Changing paradigms in ovarian stimulation: what can we learn from luteal-phase ovarian stimulation?

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ABSTRACT

The standard regimens of ovarian stimulation are started during the early follicular phase of the menstrual cycle and GnRH analogue is widely used for preventing premature LH surge. Few studies explore the possibility of performing ovarian stimulation during the luteal phase except some case reports of fertility preservation in cancer patients. We attempted to initiate ovarian stimulation in the luteal phase and confirmed that luteal-phase ovarian stimulation can provide potential oocyte and embryos. Our study firstly extended the concept to a routine IVF setting which can be utilized independent of menstruation. We found that the phenomenon of no spontaneously LH surgeduring luteal-phase ovarian stimulation but it can be triggered by GnRH agonist. The consistent LH suppression may be the actions of progesterone secreted from corpus lutein. So we hypothesized that progesterone can be used to prevent premature LH surge as an oral alternative of GnRH analogue during controlled ovarian stimulation. A prospective controlled study was performed to investigate the effects of medroxyprogesterone acetate (MPA) to prevent LH surge in patients undergoing IVF/ICSI treatments and to compare cycle characteristics during COH and pregnancy outcome in subsequently FET cycles. 300 infertile women with 25-42 year and normal cycle were allocated into two groups. In experimental group, HMG 150-225IU/d and MPA 10mg were given from cycle day 3 onwards. Ovulation was induced with GnRHa 0.1mg or co-trigger by GnRHa 0.1mg and hCG 1000IU when dominant follicles mature. Short protocol was used as control. The viable embryos were cryopreserved for a later transfer. The primary outcome was the number of oocyte retrieved and the incidence of premature LH surge. Secondary outcomes included the number of mature oocytes, fertilization rate and pregnancy outcomes from FETs. The results showed that the number of oocyte retrieved was similar between the two groups (10.4±7.9 vs 9.6±6.0, P>0.05) while higher dose of HMG administration used in the HMG+MPA group (P<0.05). The LH level in the HMG+MPA group contained in suppression during the ovarian stimulation and the mean LH was 1.8IU/l on the trigger day. The incidence of premature LH surge was 0.7% (1/150) in this study. The FET results showed that no difference was found in the pregnancy rate (47.8% vs. 43.3%) and implantation rate (31.9% vs 27.7%) in the FET cycles of HMG+MPA and short protocol. So we conclude that MPA is an effective oral alternative for prevention of premature LH surge in woman undergoing ovarian stimulation for IVF, which will open a new regimen of ovarian stimulation without GnRH analogue in combination with embryo cryopreservation.