

EFFECT OF INCREASED MID-CYCLE ANDROGEN LEVELS FOLLOWING CONTROLLED OVARIAN HYPERSTIMULATION DURING IVF ON FERTILIZATION / PREGNANCY RATES

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ABSTRACT

The only androgen to rise significantly above normal levels during controlled ovarian hyperstimulation for IVF was androstenedione. No adverse effect on fertilization or pregnancy rates were found.

INTRODUCTION

The present study was conducted to evaluate the mid-cycle rise in serum estradiol (E₂), testosterone (T), androstenedione (A), and dehydroepiandrosterone sulfate (DHEA-s) following controlled ovarian hyperstimulation (COH) using the long-leuprolide-hMG technique (Meldrum et al, 1989) for IVF-ET in a group of women whose baseline androgens were normal. Fertilization / pregnancy rates were compared in women whose androgens increased above the normal range versus those in whom levels remained normal.

MATERIALS / METHODS

A total of 48 consecutive patients undergoing IVF-ET who had normal baseline testosterone (T), androstenedione (A), and dehydroepiandrosterone sulfate (DHEA-s) were studied. The indications for IVF included tubal factor, immunological factor, male factor, as well as unexplained infertility. Patients were treated with leuprolide acetate and hMG to achieve hyperstimulation for transvaginal oocyte retrieval. Serum samples were collected during the menstrual cycle and at the time of peak estradiol (E₂) for testosterone (T), androstenedione (A) and dehydroepiandrosterone sulfate (DHEA-s). Measurements were made by solid phase radioimmunoassay for E₂ (Diagnostic

Products Corporation, Los Angeles, CA) for **T** (ICN Biomedical Inc, Costa Mesa, CA) for **A** (Amersham Corporation, Arlington Heights, IL) and for **DHEA-s** (Diagnostic Products Corporation, Los Angeles, CA).

The mid-cycle androgen levels were evaluated, and the following normal ranges were used: **DHEA-s**, 25-410 $\mu\text{g}/\text{dl}$ was consider normal, >410 was considered elevated. Normal range for **T** was 20-80 ng/dl ; elevated **T** was defined as > 80 ng/dl . **A** was considered normal if it fell into the range 80-300 ng/dl ; levels > 300 ng/dl were considered elevated. Fertilization / pregnancy rates for patients with normal mid-cycle androgens were compared to pregnancy and fertilization rates for patients with elevated mid-cycle androgens.

Table 1. Baseline Versus Mid-cycle Androgen and Estradiol Levels Following Controlled Ovarian Hyperstimulation in 48 Women Undergoing IVF *In Vitro* Fertilization

	Base DHEA-s	Base T	Base A	Mid E ₂	Mid DHEA-s	Mid T	Mid A
X	162	34	187	1313	190	46	297
SD	83	20	69	521	98	18	99

DHEA-s = Dehydroepiandrosterone sulfate

T = testosterone

A = Androstenedione

Base = baseline

Mid = mid-cycle

E₂ = estradiol (pg/ml)

Preg = number pregnant

X = mean

SD = standard deviation

RESULTS / DISCUSSION

The levels of baseline and mid-cycle testosterone (**T**), androstenedione (**A**), dehydroepiandrosterone sulfate (**DHEA-s**), and mid-cycle E₂ for the first cycle of treatment for 48 patients having IVF are shown in Table 1. Three of the 48 patients had elevated **DHEA-s** levels, and one of 48 had elevated **T** levels. Twenty-two of the 48 (46%) had elevated **A** levels. Thus androstenedione was the only androgen to rise significantly at mid-cycle. There were 9 pregnancies (19%). When **A** was normal, 5 of 26 (19%) conceived, and when **A** was elevated 4 of 22 (18%) conceived. Similarly, when **A** was normal the fertilization rate was 52%, and when **A** was elevated the fertilization rate was 46%.

If sera androgens rise in patients treated with follicle maturing drugs where the objective is to mature as few follicles as possible, a priori, there should be a greater magnification of androgen rise following controlled ovarian hyperstimulation for IVF. The only androgen to frequently rise in individual patients above the normal level was androstenedione. However, no difference in fertilization / pregnancy rates in patients with this pattern of androgen rise was found. Thus these data contrast to earlier studies where higher androgen levels seemed to reduce pregnancy rates in non-IVF pregnancies (Dupon et al, 1973; Lawrence et al, 1976). It would appear that these patients did not clinically have polycystic ovarian (PCO) syndrome. The possibility does exist that if one would evaluate PCO patients exclusively, some adverse effect of elevated androgen might still be found.

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