Adjuvants and Add-Ons to Stimulation Protocols

Kaylen M. Silverberg, MD
Founding Partner & Medical Director
Texas Fertility Centers & Austin IVF
Austin and San Antonio, TX

While medication protocols for IVF stimulation are relatively well established, practitioners (and patients alike) continue to search for other adjuvants that will provide a potential boost in pregnancy rates. To that end, many different types of adjuvants have been proposed for both male and female infertility. Many of these products have been, and continue to be, used despite a lack of data demonstrating efficacy. This presentation will review the available data to hopefully identify and separate those products that have demonstrable efficacy from those that do not.

Well over 150 unique adjuvants have been proposed to improve male fertility. Over 90 of these have been scientifically evaluated. In that regard, 41 rigorous studies were identified, including either randomized, controlled trials or meta-analyses. These data demonstrated efficacy for 18 of the 90 studied products. The most commonly employed male adjuvants include vitamins E & C, zinc, folic acid, and selenium. Those with the most scientific support include vitamins E & C, zinc, L carnitine, and CoQ10. No scientific evidence confirming the efficacy of several commonly used supplements, including glucosamine, vitamin D, niacin, and biotin were identified. Several different medications have also been evaluated for their potential effect on male fertility. Both gonadotropins (FSH) and clomiphene citrate have been demonstrated to improve sperm counts and motility and normal morphology, respectively.

While significantly fewer adjuvants have been proposed for the enhancement of female fertility, much more related literature has been published, and many of these products have been extensively studied. Growth hormone (GH) has been proposed to enhance female fertility for over 30 years. Most studies have agreed that growth hormone produces higher estradiol levels and that GH cycles typically yield 1-2 more oocytes than cycles without GH. Data evaluating live birth rates (LBR) has been less clear. Even meta-analyses fail to agree, resulting in no clear conclusion.

DHEA has also been evaluated extensively. In a large survey of fertility practitioners world-wide, approximately 25% of practitioners recommend DHEA to their poor responder patients. Large studies and a recent meta-analysis suggest that DHEA improves both clinical pregnancy rates and LBR, but it does not appear to have a beneficial effect on reducing miscarriage rates. To the contrary, heparin, aspirin, sildenafil, intralipids and IVIg do not have any clear role in improving female fertility.

While steroids have been proposed as a valuable adjunct for years, the many different published regimens, specific drugs and doses, and initiation and duration of treatment make data interpretation very difficult. Regardless, it appears that while glucocorticoids do not improve fertility, prednisolone may – especially in selected patients with at least one previous failed IVF cycle. Finally, CoQ10 appears to both improve continuing pregnancy rates and reduce cycle cancellation rates.

In addition to adjuvants given to both men and women, several laboratory techniques have been proposed to improve IVF cycle outcome. Of these, embryo glue has been demonstrated to be effective, while assisted hatching has not.

Finally, several techniques and/or adjuvants have been used around the time of embryo transfer to try to increase the likelihood of implantation. While most techniques, including the instillation of such things as granulocyte colony stimulating factor, hCG, and platelet rich plasma into the uterus have not been studied adequately enough to fairly evaluate them, other techniques such as intentional endometrial injury (the so called "scratch test"), has failed to demonstrate efficacy in a recent large randomized controlled trial.

In conclusion, there is a very large body of scientific literature evaluating adjuvants for the enhancement of LBR in IVF cycles. Most studies are unfortunately small, poorly designed, or both. This confounds the identification of products that can truly benefit patients. This presentation is intended to educate participants to identify those agents that have demonstrated efficacy in IVF cycles.