

# The effect of length of the follicular phase on pregnancy outcome following single embryo transfer (ET) in hypergonadotropic women

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## Summary

**Objective:** To evaluate whether a short follicular phase adversely affects pregnancy rates following in vitro fertilization-embryo transfer in women with diminished egg reserve similarly to women with short follicular phases and normal egg reserve. **Methods:** A retrospective review of women with day 3 serum FSH > 12 mIU/ml having only a single embryo transfer. Pregnancy rates were determined according to length of follicular phase, i.e., until day of egg retrieval. **Results:** The ongoing/delivery pregnancy rates for women having oocyte retrievals on day 10 or earlier was 20.0% (20/63) compared to 16.1% (34/210) for those having retrievals on day 11 or later ( $p = \text{NS}$ ). **Conclusions:** Either length of the follicular phase is not an important factor for achieving a pregnancy in women with diminished egg reserve or the use of ethinyl estradiol in the follicular phase negates the adverse effect of the short follicular phase even if it fails to lengthen this phase to at least ten days.

**Key words:** Diminished egg reserve; Length of follicular phase; Ethinyl estradiol.

## Introduction

Even in the modern era of in vitro fertilization-embryo transfer (IVF-ET) using typical controlled ovarian hyperstimulation (COH) regimens, there are reports of extremely poor pregnancy outcome despite transfer of morphologically normal embryos of sufficient number when the day 3 serum follicle stimulating hormone (FSH) level is elevated [1, 2].

However a reasonable pregnancy outcome has been reported in couples with not only increased day 3 serum FSH levels but even less egg reserve when minimal or no gonadotropins were used [3, 4].

A short follicular phase has been found to be associated with a lower pregnancy rate [5, 6].

The present study had two purposes: 1) To evaluate the efficacy of single embryo transfers in women with high day 3 serum FSH levels in a larger series; 2) To determine if pregnancy outcome is affected by the length of the follicular phase.

## Materials and Methods

A retrospective review of all single embryo transfer outcomes from January 1, 1997 to January 1, 2004 was performed in women whose day 3 serum FSH was > 12 mIU/ml.

Inclusion criteria included: Serum FSH > 12 mIU/ml, and age ≤ 39 years. The women were included if serum estradiol (E2) was > 50 pg/ml as long as serum FSH > 12 mIU/ml.

Careful frequent monitoring during follicular phase with pelvic sonography to measure follicle and endometrial growth was performed. Also, measurements of concomitant serum E2, progesterone (P), luteinizing hormone (LH), and FSH levels were made.

During pregnancy an ultrasound at eight weeks and 16 weeks was performed. The end of the follicular phase was considered as the day of oocyte retrieval.

## Results

The pregnancy outcome for single embryo transfers according to length of follicular phase is shown in Table 1.

The majority of oocyte retrievals occurred between days 11-15 (160/273, 58.5%). Though there were only five retrievals on days 1-5, this may be spuriously low because the women were more likely to cancel because they were advised that our own studies suggest lower outcomes with very short follicular phases [4, 5].

There were no differences in clinical pregnancy rates or implantation rates in any of the five groups subdivided according to days of follicular phase (Table 1).

There were no differences in the ongoing/delivery pregnancy rates in women having the retrieval from day 6 to over 21 days. There were no delivered pregnancies in the day 1-5 group but there were only five transfers (Table 1).

Table 1. — Pregnancy outcome for one ET based on number of days of follicular phase.

	1-5 ≤ 39	6-10 ≤ 39	11-15 ≤ 39	16-20 ≤ 39	≥ 21 ≤ 39
# of transfers	5	58	160	35	15
Mean E2 day hCG (pg/ml)	433.8	444.7	749.0	5546.0	390.8
Mean P day hCG (ng/ml)	0.90	0.83	0.90	0.91	0.76
# of follicles	6	218	759	109	37
# of eggs retrieved	7	117	511	91	32
# of inseminations	6	108	436	83	30
# fertilized	5	67	220	39	29
% fertilized	83.3	62.0	50.5	47.0	96.7
# of pregnancies	1	16	33	7	5
% pregnancy/transfer	20.0	27.6	20.6	20.0	33.3
# of clinical pregnancies	1	14	27	6	5
% clinical/transfer	20.0	24.1	16.9	17.1	33.3
# ectopic	0	1	0	0	0
# viable	0	13	25	6	3
% of ongoing/delivered	0.0	22.4	15.6	17.1	20.0
% of SAB: clinical pregnancy	100.0	7.1	7.4	0.0	40.0

SAB: spontaneous abortion.

The ongoing/delivery pregnancy rates for women having oocyte retrievals on day 10 or earlier was 20.0% (20/63) compared to 16.1% (34/210) for those having retrievals on day 11 or greater ( $p = \text{NS}$ ).

Since there was only one embryo transferred the implantation rate equals the clinical pregnancy rate.

## Discussion

Previous non-IVF studies in women with better oocyte reserves found a lower pregnancy rate in women who ovulated before day 11 [4, 5]. It was found that delaying the follicular phase with ethinyl estradiol to  $\geq 11$  days improved the pregnancy outcome to normal [5].

At least with IVF-ET, the present data do not suggest canceling the retrieval or freezing of the embryo and not transferring if the oocyte retrieval is from days 6-10. Many of the cases not included in this study whose retrievals were day 1-5 availed themselves of the option of retrieval and cryopreservation of the embryo or cancellation of the retrieval. The present data might make some reconsider this option since one of five women did achieve a clinical pregnancy.

The method of lengthening the follicular phase was with ethinyl estradiol. Many of the patients in this study, especially the ones with early retrievals, had been on ethinyl estradiol to lower elevated day 3 FSH in an effort to restore down-regulated FSH receptors and restore sensitivity to endogenous or exogenous gonadotropins [6].

The possibility exists that the improved outcome in the one study by lengthening the follicular phase could have been a direct effect of the ethinyl estradiol and not to lengthening the follicular phase, at least based on these IVF data [5].

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