The study results show that a dual trigger of recombinant hCG in addition to GnRH-a significantly increased IVF outcomes including live birth rate in patients with DOR undergoing GnRH antagonist down-regulated IVF-ICSI cycles. These outcomes are in accord with prior publications examining dual-trigger protocols.

EDITORIAL COMMENT

(Diminished ovarian reserve remains one of the most vexing challenges facing reproductive medicine specialists. Some argue that “less is better” because small studies demonstrate no advantage of robust versus minimal stimulation in patients with DOR. Still, the majority opinion is that retrieval of additional oocytes should increase the chances of identifying a developmentally competent oocyte. The “dual-trigger” consists of a GnRH-a combined with hCG. This approach produces increased oocytes and mature (MII) oocytes, as well as improved pregnancy rates, compared with hCG trigger alone in normal and high responders undergoing ART. This study extends the dual trigger approach to patients with DOR. The study found that the dual-trigger group had higher fertilization, clinical pregnancy, and live birth rates. The spontaneous abortion and cycle cancellation rates were lower in the dual-trigger group. Mean number of retrieved oocytes or number of MII oocytes did not differ between the groups. Based on this and other studies, our center has switched to the dual-trigger method of promoting oocyte maturation during ART.—DK)

DHEA Use to Improve Likelihood of IVF/ICSI Success in Patients With Diminished Ovarian Reserve: A Systematic Review and Meta-analysis

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ABSTRACT

Despite advances in in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), poor ovarian response (POR) remains a challenging issue. The frequency of POR is estimated to occur in 5% to 18% of IVF/ICSI cycles and has a corresponding pregnancy rate of 2% to 4%. Dehydroepiandrosterone (DHEA) is an essential prohormone in ovarian follicle steroidogenesis. Administration of oral DHEA has shown beneficial effects in ovarian stimulation for patients with POR, despite the fact that the mechanism of action remains unclear.

This systematic review and meta-analysis aimed to evaluate the efficacy of DHEA administration in improving the success rate of IVF/ICSI. The databases MEDLINE and EMBASE were searched for studies that occurred between 2007 and 2017 comparing the pregnancy rate with and without DHEA in patients undergoing IVF/ICSI. Studies were included if they defined POR as 2 of 3 of the following variables: patients older than 40 years; antral follicle count lower than 5 or decreased anti-Müllerian hormone; and deficient prior ovarian response. Quantitative data extracted from the studies included DHEA doses, number of subjects, number of clinical pregnancies, number of abortions, and mean oocyte retrieval. A fixed-effects model was used for qualitative variables, and Peto method used to calculate odds ratios (OR) with 95% confidence intervals (CIs). Cohen method was used to calculate standardized mean differences between qualitative variables. The primary outcome recorded was clinical pregnancy rate per initiated cycle, and secondary outcomes included mean oocyte retrieval and abortion rate.
A total of 5 studies were included in this meta-analysis, including 910 patients undergoing IVF/ICSI and 413 receiving DHEA. In each of these studies, DHEA was administered in 25-mg doses 3 times a day. The timing of the administration relative to IVF/ICSI varied, one 6 weeks prior, three 12 weeks prior, and one 16 weeks prior. Analysis found that DHEA was significantly associated with an increase in pregnancy rate (OR, 1.8; 95% CI, 1.29–2.51; P = 0.001) and a decrease in abortion rate (OR, 0.25; 95% CI, 0.07–0.95; P = 0.045). No association was found between DHEA use and the mean number of oocytes retrieved (standardized mean difference, −0.01; 95% CI, −0.16 to 0.13; P > 0.05). Low heterogeneity was found between studies regarding DHEA use and pregnancy rate (I² = 19.6%), DHEA used and likelihood of abortion (I² = 0.0%), but not DHEA use and mean oocyte retrieval (I² = 98.6%).

The results show that DHEA administration in patients with POR increases pregnancy rate, decreases abortion rate, and does not affect mean oocyte retrieval. These findings imply that the increase in pregnancy rate may be due to an increase in oocyte quality, and further research is needed to elucidate the mechanism of action of DHEA.

EDITORIAL COMMENT

(Patients with a poor response to ovarian stimulation are among the most challenging to treat. Few options exist, besides increasing the dose of gonadotropins. Dehydroepiandrosterone is a prohormone for ovarian follicle steroidogenesis. Normally, the sulfated form of DHEA is produced in the adrenal gland and travels to the ovary, where it serves as a substrate for ovarian steroidogenesis. Oral administration of DHEA, therefore, has been proposed as a strategy to enhance ovarian activity. This systematic review and meta-analysis collated and analyzed published studies of the efficacy of DHEA in ART. It included 5 studies on 910 patients undergoing IVF/ICSI, with 413 receiving DHEA. Dehydroepiandrosterone was administered in a dose of 25-mg doses 3 times per day. The timing of the administration relative to IVF/ICSI varied from 6 to 16 weeks prior to the ART cycle. Dehydroepiandrosterone increased pregnancy rate and decreased in abortion rate. It did not, however, affect the number of oocytes retrieved. The results of this review suggest that DHEA may enhance ART outcomes in patients with poor response to ovarian stimulation. Other studies suggest that measurement of adrenal steroidogenesis, such as DHEA-S, may identify a subset of patients more likely to respond favorably to DHEA supplementation. Clearly, further studies are needed on this intriguing line of research.—DK)