PRESENT STIMULATION IS THE PAST OF TOMORROW

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Nowadays, ovarian stimulation strategy is a beautiful example of lack of intellectual precision in the process.
Long down regulation protocols are widely used introducing extended treatments and eventually temporarily menopausal symptoms. HCG for final egg maturation is still the golden standard. Multiple fresh embryo replacement is still very common. Multiple frozen embryo replacements are very common. The occurrence of 3 % of OHSS syndrome is a well accepted and documented finding.
The overall results of this approach are cumbersome, including emotional stress for the patients, multiple pregnancies and occurrence of ovarian hyperstimulation syndrome.
These protocol strategies can be drastically changed in different ways.
GnRH agonist down regulation can be replaced by GnRH antagonist, which reduces the treatment duration. If GnRH antagonists are used the cycles are short and the stimulation takes approximately ten days. Meta-analysis has clearly demonstrated that ongoing pregnancy rates after GnRH agonist and GnRH antagonist down regulation are not significantly different.
A major issue in long agonist down regulation is a 3 % occurrence of OHSS. This syndrome does have major complications which can be fatal, such as physical and emotional ones. Also the pregnancy outcome is hampered by pregnancy induced hypertension. For medical and legal reasons this approach is unacceptable.
At this writing alternative solutions exist such as the use of GnRH antagonist for down regulation and GnRH agonist to trigger ovulation.
If a patient is at risk for OHSS in GnRH antagonist cycles the conversion to change is agonist triggering instead of hCG is of paramount importance. It is well known that the risk of OHSS after GnRH agonist triggering in GnRH antagonist cycles is nihil.
In case of GnRH agonist triggering one of the strategies to be followed is the vitrification of all oocytes or embryos. The embryos obtained after thawing of the oocytes are after thawing of the embryos have to be replaced subsequently in a natural or artificial cycle.
Another strategy is luteal phase supplementation with low dose hCG (1.500 units) at the moment of egg retrieval. In an observational study out of 12 patients at risk for OHSS six became pregnant without symptoms.
In a randomized controlled trial similar pregnancy rates with agonist triggering and low dose hCG were obtained compared to the injection of 10.000 units hCG. This study was performed in a general population.
Needless to say that there are important tools available to avoid OHSS and that an algorithm can be made to avoid totally OHSS.
An easy approach could be that all first stimulation cycles have to be performed with GnRH antagonist. This allows, if the patient is at risk for OHSS (i.e. more than 20 follicles) to trigger with GnRH agonist. In this condition all oocytes can be vitrified or all embryos can be cryopreserved.
Replacement can be performed in a subsequent natural or artificial cycle.
On the same line it is mandatory that all egg donation cycles have to be performed in GnRH antagonist cycles with GnRH agonist triggering.

The approach of egg vitrification in patients at risk for OHSS has been recently documented in an observational study. The pregnancy rate after coasting was 30 % and it was 50 % after oocyte vitrification.
Conclusions
Nowadays, OHSS syndrome is totally avoidable by the combination of GnRH antagonist and GnRH agonist triggering. This approach leads to an OHSS Free Clinic.
Coda on OHSS Free Clinic
This concept of OHSS Free Clinic introduces the practice of:
1. Maximizing safely ovarian stimulation by GnRH agonist triggering,
2. A. vitrification of all oocytes or B. vitrification of all embryos,
3. Replacement of an embryo after thawing in a natural or artificial cycle.

This new concept introduces an OHSS Free Clinic by segmentation of IVF in three phases: safe ovarian stimulation, cryopreservation technology and embryo replacement in a receptive endometrium.

References:
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