ESHRE 2020 Virtual (5-8 July 2020)

Questions for the speakers

Session 39: Strategies to improve the outcomes of ovarian stimulation 2

Impact of different strategies in frozen cycles in normo responding patients undergoing IVF/ICSI cycles: a multicenter cohort study - Charalampos Siristatidis (Greece)

Q: Can you repeat what you mean by Group 3?

A: Hormone Replacement cycle (HRC) [estrogens, i. Standard estradiol valerate (Cyclacur; Bayer Hellas A.B.E.E.), 2 tabs starting from day 2 and onwards or ii. estradiol valerate increasing dose, starting at day 1 of cycle with 1 tab for 4 days, then 2 for 5 days, then 4 for 4], plus GnRHa suppression with luteal support (progesterone) (Group 3)

Q: Only 439 cycles, no RCT, no conclusions possible, as Systematic reviews based on RCTs did not show differences between HRT protocols for FET…

A: Yes, only 439 cycles; after applying strict inclusion and exclusion criteria; yes, no RCT: it was clear: that was a cohort study – it was not an RCT from the beginning.

Q: What do you think about the natural cycle for Frozen embryo transfer?

A: It is not the issue what I think; our study showed inferior results to the hormone replacement modalities.

Q: Do you suppress a cycles with OCP's ?

A: No. That was not in the design of the particular study.

Q: Can you specify groups and types of treatments?

A: •1. Natural cycle (NC), using urinary hCG (10000 IU of Pregnyl®, Merck Sharp & Dohme, NJ, USA) or recombinant hCG (250 IU of Ovitrelle®, Merck Serono Pharmaceuticals), as ovulatory trigger, without luteal support (Group 1),

•2. NC, using hCG, with luteal support [progesterone (i. vaginal tablets ii. Vaginal gel iii. IM iiii. Combination (Utrogestan®, Besins, France) three times daily using 200 mg or in the form of gel (Vasclor / Crinon)] (Group 2)

•3. Hormone Replacement cycle (HRC) [estrogens, i. Standard estradiol valerate (Cyclacur; Bayer Hellas A.B.E.E.), 2 tabs starting from day 2 and onwards or ii. estradiol valerate increasing dose, starting at day 1 of cycle with 1 tab for 4 days, then 2 for 5 days, then 4 for 4], plus GnRHa suppression with luteal support (progesterone) (Group 3)

•4. HRC without GnRHa suppression with luteal support (progesterone) (Group 4).

Q: What do you think about the natural cycle for frozen embryo transfer

A: Our study showed inferior results to the hormone replacement modalities.

Q: What are the stable and the increasing oestrogen protocols please? Could u describe both?

A: i. Standard estradiol valerate (Cyclacur; Bayer Hellas A.B.E.E.), 2 tabs starting from day 2 and onwards or ii. estradiol valerate increasing dose, starting at day 1 of cycle with 1 tab for 4 days, then 2 for 5 days, then 4 for 4], plus GnRHa suppression with luteal support (progesterone) (Group 3)

Q: Are there any differences in LBR, ongoing pregnancy rate between Kryo-ET in fresh vs. artificial cycle? Fresh cycle with HCG vs. without HCG?

A: •Live birth was higher in Group 3 as compared to Group 4, and lower when progesterone administration through the combination of tabs and gel was compared to tabs only

•Miscarriage was lower in Group 3 compared to Group 4 and when progesterone administration through the combination of tabs and gel was compared to tabs.

•**Subgroup analysis of day 3 embryo transfer**: participants of Group 3 were more likely to have a live birth and clinical pregnancy compared to Group 4

•The stable estrogen protocol compared to the increasing at day 5 was associated with higher biochemical and clinical pregnancy rates, while the progesterone through tabs was linked with lower miscarriages compared either with gel or combinations

•**Subgroup analysis, participants with 2 or more embryos** transferred (n=351 cycles; 271 women) and a stable estrogen administration were more likely to have a biochemical pregnancy compared to the increasing dose; a combination of progesterone regimens were less likely to have a clinical pregnancy compared to tabs

•Participants in Group 3 demonstrated higher rates of live birth and biochemical and clinical pregnancy compared to Group 4

For the definition of the groups please see above.

Q: What do you mean by stable estrogen protocol. Do you start 6mg dosage of estradiol for every one?

A: Please see above.

Q: What do you mean with the stable and the increasing oestrogen protocols please? Could u describe both?

A: Please see above.

Do we trust in evidence based medicine? A multicentre retrospective analysis of 2677 first IVF/ICSI cycles before and after the OPTIMIST trial. - Enrico Papaleo (Italy)

Q: Was the rFSH the same brand for every patient (cofounding biais) ? was it alpha or beta rFSH daily doses?

A: In the study, starting dose of gonadotropin of all companies were included

Q: How can opitimist be better when cumulative pregnancy rates are reduced?

A: Reduction in PR was noted only in hyper-responder patients. In this population, no difference in starting dose between the two years was reported.

Q: Did you notice any changes in safety - lower OHSS e.g.?

A: No clinical differences were noted

Q: How are donors doing during sec stimul?

A: Donors were not included in the study

Pituitary supression is not necessary for blocking LH surge during luteal-phase stimulation - Maria Cruz Palomino (Spain)

Q: In a random start in the luteal phase that crosses into the early follicular phase, who you give a medication to prevent ovulation or not.

A: In the study that we present, luteal phase stimulation is not started on a random day but is scheduled after the first oocyte retrieval

On the other hand, egg donor receive or do not receive medication to prevent ovulation during luteal phase stimulation according to the study group they were assigned after randomization

Q: Is there any other studies published so far regarding not needing of pituitary suppression in luteal stimulation

A: As far as we know, there are no studies specifically designed for this hypothesis.

Q: Is it relevant to antagonist cycles: standard follicular antagonist Rx and luteal FSH without antagonist?

A: It could be considered al alternative to conventional stimulation protocols once we have completed the study

Q: Have you compared the outcomes from the luteal phase stimulation only in the control and study group? (instead of the outcomes of both phases)

A: No, we compared clinical outcomes for both follicular and luteal phases in the control and in the study group

Q: Could you tell us if there is more complication with two ovarian puncture in the same cycle?

A: From what we have been able to observe, there has not been an increase in complications with two oocyte retrievals

Q: Do you have any idea which is the progesterone plasma level able to block the pituitary? It would possible to use antagonist to rescue?

A: Up to date, it is a piece of information that we do not yet have and that we hope to have once the study is finished

On the other hand, in the event that LH doubled its value on consecutive days, a recue antagonist would be introduced to prevent ovulation