

IVF Protocols: Hyper & Hypo-Responders, Implantation

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CONCEPTIONS

REPRODUCTIVE ASSOCIATES
OF COLORADO



Subset : DHEA

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DHEA

- DHEAS levels decrease by 50% from age 25 – 45.
- 50% of follicular fluid T is derived from *circulating* DHEA; it is also a substrate for E (1).
- FSH receptors are reduced in poor responders and androgen increases FSH receptors on granulosa cells.
- Granulosa cell apoptosis increases as women age.
- Androgen receptor mRNA correlates positively with proliferation and negatively with apoptosis in primate granulosa cells (2).
- Advancement from primordial oocyte pool to recruitable oocyte pool.

(1) Hillier et al, Mol Cell Endocrinol 1994; 100(1-2):51-4.

(2) Weil et al, J Clin Endocrinol Metab 1998; 83: 2479-85.

DHEA IVF Protocol Literature Synopsis as of 11/20/07
M. Bush, MD

P-377

Gleicher/Barad ASRM 2007

DHEA improves number of euploid embryos available for transfer in DOR patients.

“8 patients received at least one month of supplementation with DHEA (micronized, pharmaceutical grade; 25 mg, TID) prior to oocyte retrieval”

P-567

Gleicher/Barad ASRM 2007

Longitudinal review of 281 cycles from 2003-2006 in women above age 40 with DOR. By 2006, 45% of women above 40 were given DHEA. DHEA significantly improves CPR/ET. They have since adopted a policy of DHEA in all women above 40 undergoing IVF.

“Patients received micronized, pharmaceutical grade DHEA 25 mg TID for a minimum of two months prior to egg retrieval”

O-289

Brill/Gleicher ASRM 2006

DHEA leads to increased, and more rapid, conception rates.

“88 patients received DHEA supplementation at a dosage of 25mg TID for an average period of 3.7 +/- 0.3 months followed by IVF”

O-101

Barad/Gleicher ASRM 2005

DHEA pre-treatment for IVF in 45 DOR patients increases oocyte yield and percentage of high quality embryos.

“DHEA, at 25mg TID, for an average of 28 weeks +/- 15 wks (range 4 to 48 weeks)”

F&S, Vol. 84, No. 3, September 2005

Barad/Gleicher

Initial case report detailing a 43 year old with DOR who dramatically improved her oocyte production over the course of continuous treatment with 75 mg/d DHEA

DHEA

Table I. Comparison of results of IVF before and after treatment with dehydroepiandrosterone (DHEA)

	Pre-DHEA	Post-DHEA	P-value
<i>n</i>	25	25	
Age (years)	39.9 ± 0.8	40.4 ± 0.8	–
Weeks of DHEA	–	17.6 ± 2.13	–
Cancellation	8/25 (32%)	1/25 (4.3%)	0.02
Peak estradiol (pmol/l)	3493 ± 512	4065 ± 589	Not significant
Oocytes	3.4 ± 0.5	4.4 ± 0.5	<0.05
Fertilized oocytes	1.4 ± 0.3	3.0 ± 0.5	<0.001
Percentage of fertilized oocytes	39	67	<0.001
Day 3 embryo blastomeres	3.4 ± 0.4	4.7 ± 0.5	0.01
Day 3 embryo grade	2.9 ± 0.1	3.4 ± 0.09	0.02
Cumulative embryo score per oocyte retrieved	8.4 ± 1.5	16.1 ± 1.6	0.001
Transferred embryos	1.4 ± 0.2	2.4 ± 0.3	0.005
Normal day 3 embryos	1.2 ± 0.2	2.7 ± 0.4	0.001

- 25 women with DOR. 450 rec-FSH + 150 hMG/d.
- Second cycle had an average of 4 ½ months DHEA lead-in with 75/d.

DHEA

- 89 women with DOR took 75 mg/d DHEA for up to 4 months prior to IVF, controls proceeded straight to IVF without DHEA.
- Day 3 FSH 16 (+/- 1.2) in treatment v. 13.6 (+/- 1.0) controls.
- Cumulative PR (+CA after 6 weeks) 28.4% v. 11.9% (relative hazard of pregnancy, HR, 3.8; 95% CI 1.2 – 11.8, $p < 0.05$).
- Half of the pregnancies in the DHEA group occurred before IVF; yet strong trend toward higher PR remained with DHEA at IVF (20.6% v. 11.9%).

DHEA

Treatment effect on AMH

- AMH was evaluated in 55 women with DOR at IVF, given DHEA lead-in of 75/d for average of 2 ½ months.
- AMH significantly improved after DHEA ($p=0.002$). Age ($p=0.007$) and length of DHEA treatment ($p=0.019$) were independently associated with increasing AMH.
- Under age 38 all ages demonstrated higher AMH levels, and improved AMH proportionally more than females > 38.
- Longitudinal, AMH improved by ca. 60% from 0.22 ± 0.22 ng/mL to 0.35 ± 0.03 ng/ml ($p<0.0002$). Those reaching IVF had pregnancies in 23.64%. Pregnant women showed more improvement in AMH than those who did not conceive ($p=0.001$).

DHEA

Treatment effect on AMH

- Presents objective evidence for improvements in ovarian reserve (OR) after DHEA at all ages.
- Concurrent with reported clinical outcomes, it is more pronounced in younger (premature aging) than older (physiologic aging) women.
- DHEA-associated improvements in OR statistically reflect subsequent improvements in cumulative clinical pregnancy rate.
- AMH, therefore, is reflective of improving OR and pregnancy chances in women who receive DHEA supplementation.