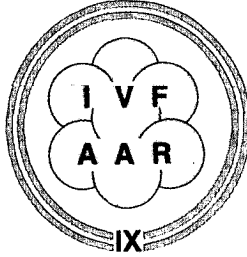


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IXA

Lowered pregnancy rates seen in IVF patients with a homogeneous hyperechogenic endometrial echo pattern prior to hCG injection (1)

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SUMMARY

The present study evaluated the influence of a hyperechogenic endometrium when the endometrial thickness was ≥ 10 mm in women undergoing in vitro fertilization-embryo transfer. 273 consecutive cycles, where endometrial thickness was ≥ 10 mm were evaluated (excluding 85 cycles we previously reported). 22 patients demonstrated the hyperechogenic pattern, 1 achieved a chemical pregnancy (Beta human chorionic gonadotropin > 500 mIU/mL), none achieved clinical pregnancies (ultrasound confirmation). In contrast, 67/251 (26.7%) conceived with other echo patterns (chi-square analysis, $p = .01$). These data thus confirm the negative influence of this type of echo pattern on subsequent pregnancy rates following the luteal phase leuprolide acetate-human menopausal gonadotropin controlled ovarian hyperstimulation regimen.

INTRODUCTION

Vaginal sonography to detect changes in endometrial texture, prior to the rise in progesterone (P), has been used to predict the likelihood of pregnancy that cycle.

Endometrial echo patterns are determined by the comparison of the echogenicity of the endometrium to that of the myometrium and the distinction of a central echogenic line within the endometrium. These echo patterns have been described as appearing either hypoechogenic with well-defined outer walls and central echogenic line, isoechogenic with a poorly defined central echogenic line or hyperechogenic with no visualization of the central echogenic line (2,3). The correlation of these echo patterns seen prior to oocyte recovery to pregnancy rates (PRs) has shown varying results in different studies of women undergoing controlled ovarian hyperstimulation (COH) for in vitro fertilization-embryo transfer (IVF-ET). Gonen et al. found that only the hypoechogenic endometrial echo pattern correlated with good PRs when the COH regimen was clomiphene citrate (CC)-human menopausal gonadotropin (hMG) and the sonographic evaluation was performed on the day following the injection of human chorionic gonadotropin (hCG) which was one day prior to oocyte recovery (3).

The study presented herein was designed to evaluate the correlation of endometrial echo patterns using the luteal phase LA-hMG COH regimen when the endometrial thickness reached a minimum of 10mm in a larger series.

MATERIALS AND METHODS

All IVF-ET cycles from September 1991 to July 1992 were evaluated in which the luteal phase LA-hMG regimen for COH was used (4). If the endometrial thickness was still <10mm, hCG was given, oocyte recovery occurred and the patient was advised to have all embryos cryopreserved.

Transvaginal endometrial sonographic evaluation was performed using a 5MHz endovaginal transducer. Thickness was measured in millimeters (mm) by placing electronic calipers on the outer walls of the endometrium as seen in the longitudinal axis of the uterine body. The endometrial echo patterns were graded I, II, or III using the following criteria: Pattern I represented the hypoechogenic endometrium with well defined outer walls and central echogenic line; pattern II was used to represent the isoechogenic endometrium with a poorly defined central echogenic line; pattern III was used to denote the homogeneous hyperechogenic endometrium in which no central echogenic line was visualized (5). All measurements and grading were performed by one experienced sonographer on one ultrasound unit to eliminate inter-observer and machine variation.

Endometrial thickness and echo pattern from the day of hCG injection were recorded. A total of 307 consecutive cycles was available for evaluation. Only cycles demonstrating an endometrial thickness of ≥ 10 mm were included in this study, thus eliminating 16 cycles. No fertilization was achieved in 18 cycles allowing for 273 cycles available for complete evaluation. No inclusion or exclusion was made based on echo pattern.

Parameters relevant to the IVF cycle, including patient's age, serum

estradiol (E_2), and P levels on day of hCG injection, number of oocytes retrieved, number of follicles observed, number of embryos transferred, and conception outcome were also recorded for each cycle. The PRs were compared according to the three different echo patterns (in all cases thickness was ≥ 10 mm). A clinical pregnancy was established only with ultrasound evidence of pregnancy; a viable pregnancy was defined as a pregnancy showing sonographic viability six weeks from retrieval.

The PRs observed were compared by echo pattern using chi-square analysis. Significant differences were further analyzed by partitioning the chi-square. Comparison between the echo pattern groups and other IVF parameters were made using analysis of variance. If the data on a variable was not normally distributed, the Kruskal-Wallis analysis of variance was used. All testing was done at the .05 level of significance.

RESULTS AND CONCLUSIONS

There were 273 cycles in which the patient's endometrium attained a thickness of at least 10mm at the time of hCG injection.

There was no difference in the mean age of the patients with each pattern type: 33.9 ± 35 years for pattern I, 33.9 ± 34 for pattern II and 31.8 ± 4.0 for pattern III (ANOVA, $p = .06$). Day 13 of the cycle was the median day in all three echo pattern groups when hCG was administered.

Comparison of the sera hormone levels E_2 and P on the day of hCG by echo pattern showed that there was no difference in the median levels observed by echo pattern (1906pg/mL and .9ng/mL for I, 1748pg/mL and .9ng/mL for II and 2060pg/mL and 1.0ng/mL for III, Kruskal-Wallis Anova, $p = .293, .345$). The distribution of echo patterns was the same for all P levels (chi-square = 4.5, $p = .337$). However, it is interesting to note that once P levels rose above 1.5ng/mL, the proportion of pattern III endometrium observed increased from 6.8% to 15.6%. The distribution of echo patterns at each E_2 level was the same (chi-square = 9.2, $df = 8$, $p = .284$).

There was a significant difference in the endometrial thickness by echo pattern with the median of 12.0mm for pattern I, 13.0mm for pattern II and 14.0mm for pattern III (Kruskal-Wallis, $p = .002$).

There was a total of 68 (24.9%) pregnancies observed, 54 (19.8%) clinical and 14 (5.1%) chemical (Beta hCG level > 500 mIU/mL but no ultrasound confirmation). The clinical PR was 24.5% for pattern I, 17.0% for pattern II and 0% for pattern III. Chi-square analysis showed that there was a significant difference in the clinical PRs by echo pattern (chi-square, $p = .01$). Further comparisons were made by partitioning the chi-square results. These comparisons showed that there was no difference in the rates for pattern I and II (chi-square, $p = .16$); however when comparing the rates for I and II combined, vs III, there was a significant difference in the PR (chi-square, $p = .02$).

Other possible factors that could contribute to the conception outcome of the IVF cycle were compared by echo pattern to see if the groups differed in these parameters. However, there was no difference in the median number of oocytes retrieved, percent fertilization, and or number of embryos transferred.

The different echo patterns have been reported to coincide with the changes of the endometrium in response to E_2 and P levels throughout the menstrual cycle. Hyperechogenic endometrium (III) is the pattern

typically seen in the mid to late secretory phase (5). We have also observed that the pattern becomes hyperechogenic once the P rises. Previous data from our clinic has found that there is a lower PR if the P rises above 1ng/mL prior to the hCG injection (6). Others have similarly made the same conclusions (7,8). We hypothesized that perhaps those with pattern III might have higher serum P levels prior to hCG injection; however no statistical differences were found amongst the three groups, though pattern III had the highest median (1.0). The reason for observing this echo pattern preovulatory is not known.

Though the percentage of patients with pattern III was more than twice as high when the serum P was ≥ 1.6 ng/mL than when it was ≤ 1 ng/mL (5/32 or 15.6% vs 11/162 or 6.8%), more than half of those patients with serum P levels > 2 ng/mL still had type I patterns. Thus our data do not support the hypothesis that higher serum P levels are responsible for the preovulatory observation of pattern III and could thus explain the poor PR by over advancement of the endometrium by excessive P.

Though the exact mechanism is not known, at this time our data would suggest that if a patient has met the normal follicular maturation criteria to give hCG in an IVF program, if a type III endometrium is seen one should consider cryopreservation. Whether pushing the stimulation further can change the echo pattern remains to be determined by further studies.

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