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Original Research

Adjusting progesterone (P) dosage to compensate for a non-homogeneous hyperechogenic (HH) echo pattern three days after embryo transfer

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Summary

Purpose: To determine if in the modern era failing to attain a homogenous hyperechogenic (HH) pattern three days after embryo transfer is still associated with a lower pregnancy rates. The study evaluates the efficacy of adding extra progesterone (P) at the time of the non-HH pattern. *Materials and Methods:* A five-year retrospective cohort analysis was performed evaluating two age groups (≤ 34 *vs*. 35-39 years). If an HH pattern was not attained, 50 mg IMP was added to the vaginal P supplementation already given in the IVF-ET cycle. The first two IVF cycles were evaluated. *Results:* There was no difference in live delivered pregnancy rates in younger women not attaining the HH pattern but it was lower in those aged 36-39 years. *Conclusions:* A randomized study adding extra IM P or not in women aged 36-39 or even the younger women is needed to determine if adding extra IM P improves the pregnancy rates or not.

Key words: Mid-luteal phase; Endometrial echo pattern; In vitro fertilization; Live delivered pregnancy rate.

Introduction

There are three well known sonographic echo patterns: triple-line, isoechogenic, and homogeneous hyperechogenic. The sonographic appearance of the endometrium changes throughout the menstrual cycle. In the proliferative phase, the endometrium has a hypoechogenic structure with a well defined central echogenic line. This texture changes in the secretory (luteal) phase becoming hyperechogenic with no visualization of the central echogenic line. This is known as a homogeneous hyperechogenic pattern (HH) [1-3].

A previous study was performed where women with at least six months of infertility with a history of patent fallopian tubes and a husband with normal semen parameters were evaluated sonographically and hormonally to see if they attained a mature follicle of 18-24 mm with a serum E2 >200 pg/mL, a post-coital test was evaluated, follicular collapse of at least 5-mm two days after the luteinizing hormone (LH) surge indicative of oocyte release was determined and then an evaluation was performed of the sonographic echo pattern seven days after ovulation [4]. Those who did not attain a mature follicle or had not demonstrated sperm with progressive motion on post-coital tests were eliminated [4].

Evaluating 296 natural cycles, 165 attained an HH pattern (55.7%) and 131 non-HH [4]. The viable pregnancy rates by simply treating with careful vigilance and benign neglect was 8.5% (14/165) for HH and 2.2% (3/131) for non-HH ($p < 0.05$) [4].

A prospective observational study performed in the "old" era of IVF found a 29.3% live delivered pregnancy rate when the HH pattern was achieved three days after ET *vs*. only 7.1% with a non-HH pattern [5]. The natural cycle study involved no luteal phase support, whereas the IVF-ET study used the typical luteal phase support with vaginal progesterone (P) [4, 5].

The purpose of the present study was to determine if increasing the P supplementation dosage with a non-HH pattern could narrow the gap between live delivered pregnancy rate with HH *vs*. non-HH. Since the HH pattern conversion occurs in the luteal phase, it seems logical that P is involved in the change in architecture leading to sonographic changes. We considered that failing to attain an HH pattern may be related to the need for more P and possibly even increasing the level at the mid-luteal phase could improve the chance of a successful pregnancy.

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Table 1. — *Live delivered pregnancy rates following IVF-ET according to age and attaining or not a homogeneous hyperechogenic endometrial echo pattern in mid-luteal phase.*

	Age < 35 years			
		Cycle 1	Cycle 2	
	Non-HH	HH	Non-HH	HH
No. of cycles	175	476	45	122
Clinical pregnancy	88	244	20	57
Live delivered pregnancies (rate)/transfer	76 (43.4%)	218 (45.8%)	17 (37.8%)	51 (41.8%)
	Age 35-38 years			
		Cycle 1	Cycle 2	
	Non-HH	HH	Non-HH	HH
No. of cycles	75	202	17	63
Clinical pregnancy	27	90	4	34
Live delivered pregnancies (rate)/transfer	21 (28%)	77 (38.1%)	4 (23.5%)	28 (44.4%)

Materials and Methods

A five-year retrospective cohort analysis was performed comparing pregnancy rates following IVF-ET in women who attained an HH pattern *vs*. those who did not three days after ET. All women were taking some type of vaginal P preparation starting the day after oocyte retrieval.

The policy was to add 50 mg I.M. P starting on the day of the mid-luteal phase sonographic determination of echo pattern if an HH pattern was not attained. If 50 mg I.M. P was not given, the cycle was not included in the study.

If a pregnancy was not accomplished, the dosage of vaginal P would be increased in the next IVF cycle but kept the same for those with HH. If either the group who originally achieved an HH pattern or those who did not successfully conceive in cycle 1 failed to have a mid-luteal HH pattern in the second IVF-ET cycle, again 50 mg I.M. P was given from mid-luteal phase. The data were stratified into two age groups for comparison: age < 35 and 35-38 years.

Results

The clinical and live delivered pregnancy rates according to mid-luteal echo pattern and age are seen in Table 1. For first IVF cycles with conventional P supplemental dosages, both age groups had a 70% rate of attaining an HH mid-luteal phase sonographic echo pattern. For second cycles raising the dosage of P for those not attaining an HH pattern in cycle 1 the percentage rate of HH was the same (73%) in the younger group and very slightly higher 78% (but statistically not significant) for women of 35-38 years.

Adding extra P at the time of a non-HH echo pattern three days after transfer and/or the improvement in IVF technology leading to heartier embryos resulted in similar pregnancy rates for younger women (age ≤ 35 years) receiving P supplementation after oocyte retrieval even with a non-HH pattern at mid-luteal phase (Table 1).

For the age group of 35-38 years, the results from the first two cycles (including those receiving extra P at the time of non-HH pattern) were combined to attain more power. The live delivered pregnancy rate was 27.1% (25/92) for non-HH *vs*. 39.5% (105/261) for HH ($p = 0.044$, chi-square analysis).

Discussion

For women aged 35-38 years, the addition of I.M. P at the time of non-HH pattern improved the live delivered pregnancy rates to a similar percentage as those with an HH pattern. This could suggest that the main reason for similar pregnancy rates for both patterns in the younger group is the heartiness of the embryo with the combination of new technology and chronologically younger oocytes, rather than saving the cycle with extra P.

Though the architectural changes in the endometrium occurs at the time of peak serum P, and (probably P plays some role in the changes), there seems to be other factors which when not appropriate may fail to produce a totally appropriate endometrium for implantation, especially from an embryo with somewhat compromised implantation potential.

The question arises as to whether the adverse effect of a non-HH pattern in women of intermediate age following embryo transfer reflects an endometrial defect that is partially related to an adverse effect of controlled ovarian hyperstimulation. This raises the question if these women are more prone to repeating in subsequent IVF-ET cycles a non-HH pattern three days from ET, would this group fair better with cryopreservation with deferred transfer? It is thus not clear if the failure to show a difference in pregnancy rates according to mid-luteal echo pattern in younger women is related to the addition of I.M. P at that time or improvement in IVF technology. The continued observed difference in pregnancy rates in the women aged 36-39 years does not necessarily indicate that adding I.M. P at that time did not help at all, since it is possible the difference would have been greater if it had not been given. A randomized study adding I.M. P or not could help to answer this question.

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