DRUG REVIEW PROSPECTIVE SELF-CONTROL STUDY

Dehydroepiandrosterone: Is it a Magic Drug?

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Abstract

With infertility populations in the developed world rapidly aging, treatment of diminished ovarian reserve (DOR) assumes increasing clinical importance. In developing countries like India, many patients due to economic and cultural restraints are not able to afford ovum donation or other assisted reproductive techniques. Thus, the possibility of a significant improvement in ovarian response with such an intervention in cases of DOR seems to be very promising. Our findings show only an improvement in anti-mullerian hormone (AMH) levels and antral follicle count in women with poor ovarian reserve, which was statistically significant. But we need a bigger sampling size.

Keywords: Anti-mullerian hormone, Dehydroepiandrosterone, Infertility, Poor ovarian reserve.

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Introduction

As we know infertility populations is rising all over the world, managing diminished ovarian reserve (DOR) is very important.

Many studies have been reported to have improve outcome with dehydroepiandrosterone (DHEA) pretreatment.

Diminished ovarian reserve is where the ovaries lose it capability to act in a desired manner affecting reproductive outcome.

Anti-mullerian Hormone

- There is no specific time for the test.
- Low values of anti-mullerian hormone (AMH) are associated with poor ovarian response but it does not predict failure to conceive.

AFC (Antral Follicle Count) Ideally to be Seen on Day 2/ Day 3

- Number of visible follicles (2–10 mm) during transvaginal ultrasound.
- Performed on cycle days 2–5.
- Number of antral follicles correlates with ovarian response to stimulation.
- Does not predict failure to conceive.

Action

Dehydroepiandrosterone is an endogenous steroid hormone.

It is produced in the adrenal glands *(zona reticularis)* and the gonads, and functions predominantly as a metabolic intermediate in the biosynthesis of the androgen and estrogen sex steroids.

Dehydroepiandrosterone does show many effects on reproduction and has a binding effect on an array of receptors (Fig. 1).

Mechanism of Action

We still are unsure of the direct mechanism of DHEA on ovary.

- Acts as prehormone of the follicular fluid testosterone during the administration of gonadotropins for ovulation induction, which leads to the formation of estradiol.[1]
- Barad et al. (2006)—androgens can be a metabolic precursor for steroid production and it acts as ligands for androgen receptors, thus influencing follicular growth in ovaries.[2]

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- From the theory by Barad et al., we know that DHEA acts like PCO creation to an aging ovary.[2]
- Casson et al. also hypothesized that the beneficial effect of DHEA may be due to an increase in insulin-like growth factor-I.[3]
- From many studies, we know DHEA has a cumulative effect.[4] This increase in preantral and antral follicles leads to an increase in AMH production and more follicles become available for induction with gonadotropins which is reflected by a fall in serum FSH and rise in serum estradiol.
- As an immune regulator, it enhances the Th1 immune response and regulates the balance of the Th1/Th2 response. Upregulation of the CD8+ T lymphocyte population in ovarian tissue, thus regulating the balance of CD4+/CD8+ T cells.[5]

Aim

- To assess the effect of DHEA supplementation on diminished ovarian reserve in infertile patients

Objective

- To evaluate the effect of DHEA supplementation on ovarian reserve by measuring markers, such as, antral follicle count and serum AMH in patients with diminished ovarian reserve.

Materials and Methods

- A prospective self-controlled study was conducted at Rainbow IVF Hospital, Agra from January 2019 to January 2020.
- Total 30 patients of infertility were recruited based on inclusion and exclusion criteria.

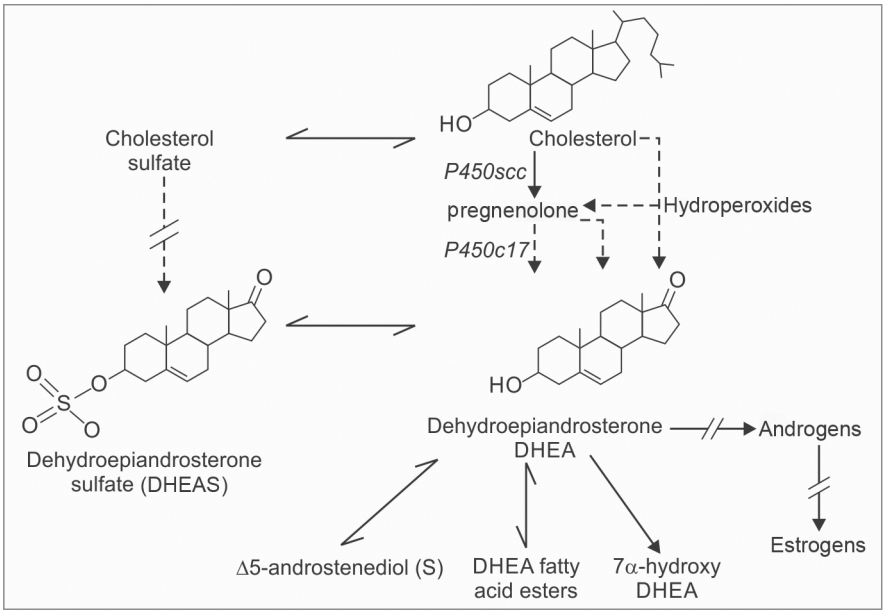

Fig. 1: Synthesis of dehydroepiandrosterone

- Informed consent was taken for all patients.
- The study population was divided into two age groups (<35 and ≥35 years) to determine whether there was a difference in the effect of DHEA supplementation between younger and older patients with diminished ovarian reserve.
- Baseline serum AMH and antral follicle count (D2 Ultrasound) were noted.
- All patients received DHEA supplementation in the form of 75 mg sustained release tablet to be taken once daily for 3 months.
- A repeat serum AMH and antral follicle count were done after 3 months.
- Difference in the AMH and AFC before and after DHEA supplementation was noted. To evaluate whether change in AMH and AFC was significant, Mc Nemar test was applied using SPSS 20.

Outcome

Primary Outcome

- Improvement in serum AMH level.
- Improvement in antral follicle count.

Secondary Outcome

- Determined whether there was a difference in the effect of DHEA supplementation between younger and older patients with diminished ovarian reserve.

Inclusion Criteria

- Women seeking treatment for infertility with an abnormal ovarian reserve test
- Antral follicle count ≤5 and/or anti-mullerian hormone ≤1 ng/mL.

Exclusion Criteria

- H/o ovarian cystectomy/oopherectomy
- Diagnosis of endometriosis
- Abnormal thyroid/liver/kidney function
- On anticonvulsant therapy

Discussion

- With infertility populations in the developed world rapidly aging, treatment of DOR assumes increasing clinical importance.
- In developing countries like India, many patients due to economic and cultural restraints are not able to afford ovum donation or other assisted reproductive techniques. Thus, the possibility of a significant improvement in ovarian response with such an intervention in cases of DOR seems to be very promising.
- Our findings show only an improvement in AMH levels and antral follicle count in women with poor ovarian reserve which was statistically significant.
- On close observation, the mean increase in AMH and AFC is more in the younger population (<35 years) indicating more beneficial role in younger population with diminished reserve and further emphasizing the role of age as a marker for ovarian reserve (Tables 1 and 2).
- The data support the meta-analysis of 2011, which says that role of DHEA in improving ovarian reserve is effective (Figs 2 and 3).

Limitation

The sample size is small so we need to further study to draw significant conclusions.

Table 1: Study statistics

Age group	*Baseline AMH (mean ± SD) (ng/mL)*	*AMH after 3 months (mean ± SD) (ng/mL)*	*Mean difference (95% confidence interval)*	*p value*
<35 years (*n* = 14)	1 ± 0.32	1.4 ± 0.28	0.4 (0.16–0.66)	0.001
≥35 years (*n* = 16)	0.78 ± 0.23	0.97 ± 0.24	0.19 (0.02–0.35)	0.003

Table 2: Our study statistics

Age group	*Baseline AFC (mean ± SD)*	*AFC after 3 months (mean ± SD)*	*Mean difference (95% confidence interval)*	*p value*
<35 years ($n = 14$)	2.14 ± 0.66	3.57 ± 0.94	1.4 (0.79–2.06)	0.001
≥35 years ($n = 16$)	1.63 ± 0.81	2.00 ± 0.73	0.38 (0.05–0.70)	0.02

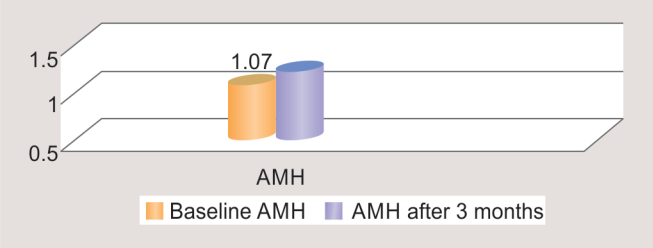

Fig. 2: Comparison of AMH levels before and after DHEA supplementation for 3 months

Conclusion

- Our findings show an improvement in AMH levels and antral follicle count in women with poor ovarian reserve which was statistically significant.
- The improvement in mean levels of AMH and AFC was more in younger age group (<35 years).
- But due to small sample size, there is a need to continue this study and draw conclusions on a larger sample size.

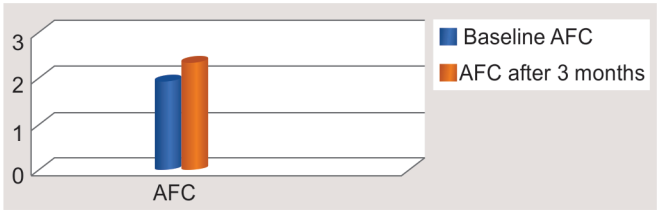

Fig. 3: Comparison of AFC levels before and after DHEA supplementation for 3 months

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