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Can Endometriosis Affect the Clinical Outcomes in Patients Undergoing IVF-ET ?

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자궁내막증을 갖는 불임환자의 체외수정시술에 관한 연구

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연구목적: 전반적인 자궁내막증이 체외수정시술에 미치는 영향을 알아보고, 특히 stage III-IV 자궁내막증을 갖는 불임환자 체외수정시술 결과에 대하여 알아보고자 본 연구를 시행하였다.

연구재료 및 방법: 1998년 9월부터 2001년 9월까지 진단복강경을 통해 자궁내막증으로 진단된 환자 중 체외수정시술을 시행 받은 91명 131주기를 대상으로 하였으며 이중 stage III-IV의 자궁내막증을 갖는 환자는 27명 34주기였다. 비교군은 이시기에 진단된 순수 난관원인으로 체외수정시술을 시행한 40명 56주기를 대상으로 하였다. 통계학적 검사는 Student's *t*-test와 Chi-square test를 시행하였고, $p<0.05$를 유의성이 있는 것으로 판정하였다.

결 과: 전체 자궁내막증 환자와 난관인자의 체외수정시술에서 두 군간의 나이는 31.6±3.3, 32.6±3.6세로 비슷하였다. 채취된 난자의 수 (10.3±6.6 vs 11.7±5.1), 성숙난자 수 (7.4±4.7 vs 7.7±4.9), 수정율 (70.2±32.4% vs 73.7±20.0%), Good embryo quality rate (8세포 (G1+G2)를 2PN의 개수로 나눈 값) (32.6% vs 32.4%) 및 배아이식 수 (4.6±1.4 vs 4.8±1.1)로 두 군간에 차이는 없었다. 또한 임상적 임신율의 경우도 각각 30.7%, 42.8%로 비슷하였다. 중등도 및 중증의 자궁내막증과 난관인자의 비교에서 성숙난자 및 채취된 난자의 개수는 각각 8.8±4.9, 7.7±3.9, 11.3±7.0, 11.7±5.1개로 두 군간에 차이는 없었다. 수정율은 stage III와 IV 군에서 감소되는 경향을 보였으나 통계학적인 유의성은 없었다 (66.2±30.0% vs 73.7±20.0%). Good qulity embryo rate (GQER)는 stage III-IV 자궁내막증 환자군에서 22.0%로 순수 난관인자의 32.4%에 비하여 감소하는 경향을 보였으나 통계학적인 유의성은 없었다 ($p=0.15$, Chi-square test). 배아이식 수의 경우는 각각 4.7±1.5, 4.8±1.1개로 차이가 없었다. 배아이식 주기당 임상적 임신율의 경우는 stage III-IV 군에서 25.0% (8/32), 난관인자 군의 42.8% (24/56)로 통계학적인 유의성은 없었으나 ($p=0.06$, Chi-square test), 중등도 및 중증의 자궁내막증을 갖는 환자에서 임신율이 감소하는 경향을 보였다.

결 론: 체외수정시술시 자궁내막증이 임신율에 나쁜 영향을 미치지 않지만, 중등도 및 중증의 자궁내막증을 갖는 불임환자의 체외수정시술에서는 임신율에 나쁜 영향을 끼칠 가능성이 있을 것으로 사료된다.

Key Words: Endometriosis, Good quality embryo rate, IVF-ET

Endometriosis is a common and enigmatic disease that has been linked to decreased fertility. The relationship between endometriosis and infertility is still debated.

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In vitro fertilization and embryo transfer (IVF-ET) has become a recognized treatment of endometriosis-associated infertility. Using IVF-ET, it is possible to bypass the suspected deteriorated pelvic condition or disturbed function. However, the results from IVF-ET cycles also are controversial. Some investigators have reported high success rates with IVF treatment.[1~2] Other investigators, however, reported a poor outcome of IVF in patients with endometriosis compared with tubal-factor infertility.[3~5] Many investigators also reported that endometriosis can not impact PR and IR in IVF cycles.[6~9] The role of IVF treatment according to stage by stage endometriosis are also controversial.[4]

The purpose of this retrospective analysis to compared the impact of endometrisis on IVF and its outcomes between a group of patients who had stage III and IV endometriosis and a corresponding group with tubal factor infertility.

MATERIALS AND METHODS

We reviewed the medical records of 91 patients diagnosed with endometriosis who were undergoing 131 cycles of IVF procedures in our unit between September 1998 and December 2001. Of these patients, 27 patients of 34 cycles with stage III and IV endometriosis included, categorized according to the revised classification of the American Fertility Society. Meanwhile, they were compared with an age-matched control group (56 cycles, 40 patients) with only tubal factor infertility.

Controlled ovarian stimulation was performed with long protocol of GnRH agonist (Lucrin Sub Q, Abott) and Pure FSH (Metrodine HP, Serono) and hMG (Pergonal, Serono). When at least two follicles reached 18 mm or more in diameter, 10,000 IU of hCG (Profasi, Serono) was administered. Transvaginal ultrasound-guided oocyte retrieval was performed 36 hours after hCG administration. Oocyte were suspended and inseminated in P1 medium, supplemented with 10% SSS. ET was performed after 72 hours at the eight cell stage. Good quality embryo rate (GQER) defined as a number of 8 cell grade I and II divided by number of 2PN.

Statistical analysis was conducted using $?^2$ test, Student's *t*-test. The results are presented as mean±SD.

Table 1. Comparison between all stages of EMS and tubal factor

	Endometriosis (n=131)	Control (n=56)
Age	31.6±3.3	32.6±3.6
Total cycle	1.6±1.0	1.3±0.6
No. of oocyte retrieval	10.3±6.6	11.7±5.1
Mature oocytes	7.4±4.7	7.7±3.9
FR (%)	70.2±32.4	73.7±20.0
GQER (%)	32.6±29.1	32.4±24.7
No. of ET	4.6±1.4	4.8±1.1
PR Per ET (%)	31 (40/129)	42.8 (24/56)

NS
GQER: good quality embro rate (8 cell (GI+GII)/2PN)

RESULTS

Table 1 compares the IVF outcome in patients with all stage of endometriosis and those who had tubal factor infertility. The age of patients, number of total IVF cycle were not significantly different between the groups. Similarly, the number of oocytes retrieval, and number of embryos transferred in each group were comparable. The pregnancy rates were comparable in women with endometriosis patients and with tubal factor patients.

Table 2 compares the outcome in patients with minimal to mild (stage I-II) endometriosis and those who had moderate to severe endometriosis (stage III-IV). although stage III-IV patients appe-

Table 2. Comparison between stage I-II and stage III-IV endometriosis

	Endometriosis stage I-II (n=97)	Endometriosis stage II-IV (n=34)
Age	31.6±3.5	31.1±2.8
Total cycle	1.6±1.0	1.8±1.0
No. of oocyte retrieval	10.0±6.4	11.3±7.0
Mature oocytes	6.9±4.5	8.8±4.9*
FR (%)	71.6±33.2	66.2±30.0
No. of ET	4.5±1.4	4.7±1.5
GQER (%)	36.4±30.0	21.6±20.0†
PR Per ET (%)	33.3 (32/96)	25.0 (8/32)

*p=0.04, †p=0.01

Table 3. Comparison between stage III-IV endometriosis and tubal factor

	Endometriosis stage III-IV (n=34)	Tubal factor (n=56)
Age	31.1±2.8	32.6±3.6
No. of oocyte retrieval	11.3±7.0	11.7±5.1
Mature oocytes	8.8±4.9	7.7±3.9
FR (%)	66.2±30.0	73.7±20.0
GQER (%)	22.0±20.1	32.4±24.7*
No. of ET	4.7±1.5	4.8±1.1
PR Per ET (%)	25.0 (8/32)	42.8 (24/56)†

*p=0.04, †p=0.06

ared to have significantly higher number of mature oocytes, the GQER was significantly lower in stage III-IV. The pregnancy rate, however, was not significantly different between the groups.

Table 3 compares the IVF outcome in patients with stage III-IV endometriosis and those who had tubal factor infertility. The data showed a reduced GQER and pregnancy rate among patients with stage III-IV compared with tubal factor patients (p=0.04). But there was no significant statistical difference in pregnancy rate (p=0.06, ?[2]).

DISCUSSION

The association between endometriosis and infertility has been extensively reported. Much of the controversy exists because in many cases there is no clear mechanism by which endometriosis might be causing infertility.

IVF-ET has become a common technique to help women with endometriosis-associated infertility.[6] Some investigators reported a poor outcome of IVF in patient with endometriosis compared with tubal infertility.[3~5] However, other authors reported that pregnancy rates were comparable in women with or without endometriosis.[6~9] The impact of endometriosis stage on IVF-ET was also controversial. Azem et al (1999)[4] reported that patients with advanced endometriosis have poorer outcome. However, Olivennes et al (1995)[6] reported that PRs were comparable between women who had endometriosis and those who did not. Dmowski et al (1995)[7] reported that IVF success rates were comparable in women with and without endometriosis regardless of the stage of the endometriosis.

Our study shows that the number of oocyte retrieved and fertilization, good quality embryo rate and pregnancy rate were similar to patients with tubal factor. Our results did not find a significant difference between pregnancy rates and the stage of endometriosis. But interestingly, GQERs were significantly decreased in patients with stage III-IV endometriosis, the PRs were similar to patients with stage I-II endometriosis. Out study, however, shows that patients with moderate to severe endometriosis have a tendency toward lower pregnancy rate than patients with tubal infertility. (p=0.06)

In patients with endometriosis, we find that the number of oocytes retrieved and fertilization rates were similar to patients with tubal factor, the embryo quality was significant decreased in patients

with moderate to severe endometriosis.

Good quality embryo may be another consequence of alterations within the oocyte. Endometriotic lesions produce different cytokines such as IL-1ß, IL-6, TNF-a. We hvae recently carried out a pilot study on the effect of endometriosis on IVF outcomes on the basis of the measurement of estradiol, progesterone, IL-1ß, IL-6, VEGF in follicular fluid of patients with endometriosis undergoing IVF. It has been indicated that there was a significant increase of IL-1ß level in follicular fluid of patients with severe endometriosis (not published). The present study, however, gives no indication of abnormal folliculogenesis and lower fertilization rate. A previous study by Brizek et al (1995)[10] reported that patients with endometriosis have increased incidence of aberrant morphological phenotypes. They also indicated that although the effects of endometriosis may not be seen in terms of follicular development or oocyte quality at the time of aspiration, toxic exposure most likely occurs during folliculogenesis resulting in the aberrant embryo morphology. Additional supports for their reports found in Shulman et al (1993)[11] and Simon et al (1994)[12] studies. However, Bergendal et al (1998)[13] indicated that once the oocyte is fertilized, it seems that the embryo has a normal chance of implantation, leading to similar pregnancy rates.

The present study has its limitation in being not only retrospective, but also the number of cases was small, and a few had also ever undergone pelviscopic cystectomy and fulguration.

In conclusion, the presence of endometriosis may not affect clinical outcomes in patients undergoing IVF-ET when all stages of endometriosis were pooled. There might be, however, an unfavorable outcome of IVF-ET in patients with moderate to severe endometriosis because it might be affecting embryo quality by toxic exposure during folliculogenesis.

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