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Relationship of Endometrial Thickness and Sonographic Echo Pattern to Endometriosis in Non-in vitro Fertilization Cycles

Key Words

Endometrial thickness
Endometriosis
Sonographic echo pattern

Abstract

The objective of this study was to investigate the effect of endometriosis on the proliferation of the endometrium as determined by sonographic measurements of endometrial thickness and echo pattern at peak follicular maturation. A prospective study of 60 infertility patients was conducted in which the endometrium was evaluated sonographically, both before and after laparoscopy. Prior to laparoscopy, the mean endometrial thickness was 10.5 ± 1.9 mm in the group without endometriosis ($n = 20$) and 11.7 ± 2.8 mm in the group with endometriosis ($n = 40$) ($p > 0.05$). Following the laparoscopy, there was no change in the mean thickness within each group. The incidence of an unfavorable echo pattern was negligible in both groups. Endometriosis does not cause a reduction in endometrial thickness, nor does it appear to influence the development of an unfavorable echo pattern at time of peak follicular maturation.

Introduction

Although many explanations have been proposed for the mechanisms by which pelvic endometriosis might cause infertility, none have yet been determined with certainty. Some reports have suggested hormonal abnormalities in the pattern of luteinizing hormone (LH) surge [1] and hormonal patterns during the luteal phase [1-3]; others find ovarian abnormalities that effect follicular rupture and release of oocytes [2, 4]; some researchers favor peritoneal factors with increased volumes of fluid [5, 6], increased activity of peritoneal macrophages [6-8] and the presence of an embryotoxic factor in the peritoneal fluid [9-12] as possible explanations.

Some studies have demonstrated reduced fecundity, even in mild cases where the presence of endometriosis has caused no apparent mechanical disruption to tube-oocyte pick-up [13, 14]. Patients with all infertility factors corrected but mild endometriosis had an improved pregnancy rate (PR) when their implants were thermally fulgurated laparoscopically compared to nonfulgurated controls.

Previous studies have demonstrated a decreased PR in patients following in vitro fertilization embryo transfer with an endometrium that is too thin at the time of human chorionic gonadotropin (hCG) injection [15-19]; also, a thin endometrium was associated with a lower PR following transfer of embryos derived from donor oocytes

to recipients in ovarian failure [20]. Furthermore, decreased PRs have been associated with a homogeneous hyperechogenic endometrial pattern on sonography prior to hCG injection [15–18, 20–22]. Also, some have claimed that thin endometria or abnormal echo patterns are associated with decreased PRs in cycles not using assisted reproductive technology [23].

It was hypothesized that perhaps endometriosis has a negative effect on the endometrium, inhibiting endometrial proliferation and implantation and surgical treatment was instrumental in fostering conditions for improving the development of a better endometrium.

The purpose of this study was to investigate the effect of endometriosis on the thickness and echo pattern of the endometrium measured by pelvic sonographic studies at the time of peak follicular maturation by comparing the thickness and echo patterns by diagnosis before and after laparoscopy.

Material and Methods

Within a 6-month period, the first 60 patients who underwent a laparoscopy as part of their initial evaluation for infertility treatment were included in this study; 31 of the patients were seeking treatment for primary infertility and 29 for secondary infertility. A previous history of treated endometriosis was present in 5 cases.

Patients were monitored sonographically throughout the follicular phase of the cycle. Peak follicular maturation was identified as the time in which a follicle attained a diameter >18 mm together with a sera estradiol (E_2) level of >200 pg/ml. Ovulation was confirmed by a subsequent ultrasound that demonstrated collapse of the lead follicle. Sonographic measurement of the endometrial thickness and echo pattern taken at the time of peak follicular maturation were used as baseline measurement in this study. Endometrial sonographic measurements were made using an ATL Ultramark 4 Unit (Advanced Technology Laboratories, Bothell, Wash., USA) equipped with a 5-MHz vaginal transducer. Endometrial thickness was measured in millimeters by placing electronic calipers on the outer walls of the endometrium in the longitudinal axis of the uterine body. The endometrial patterns visualized sonographically were graded A, B or C using the following criteria: *pattern A* presented as a triple-line pattern or a multilayered endometrium in which hyperechogenic outer lines and a well-defined central echogenic line were visualized with hyperechogenic or black areas seen between these lines; *pattern B* was an intermediate pattern in which the endometrium had the same echogenicity as the myometrium with a poorly defined central echogenic line, and *pattern C* was an entirely homogeneous, echo-dense endometrium in comparison with the myometrium in which no central echogenic line could be visualized.

All measurements were performed on ovulatory cycles. Those patients with ovulation disorders were treated with ultra-low dose gonadotropin therapy prior to endometrial measurements. The ultra-low dose gonadotropin regimen was started with one ampule of human menopausal gonadotropin (hMG) (75 IU follicle-stimulating hormone (FSH) and LH, or 75 IU pFSH, Pergonal and Metrodin;

Serono Laboratories, Randolph, Mass., USA) daily from day 5 of the menstrual cycle and continued at this dosage unless there was an inadequate rise in serum E_2 , when the dosage was increased to 1½ ampules. The patients were given 10,000 IU hCG when at least one follicle attained an average of 18–24 mm diameter by sonography and the serum E_2 >200 pg/ml. Following oocyte release, the luteal phase was supplemented by oral micronized progesterone (P) 50 mg 4 × /day.

On the day of peak follicular maturation, baseline sera hormone levels were measured for E_2 , LH and P. The number of mature follicles (>18 mm in diameter) and the use of ovulation induction therapy was noted. Within 3 months of the laparoscopy, a patient's cycle was again monitored and the sonographic measurements taken at the time of peak follicular maturation were used as the postsurgery measurements reported in the study.

Based on the findings of the laparoscopy, patients were classified by stage of endometriosis using the American Fertility Society (AFS) classification [24]. Patients were then classified into two groups: the control group consisted of patients whose laparoscopy was negative, i.e., no endometriosis and the study group consisted of patients whose laparoscopy was positive, i.e., some evidence of endometriosis.

The endometrial thickness, sera hormone levels and number of follicles were compared by presence of endometriosis using t test for independent groups. The distribution of echo patterns was compared between the groups using χ^2 analysis. The measurements obtained pre- and postsurgery were compared using paired t test. All significance tests were done at the 0.05 level. This study had 80% power to detect a difference of at least 2 mm in the mean endometrial thickness between the two groups at the 0.05 level of significance.

When endometriosis is identified laparoscopically, implants are ablated using a CO₂ laser. Vaporization is carried out using 12–15 W of power on continuous mode. Implants that are deep or over the ureters are excised using sharp dissection taking care not to damage underlying structures. Endometriomas are removed via laparoscopic cystectomy or cystotomy with laser ablation of the cyst wall.

Results

The women in the study ranged from 24 to 44 years of age with a mean of 33.8 years and a standard deviation of 4.5 years. Based on the findings of the laparoscopy, patients were classified into two groups: group 1 had no endometriosis (n = 20), and group 2 consisted of patients with endometriosis (n = 40): 24 with stage I, 11 with stage II, and 5 with stage III or IV.

At the time of peak follicular maturation, the sera hormone levels were similar in the two groups. For the group without endometriosis, the mean midcycle hormone levels were: LH 45.3 ± 58.2 (mIU/ml), P 0.5 ± 0.3 ng/ml, and E_2 365.6 ± 247.8 pg/ml. For the group with endometriosis the mean midcycle hormone levels were: LH 46.4 ± 56.7 (mIU/ml), P 0.5 ± 0.4 ng/ml, and E_2 470.0 ± 499.2 pg/ml.

Table 1. Comparison of endometrial characteristics pre- and postlaparoscopy by endometriosis diagnosis

		No endometriosis (n = 20)		Endometriosis group (n = 40)	
		pre	post	pre	post
Thickness, mean \pm SD ^a		10.5 \pm 1.9 ^c	10.1 \pm 1.8	11.7 \pm 2.8 ^c	11.8 \pm 3.0
Proportion with thin endometrium ($<$ 10 mm) ^b		35.0% ^d	35.3%	22.5% ^d	15.0%
Echo pattern ^b	A	45.0% ^d	45.0%	60.0% ^d	62.5%
	B	55.0%	55.0%	35.0%	28.1%
	C	0.0%	0.0%	5.0%	9.4%

^a $p > 0.05$, t test between groups.

^b $p > 0.05$, χ^2 between groups.

^c $p > 0.05$, paired t test within groups.

^d $p > 0.05$, χ^2 within groups.

The mean number of follicles observed in each group was 1.5 ± 0.9 mm in the group without endometriosis and 1.5 ± 1.1 mm in the group with endometriosis. Peak follicular maturation occurred on average on day 14 ± 3 in the control group and on day 13 ± 3 in the endometriosis group.

There was no difference in the mean baseline (or post-treatment) endometrial thickness between the groups ($p > 0.05$; table 1). Prior to laparoscopy, patients without endometriosis had a mean endometrial thickness of 10.5 mm as compared to 11.7 mm for patients with endometriosis. Within each group there was no difference in the mean thickness pre- or postsurgery. The proportion of patients with thin endometria ($<$ 10 mm) was 35.3% in the group with no endometriosis and 22.5% in the group with endometriosis presurgery ($p > 0.05$, χ^2). Following surgery, the proportion of patients with thin endometria were 35.3 and 15%, respectively.

Thirty (50%) of the 60 women in the study were treated with ovulation induction therapy, 10 in the control group and 20 in the study group. The mean endometrial thickness did not differ by usage of ovulation-inducing drugs. In the control group, those not taking these medications had a mean endometrial thickness of 10.5 ± 1.9 mm in the cycle before the laparoscopy as compared to 10.5 ± 2.1 mm for those taking follicular medications. In the study group, the mean endometrial thickness before the laparoscopy was 11.3 ± 2.5 mm for those not taking follicle-maturing drugs and 12.2 ± 3.0 mm for those taking them ($p > 0.05$).

The distribution of echo patterns was similar for patients with and without endometriosis (table 1). These

patterns did not change significantly pre- and postsurgery. Irrespective of endometriosis diagnosis, patterns A and B were most prevalent, with pattern C rarely observed.

Discussion

Two aspects of the endometrium change progressively throughout the follicular phase of cycle: thickness and reflectivity. Transvaginal ultrasound provides an efficient methodology for tracking these developments. Since failure to attain adequate thickness and the presence of a homogeneous hyperechogenic endometrium have been shown to impair implantation and PRs, it was hypothesized that one possible mechanism by which endometriosis could cause infertility is by inhibiting the proliferation of the endometrium.

Sonographic observation has shown that the endometrium thickens from $<$ 4 to $>$ 10 mm at midcycle and this thick diameter is maintained until the next menses. Cohen et al. [23] have shown that the incidence of viable pregnancy rates decreases when the endometrium is $<$ 8 mm and the echo pattern is totally echogenic. We hypothesized that endometriosis may impede implantation because it caused a reduction in endometrial thickness. These data showed that this was not the case. The mean endometrial thickness observed was 1 mm greater for the group with endometriosis.

This study had 80% power to detect a difference of at least 2 mm between the mean endometrial thickness in the two groups. Two millimeters correspond to 20% of the thickness observed in the group without endometriosis.

Based on these data, there is no evidence of a negative effect of endometriosis on the endometrium as measured by thickness and echo pattern at peak follicular maturation both before and after laparoscopy.

Since there was no change in the sonographic measurements before and after laparoscopy within each group, it

can be concluded that the surgery had no effect on subsequent endometrial development.

Although there is no consensus why endometriosis causes infertility in some women, our data indicate that it is not due to detrimental effects on the thickness or echo pattern of the endometrium.

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