GnRH agonist trigger – does one size fit all?

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The use of GnRH agonist for ovulation trigger in GnRH antagonist-based protocol eliminates clinically significant OHSS. It displaces the GnRH antagonist from the pituitary receptors resulting in the immediate LH and FSH surge which is followed by receptor down-regulation. Short half-life of GnRH agonist and desensitization of the pituitary almost completely eliminates the risk of OHSS due to onset of complete and irreversible luteolysis. The FSH surge may have an effect on the resumption of the oocyte meiosis and oocyte maturation.

Despite its widespread use there are a number of issues which need to be resolved.

There is no consensus on the type and the dose of GnRH agonist used. Leuprolide acetate is used in several different dosages ranging from 0.5 mg, 1, 1.5, 2 and 4 mg. The minimum most effective dose of buselserin to induce GnRH surge is 0.5 mg. The dose of triptorelin has been the most consistent and is 0.2 mg.

Supplementation of GnRH agonist trigger with a low dose of hCG, the so-called dual trigger, has been introduced in high responders to aid in oocyte maturation and to provide more sustained support of corpus luteum. Currently there is no consensus on the doses of hCG used for dual trigger and the evidence is mostly of low quality.

The concept of GnRH trigger with ‘freeze all’ policy (segmentation) results in OHSS free clinic. Until now, ‘freeze all’ is applied only in a proportion of patients, many clinics still opt for fresh ET. There are two different approaches to compensate for the luteal phase defect after GnRH agonist trigger, the European, the so called ‘Humaidan’ approach, with addition of low dose of hCG post pick-up and estradiol in the luteal phase as well as vaginal progesterone and the American intensive luteal phase support using intramuscular progesterone and transdermal or oral estradiol.

It has also been recognized that GnRH agonist trigger will not result in an adequate oocyte yield in a small subset of patients. This failure can range from empty follicle syndrome to a retrieval of much fewer oocytes than expected from the number of mature follicles on the day of trigger. Identifying patients at risk of low oocyte yield with GnRH agonist trigger prior or at the beginning of ovarian stimulation would allow the clinician to adjust the strategy according to the individual patient characteristics.

In conclusion, one size of the GnRH agonist trigger does not fit all and further protocol optimization is necessary.