quality embryos, the implantation and pregnancy rate were similar in the two groups. Our results showed that transvaginal aspiration for recurrent endometriomas (< 3 cm in diameter) before IVF-ET/ICSI cycles does not improve the outcome.

5. CONCLUSION

Our study demonstrated that pelvic endometriosis had a smaller adverse effect on the ovarian reserve than endometrioma. No advantage was found in transvaginal aspiration for recurrent endometriomas (< 3 cm in diameter) before IVF-ET/ICSI cycles in terms of number of retrieved oocytes and implantation and pregnancy rates.

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REFERENCES

1. Hart R. Unexplained infertility, endometriosis, and fibroids. BMJ. 2003; 327(7417): 721-4.
2. Busacca M, Vignali M. Ovarian endometriosis: from pathogenesis to surgical treatment. Curr Opin Obstet Gynecol. 2003; 15(4): 321-6.
3. Jenkins S, Olive DL, Haney AF. Endometriosis: pathogenetic implications of the anatomic distribution. Obstet Gynecol. 1986; 67(3): 335-8.
4. Redwine DB. Ovarian endometriosis: a marker for more extensive pelvic and intestinal disease. Fertil Steril. 1999; 72(2): 310-15.
5. Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. Fertil Steril. 1998; 70(6): 1176-80.
6. Ho HY, Lee RK, Hwu YM, Lin MH, Su JT, Tsai YC. Poor response of ovaries with endometrioma previously treated with cystectomy to controlled ovarian hyperstimulation. J Assist Reprod Genet. 2002; 19(11): 507-11.
7. Somigliana E, Ragni G, Benedetti F, Borroni R, Vegetti W, Crosignani PG. Does laparoscopic excision of endometriotic ovarian cysts significantly affect ovarian reserve? Insights from IVF cycles. Hum Reprod. 2003; 18(11): 2450-3.
8. Suganuma N, Wakahara Y, Ishida D, Asano M, Kitagawa T, Katsumata Y, et al. Pretreatment for ovarian endome-

trial cyst before in vitro fertilization. Gynecol Obstet Invest. 2002; 54 Suppl 1: 36-40; discussion 41-42.
9. Bergendal A, Naffah S, Nagy C, Bergqvist A, Sjoblom P, Hillensjo T. Outcome of IVF in patients with endometriosis in comparison with tubal-factor infertility. J Assist Reprod Genet. 1998; 15(9): 530-4.
10. Azem F, Lessing JB, Geva E, Shahar A, Lerner-Geva L, Yovel I, et al. Patients with stages III and IV endometriosis have a poorer outcome of in vitro fertilization-embryo transfer than patients with tubal infertility. Fertil Steril. 1999; 72(6): 1107-9.
11. Wu MH, Tsai SJ, Pan HA, Hsiao KY, Chang FM. Three-dimensional power Doppler imaging of ovarian stromal blood flow in women with endometriosis undergoing in vitro fertilization. Ultrasound Obstet Gyneco.l 2003; 21(5): 480-5.
12. Pabuccu R, Onalan G, Goktolga U, Kucuk T, Orhon E, Ceyhan T. Aspiration of ovarian endometriomas before intracytoplasmic sperm injection. Fertil Steril. 2004; 82(3): 705-11.
13. Esinler I, Bozdag G, Aybar F, Bayar U, Yarali H. Outcome of in vitro fertilization/intracytoplasmic sperm injection after laparoscopic cystectomy for endometriomas. Fertil Steril. 2006; 85(6): 1730-5.
14. D'Hooghe TM, Debrock S, Hill JA, Meuleman C. Endometriosis and subfertility: is the relationship resolved? Semin Reprod Med. 2003; 21(2): 243-54.
15. Schenken RS, Asch RH, Williams RF, Hodgen GD. Etiology of infertility in monkeys with endometriosis: luteinized unruptured follicles, luteal phase defects, pelvic adhesions, and spontaneous abortions. Fertil Steril. 1984; 41(1): 122-30.
16. Yoo JH, Cha SH, Park CW, Kim JY, Yang KM, Song IO, et al. Serum anti-Mullerian hormone is a better predictor of ovarian response than FSH and age in IVF patients with endometriosis. Clin Exp Reprod Med. 38(4): 222-7.
17. Coccia ME, Rizzello F, Mariani G, Bulletti C, Palagiano A, Scarselli G. Impact of endometriosis on in vitro fertilization and embryo transfer cycles in young women: a stage-dependent interference. Acta Obstet Gynecol Scand. 90(11): 1232-8.
18. Chen ML, Lee KC, Yang CT, Hung KH, Wu MH. Simultaneous laparoscopy for endometriotic women undergoing in vitro fertilization. Taiwan J Obstet Gynecol. 51(1): 66-70.
19. Xiao Y, Sun X, Yang X, Zhang J, Xue Q, Cai B, et al. Leukemia inhibitory factor is dysregulated in the endometrium and uterine flushing fluid of patients with adenomyosis during implantation window. Fertil Steril. 94(1): 85-9.
20. Dimitriadis E, Stoikos C, Stafford-Bell M, Clark I, Paiva P, Kovacs G, et al. Interleukin-11, IL-11 receptoralpha and leukemia inhibitory factor are dysregulated in endometrium of infertile women with endometriosis during the implantation window. J Reprod Immunol. 2006; 69(1): 53-64.
21. Lu H, Yang X, Zhang Y, Lu R, Wang X. Epigenetic disorder may cause downregulation of HOXA10 in the eutopic endometrium of fertile women with endometriosis. Reprod Sci. 20(1): 78-84.
22. Garrido N, Navarro J, Remohi J, Simon C, Pellicer A. Follicular hormonal environment and embryo quality in women with endometriosis. Hum Reprod Update. 2000; 6(1): 67-74.
23. Mansour G, Sharma RK, Agarwal A, Falcone T. Endometriosis-induced alterations in mouse metaphase II oocyte microtubules and chromosomal alignment: a possible cause of infertility. Fertil Steril. 94(5): 1894-9.
24. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod. 2005; 20(10): 2698-2704.
25. Kuivasaari P, Hippelainen M, Anttila M, Heinonen S. Effect of endometriosis on IVF/ICSI outcome: stage III/IV endometriosis worsens cumulative pregnancy and live-born rates. Hum Reprod. 2005; 20(11): 3130-5.
26. Koch J, Rowan K, Rombauts L, Yazdani A, Chapman M, Johnson N. Endometriosis and infertility–a consensus statement from ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence). Aust N Z J Obstet Gynaecol. 52(6): 513-22.
27. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. Fertil Steril. 2002; 77(6): 1148-55.
28. Koga K, Takemura Y, Osuga Y, Yoshino O, Hirota Y, Hirata T, et al. Recurrence of ovarian endometrioma after laparoscopic excision. Hum Reprod. 2006; 21(8): 2171-4.