ESHRE 2021 Virtual (26 June – 1 July 2021)

Questions for the speakers

PCC10: The highs and lows of IVF

When pretreatment ovarian response testing does not match the age of the patient: Significance and clinical decision making - Frank J. Broekmans (The Netherlands)

Q: In the 'one size fits all' era', do ov reserve markers have a place in management options during ovarian stimulation or are only good for counselling?

A: In fact if would apply the one size fits all strategy (150 IU, Antagonist), then OR markers assessment is not meaningful. However, today most of us wish to apply an individualized approach and then OR testing is a mandatory step. But we need to consider clearly that the MAIN purpose here is preventing HIGH/Excessive response and prevent/manage OHSS risk.

Q: Would you increase the stimulation dose in patients with FSH-polymorphism?

A: Not necessarily. We first need studies that compare standard versus increased dosage in this specific patient group to firmly assess that getting a few more oocytes will make the difference for LIVE birth..

Remember that using 150 IUI creates a maximal response in the vast majority of patients, so that in these FSH receptor variation cases one will anyhow compensate for a slightly lower receptor sensitivity.

Q: You touched on androgen for poor responder but did not expand. Would you advise please testosterone or DHEA?

A: Androgen effects may be achieved by exogenous androgen or compounds such as human chorionic gonadotropin (hCG) to stimulate local ovarian production of androgen. As of today, neither of both has offered any evidence based beneficial effect, despite a plethora of small studies. So, these compounds like Testo and DHEAS should only be used in large RCTs. If you want to apply it still, then I would prefer using DHEAS for reasons of fewer side effects.

Q: In low reserve patients, which protocol is preferred Agonist or Antagonist?

A: In general, there is no preference for one or the other. The only condition that needs to be addresses is an Imminent Ovarian Failure (IOF) condition with abnormal ovarian reserve testing, still regular cycles, but with shortening of the cycles to 22-25 days. If the antagonist protocol is applied in this IOF condition it may occur that dominant follicle growth starts already in the luteal phase preceding the Antagonist starting cycle, creating a condition where the exogenous FSH may be initiated too late. In such cases I would prefer to use a long suppression agonist scheme OR brief pretreatment with OC.

Q: How about the long agonist protocol with GNRH agonist: is there benefit for the old low responder compared to short agonist flare protocol?

A: The same answer as in the previous question: the flare up short agonist protocol used in an IOF patient may not be a good choice. So, in the low responder long suppression, flare up agonist and Antagonist may have the same results, with exception of the IOF case condition.

Q: Do you not consider the weight of the patient as a significant factor in dose determination and what about measuring circulating FSH levels during stimulation?

A: Measuring FSH in relation to ovarian response has not been well studied. We have observed NO clear relation between ovarian response and FSH level or change in FSH after the start of FSH stimulation in couples with a fixed FSH dosage of 150 IU, see Oudshoorn, HR 2017. Regarding body weight, opinions may be quite variable: Pharmacokinetics of FSH are not very informative, some dose picking algorithms do, others do not, find an added value of knowing body weight for chosing the best dosage of FSH, and in the optimist trial, for all cases using 150 IU as FSH dosage, the relation between BW and Number of oocytes was surprisingly weak.

High responders: Avoiding high risk - Roy Homburg (United Kingdom)

Q: Why is the lean patient specifically at risk for OHSS/High response? Are most of your young women, PCOS?

A: In the overweight and obese some of the administered gonadotrophins are absorbed in fat and do not reach the ovaries. In the lean patient of course this does not happen so they respond more to the same dose of gonadotrophins.

Q: Do we need to manage Insufficient endogenous LH response to the ago trigger by measuting LH at day of trigger and add 1500 hCG with the ago trigger??

A: This is a very good question for which we not yet have a definite answer. My guess is that measuring both LH and progesterone 12 hours after the trigger will give us some cut-off points below which giving a small dose of hCG or topping up the administered progesterone will be beneficial.

Q: Why use addictive small hCG doses adding a risk of OHSS when we can freeze-all and do it in an immediate FET cycle?

A: You are quite right asking this question. I'm sure that in the future this will be the case but there are still some objections such as the extra wait involved for patients, extra expense etc. I believe that each unit should define a cut-off point (e.g. no. of follicles or AMH)to decide when to go to freeze-all.

Q: Patients with PCOS sometimes do not respond to the standard dose of FSH of 150 IE/day. How far would you go with the stimulation dose?

A: The PCOS women with extremely high AMH levels are the ones who may not respond to 150 IU FSH. In that case I would increase the dose by 75 units and observe the response carefully. A complete failure to respond may indicate ovarian puncture to reduce the AMH and induce ovulation.

Q: When you start with small dose and the response is low do you step up or cancel the cycle and start with higher dose?

A: I step up but very carefully watching out for the first signs of a response.

Q: Wonderful presentation. What is your opinion on starting an IVF cycle with LH levels higher than 15 despite pretreatment with Ocp?

A: This is a virtual impossibility if the patient has taken the OCP properly for 10 days or more. Although the antagonist should solve the problem, personally I would prefer starting with a low LH.

High or low intensity monitoring during ovarian stimulation? - Ernesto Bosch Aparicio (Spain)

Q: Don't you get many degenerated oocytes, if you wait too long with triggering?

A: yes. Trigger has to be at the right time, neither too early nor too late

Q: Which is your view on duration of stimulation. Should we avoid in Antag. for example going beyond 11 or 12 days? Does the type of triggering signal play a role?

A: No; it depends just on follicular size

Q: Do you monitor LH levels in case of antagonist protocol agonist trigger to control whether trigger is working?

A: We don´t

Q: In some women , even with antag , good lh supression , ovulation at 34hrs before opu occurs , could there be some women with fragile foll wall ? older women ?

A: Older women have this risk. This is caused by prostaglandins, that's why Indometacin or Ibuprofen help

Q: What is the progesterone threshold that you use to freeze all? What about monitoring hormones ,estradiol and progesterone in a frozen cycle

A: We freezde all if PZ1.5 ng/mL; Only in fresh cycles

Q: In case most follicles are in size more than 19 mm,but estradiol is still low, do you trigger or proceed with stimulation? what is more relevant: size or hormone

A: We would trigger. Size leads

Q: Can you explain a bit more on when to trigger when not using 3 >= 17mm what do you tell your young doctors?

A: We tell them to wait that most of the follicles are between 15 and 20 mm, putting an eye on P levels