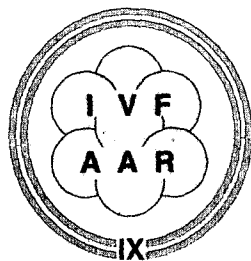


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IX

The relationship of endometriosis and pre-hCG endometrial sonographic studies in patients undergoing in vitro fertilization embryo transfer (IVF-ET) (1)

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SUMMARY

Presented herein is a prospective comparative study whose objective was to investigate the relationship of endometriosis to endometrial thickness and sonographic echo pattern prior to the administration of human chorionic gonadotropin (hCG) in 210 in vitro fertilization (IVF) patients. Patients were matched by age and controlled ovarian hyperstimulation (COH) protocol. 105 women with laparoscopic confirmation of endometriosis were compared to an equal number of patients without endometriosis. Mean endometrial thickness did not differ between groups (12.7 ± 2.9 vs 12.2 ± 2.5 mm). The distribution of echo patterns was also the same irrespective of diagnosis. Evaluation of clinical pregnancy rates (PRs) showed no reduction in patients with endometriosis, regardless of stage compared to controls.

INTRODUCTION

Some studies have reported reduced PRs in patients with moderate to severe endometriosis following IVF-embryo transfer (ET) (2-5).

The purpose of this study was to investigate the effect of endometriosis on the thickness and echo pattern of the endometrium as measured by transvaginal sonography on the day of hCG administration for IVF-ET. Since many reports (6-12) have shown a reduced PR following IVF-ET in cases with a thinner endometrium or cases in which the echo pattern was of the homogeneous hyperechogenic pattern on the day of hCG injection, it was hypothesized that perhaps endometriosis has a negative effect on the endometrium, inhibiting endometrial proliferation and implantation.

To study this hypothesis, the sonographic endometrial characteristics of women with endometriosis were compared to those of a control group comprised of women with no endometriosis.

MATERIALS AND METHODS

One hundred and five IVF cycles performed between November, 1991 and July, 1993 at the Cooper Center for IVF-ET in which the primary cause of infertility was endometriosis were evaluated. All of these patients had a laparoscopy performed within one year of the IVF cycle to confirm diagnosis of endometriosis. Stage determinations were made using the American Fertility Society (AFS) classification (13).

Each patient with endometriosis was matched with a patient who had a diagnosis of no endometriosis based on laparoscopic screening; the matched pair followed the same COH regimen and was within two years of age. Patients with endometriosis as the sole infertility factor were matched to patients with either tubal factor or unexplained infertility. Endometriosis patients with multiple infertility factors were matched with patients without endometriosis who had similar additional factors.

Patients were hyperstimulated using either the luteal phase-leuprolide-acetate (LA)/human menopausal gonadotropin (hMG) protocol (14), the flare protocol (15) or the clomiphene citrate (CC)/hMG protocol in which 100mg/day of CC is given on days 3 to 7 together with 75IU of hMG on days 3 to 6. The hMG is increased to 150 or 225 IU/day until hCG is administered. The decision as to which protocol to use was based on past history of response to stimulation, age and baseline follicular phase follicle stimulating hormone (FSH) levels. The dosage of hMG, FSH and/or CC administered was noted to guarantee the effectiveness of the matching.

Prior to the administration of hCG, endometrial sonographic measurements were made using a 5-MHz vaginal transducer. Endometrial thickness was measured in millimeters (mm) by placing electronic calipers on the outer walls of the endometrium in the longitudinal axis of the uterine body. The endometrial echo patterns visualized sonographically were graded A, B or C as previously described (9).

On the day of the sonographic studies, sera hormone levels were drawn for estradiol (E_2) and progesterone (P). The number of follicles ≥ 15 mm ≥ 18 mm was also noted. Other variables measured included number of oocytes retrieved, fertilization rate, number of embryos transferred and outcome. A clinical pregnancy was defined as one in

which an intrauterine gestational sac was visualized sonographically.

The endometrial thickness, sera hormone levels, number of follicles, number of oocytes retrieved, and number of embryos transferred were compared between the study (endometriosis) and control groups using paired t-tests. Variables were compared by stage of endometriosis using analysis of variance. The distribution of echo patterns was compared between the groups using chi-square analysis. PRs achieved by the endometriosis and control groups were compared using the McNemar test for paired samples. PRs were compared by stage of endometriosis using chi-square analysis. All significance tests were done at the .05 level.

Power analysis demonstrated that this study had 80% power at the 5% significance level to detect a difference of at least .5 mm between the endometrial thickness of the control group and the endometriosis group. It had 80% power to detect a difference of at least 1 mm between the groups classified by stage of endometriosis. Furthermore, this study had 80% power at the 5% significance levels to detect a difference of at least 15% between the PRs of the control and endometriosis groups and to detect a difference of at least 35% between the groups classified by stage of endometriosis.

RESULTS AND CONCLUSIONS

There were 105 patients in each group. Patients with and without endometriosis were an average (\pm standard deviation) of 34.5 ± 3.5 years old vs an average of 34.6 ± 3.3 years old. 66 pairs used the LA/hMG COH; 29 pairs used the flare COH and 10 pairs used the CC/hMG COH. The average number of ampules of ovulation inducing medication was the same in both groups.

On the day of hCG administration there was no difference in the mean sera E_2 levels, P levels, number of follicles ≥ 15 mm or number of follicles ≥ 18 mm between the two groups. An average of 12.6 ± 8.7 oocytes were retrieved in the endometriosis group vs 11.8 ± 6.8 oocytes in controls (paired t-test, $p > .05$). There was no difference in the fertilization rate or average number of embryos transferred in the two groups.

The average endometrial thickness in the endometriosis group was 12.7 ± 2.9 mm vs 12.2 ± 2.5 mm in controls (paired t-test, $p > .05$). Median endometrial thickness was 12mm in both groups. Thin endometria (< 10 mm) were observed in 12.4% of the endometriosis group and 10.5% of the control group.

There was no difference in the distribution of sonographic echo patterns in the two groups ($p > .05$). In the endometriosis group, Pattern A was observed 53.3% of the time, Pattern B 41.9% and pattern C 4.8%. In the control group, A was observed 49.5%, B 41.9% and C, 8.8%.

There were 4 abortions in this study, 3 in the control group (3/33, 9.1%) and 1 in the endometriosis group (1/25, 4%). No differences were seen according to echo pattern. The abortion rates by thickness were 12.5% (1/8) for those < 10 mm and 6.0% (3/50) for those ≥ 10 mm.

25 clinical pregnancies (23.8%) were achieved in the endometriosis group as compared to 33 (31.4%) in controls ($p > .05$). The ongoing/delivered rates were 22.9% vs 28.6% ($p > .05$).

Comparisons of mean endometrial thickness, distribution of echo patterns and PRs were also made by stage of endometriosis. There were no statistically significant differences in thickness, pattern or PR by stage

of endometriosis. Interestingly, Pattern C was most associated with reduced PRs and rarely observed in patients with stage III and IV endometriosis. No reduction in PR was observed as the stage of endometriosis became more severe. The clinical PR/transfer was 25.0% for stage I, 16.2% for stage II, 26.9% for stage III and 31.8% for Stage IV. There was no difference in the endometrial characteristics of patients with endometriosis as the sole infertility factor and those with endometriosis and other factors.

Based on these data, there is no evidence of a negative effect of endometriosis on the endometrium as measured by thickness and echo pattern on the day of hCG. These results are consistent with our findings for women with endometriosis who were sonographically followed in the cycle before and after laparoscopic treatment for endometriosis (16). In that study, the mean endometrial thickness was the same for patients with endometriosis and the control group both before and after surgical treatment for endometriosis.

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