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Abstract title:

Pituitary supression is not necessary for blocking LH surge during luteal-phase stimulation

Biography

Dra. María Cruz, PhD is professor from the Master's Degree in Biology and Technology Applied to Assisted Human Reproduction IVI Madrid-European University of Madrid, and clinical embryologist. She graduated from the Complutense University of Madrid in Biological Sciences and achieved her PhD in from Valencia University. Dra. Cruz completed her training by studying a Master's Degree in Biotechnology of Assisted Human Reproduction and a course of Research Methodology applied to Design and Statistics in Health sciences form Autonoma University of Barcelona.

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Study question:

Can we avoid the administration of pituitary suppressors during a luteal phase stimulation without affecting the ovarian response?

Summary answer:
In absence of pituitary supressors during luteal-phase stimulation, it is posible to block a physiological LH surge without impacting normal ovarian response

What is known already:
New stimulation approaches allow for a total disarticulation between the time of the menstrual cycle, ovarian stimulation start and embryo transfer. Double stimulation (DuoStim) was initially designed to optimize clinical outcomes in poor ovarian response, but it could be also useful in fertility preservation for non-medical reasons, especially for oocyte/embryo accumulation. Pituitary suppressors block the LH surge; however, in a protocol as specific as DuoStim, it could be assumed that these suppressors are not necessary in the luteal phase because the endogenous progesterone released during follicular phase is sufficient to block the LH surge during the luteal phase

Study design, size, duration:
Prospective and observational analysis performed in IVI Madrid between September and December 2019. Participants were randomly assigned to each of the study groups. Participants underwent the same stimulation protocol in the follicular phase and for luteal phase stimulation, they were allocated in a control group with pituitary suppressors (n=10) or in a study group, where this medication was not administered (n=10). Statistical analysis was performed by ANOVA and Chi-squared where applicable.

Participants/materials, setting, methods:
Follicular-phase stimulation was the same for both study groups; daily tablet of 10 mg of acetate of medroxyprogesterone (AMP) from first day of stimulation, 225 IU/day ecombinant FSH and triggering with 0.1 mg GnRH agonist. For the control group, luteal-stimulation is identical to the previous one; and in the study group, the only difference is that AMP was not administered daily from the start of the stimulation. LH, estradiol and progesterone were monitored during luteal-phase.

Main results and the role of chance:

As expected, and in the case of a homogeneous population such as oocyte donors, no differences were observed between the two study groups in follicular-phase stimulation, either with respect to endocrine profile or ovarian response. For control and study group respectively, the results were as follows: basal LH (6.11±1.6 IU vs 6.6±2.4 IU, p=0.680); LH on the triggering day (3.1±1.8 IU vs 2.3±0.7 IU, p=0.548); progesterone on the triggering day (1.4±0.3 ng/ml vs. 1.1±0.1 ng/ml, p=0.180); retrieved oocytes (16.7±3.0 vs. 20.1±5.4, p=0.389);and metaphase II oocytes (14.2±3.5 vs. 16.7±4.5, p=0.496).

These results are maintained for the luteal-phase stimulation, meaning that the endogenous profile in the stimulated folicular-phase is capable of inhibiting LH surge, not affecting the results derived from this second stimulation. For control and study group respectively, the results were as follows: basal LH (1.6±1.3 IU vs 1.7±0.6 IU, p=0.335); LH on the triggering day (0.5±0.4 IU vs 1.5±0.6 IU, p=0.300); progesterone on the triggering day (0.6±0.1 ng/ml vs. 0.4±0.1 ng/ml, p=0.398); retrieved oocytes (14.5±1.6 vs. 12.8±2.1, p=0.575);and metaphase II oocytes (11.7±1.0 vs. 10.4±2.3, p=0.609).

Finally, it should be noted that no rescue protocol with administration of GnRH antagonist was applied in the study group, because of ovulation risk

Limitations, reasons for caution:
These results could be considered as an interim analysis, as they are framed within a pilot study prior to conducting a larger study so, although the current data are encouraging, we are not able to draw solid evidences due to our small simple size

Wider implications of the findings:
In a certain group of patients such as oocyte donors, double stimulation implies advantages such as the possibility of achieving more oocytes in less time, optimizing the economic profitability of the egg donation program without compromising clinical results becuase of the absence of pituitary supresor during luteal-phase.

Keywords:
dual stimulation
acetate of medroxyprogesterona
LH surge