Letters to the Editor

Effects of transdermal testosterone application on the ovarian response to FSH in poor responders undergoing assisted reproduction technique—a prospective, randomized, double-blind study

Sir,

Massin et al. (2006) reported no significant beneficial effects of testosterone administration on the ovarian response to FSH in poor responders. We, however, would like to caution against preliminary conclusions, which may turn out to be misleading.

Our caution is based on prior experiences: Casson et al. (2000) were the first to attempt treatment with the mild androgen, dehydroepiandrosterone (DHEA), in women with diminished ovarian reserve. Probably because the beneficial effects of DHEA were rather disappointing, nobody pursued such treatment any further, until one of our patients, without our knowledge, started self-treatment with rather startling results (Barad and Gleicher, 2005).

As her case and subsequent experience with larger patient numbers (Barad and Gleicher, in press) well demonstrate, the beneficial effects of DHEA peak only after at least 4 months of treatment (Barad and Gleicher, in press, 2005). Casson et al. (2000) had used DHEA, however, for only much shorter time.

The failure of Massin et al. (2006) to detect significant effects on ovarian function after 15–20 days of testosterone application, therefore, should be viewed with caution. In analogy to the DHEA experience, it is possible that longer use would have resulted in different and more pronounced effects.

We would also caution against equating testosterone effects with androgen effects, as the authors have done in the abstract and discussion section of their article. While they well described the physiologic rationale for the potential effects of androgens within the two-cell/two-gonadotrophin theory, different androgens may have varying effects on ovarian physiology and may, therefore, be effective to varying degrees in the treatment of women with diminished ovarian reserve.

We also agree with the authors of this letter that a longer duration of androgen administration should have been more effective, and this issue has been extensively discussed in our article.

Nevertheless, we emphasize that similar caution should be exercised when the authors conclude from their own data on the beneficial effects of dehydroepiandrosterone (DHEA) administration. Major drawbacks of their reports came from methodological aspects. The first publication described a case report in 43-year-old woman. In this unique case, both acupuncture and DHEA interventions have been assumed to improve ovarian response in nine consecutive cycles. However, conclusions from this study are entirely speculative. The second study, presented in an abstract form at the American Society of Reproductive Medicine (ASRM) meeting in 2005, assessed the effects of DHEA in elderly women. However, several methodological flaws could have led the authors to misleading conclusion.

(i) First, this study was not prospectively randomized and did not include any placebo control group. Interestingly, our placebo-controlled study demonstrated a similar improvement in the number of follicles and oocytes in patients without any androgen supplementation. These data emphasize that valuable data can be only obtained from strictly designed, randomized and placebo-controlled clinical trials. This rule is particularly

References

Barad DH and Gleicher N (in press) Effect of dehydroepiandrosterone (DHEA) on clinical pregnancy rates, oocyte and embryo yields, embryo grade and cell numbers in IVF. Hum Reprod.


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Reply: Effects of transdermal testosterone application on the ovarian response to FSH in poor responders undergoing assisted reproduction technique—a prospective, randomized, double-blind study

Sir,

We express our best thanks to N. Gleicher and D.H. Barad for their interest in our newly published study. We agree with their statement that caution must be exercised before drawing any firm conclusions on the impact of medical interventions on IVF outcomes from studies performed with a limited number of patients.

We also agree with the authors of this letter that a longer duration of androgen administration should have been more effective, and this issue has been extensively discussed in our article.

Nevertheless, we emphasize that similar caution should be exercised when the authors conclude from their own data on the beneficial effects of dehydroepiandrosterone (DHEA) supplementation. Major drawbacks of their reports came from methodological aspects. The first publication described a case report in 43-year-old woman. In this unique case, both acupuncture and DHEA interventions have been assumed to improve ovarian response in nine consecutive cycles. However, conclusions from this study are entirely speculative. The second study, presented in an abstract form at the American Society of Reproductive Medicine (ASRM) meeting in 2005, assessed the effects of DHEA in elderly women. However, several methodological flaws could have led the authors to misleading conclusion.