Hormonal Predictions in Previously Failed IVF Cycles Determined by Estradiol Values

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Abstract: The prediction of IVF success was based on the quantitative levels of estradiol on a specific day in down-regulated cycle, however its role beyond that stage remains controversial. On the day of hCG trigger, due to increased number of follicles, high estradiol levels lead to low endometrial receptivity and thus decreased pregnancy rates in IVF cycles. Different cutoffs of serum estradiol levels have been observed on day 4–6 and on the day of hCG trigger during the stimulation cycle. Based on the aforesaid facts, the aim of our study was to assess the role of serum estradiol levels and treatment in previously failed IVF cycles.

Key Words: estradiol, IVF, follicles.

INTRODUCTION

The prime concern in in vitro fertilization (IVF) cycle is to obtain sufficient number of mature oocytes, good quality embryos, and finally achieve a successful pregnancy. The high cost and relatively low implantation rates in IVF have given rise to the need to evaluate the predictors of success in these women. Prediction of successful IVF outcome has focused on clinical research for many years. Previous reports suggest the role of various parameters like levels of hormones [follicular stimulating hormone (FSH), estradiol/ E2 , inhibin A, and inhibin B], number of ovarian antral follicles, value of progesterone ,anti-mullerian hormone, and the influence of woman's age in predicting successful pregnancy in IVF cycles . Clearly the cut off value of serum Progesterone hormone (p4) remains the main prerequisite for planning an embryo transfer . If the Progesterone value must be low than 1.2 ng/ml to perform an embryo transfer and for a successful pregnancy in an IVF outcome.

The role of estradiol (E_2) in IVF cycles is well known up to the fertilization stage, however its role beyond that stage remains controversial. On the day of hCG trigger, due to increased number of follicles, high estradiol levels lead to ovarian hyper stimulation (OHSS) and low endometrial receptivity causing decreased pregnancy rates in IVF cycles.

MATERIALS AND METHODS

Materials and Instruments:
Culture media, oil.
Instruments:
Microscope, Incubators, Laminar Air Flow, Micromanipulator, Heating blocks, Stopwatches, Culture dishes, Centre well dishes, Glass pipette, Collection containers.

METHODOLOGY

- The study was performed on women underwent IVF procedure. All patients who underwent ET procedures were accountable for this study from August 2022 to January 2023.
- Ethics committee approval was not required for this study because it involved retrospective data analysis.
- To generate homogeneous study groups we excluded women aged ≥40years at the time of ET.
- To ensure a similar endometrial receptivity between the groups, serum estradiol (E2) levels were determined on the human chorionic gonadotropin (hCG) day of the fresh ET cycle and endometrial preparation cycle in the frozen embryo transfer cycle .
- The live birth rate was considered the primary outcome. The clinical pregnancy and miscarriage rates were considered secondary outcomes.
- There was no restriction on the stimulation protocol among the participants recruited for the pooling group.

- However, for the final oocyte maturation, a fixed 250 µg of recombinant hCG was used subcutaneously for all stimulated cycles. All the embryos were generated by intracytoplasmic sperm injection (ICSI) and vitrified afterwards.
- At least two ICSI cycles were performed. Embryos recruited from the last cycle were also vitrified.
- The embryo obtained for each cycle was kept in culture until the blastocyst stage in women undergoing blastocyst ET. Embryo that reached the blastocyst stage was frozen.
- In women undergoing ET at the cleavage stage, the obtained embryo that reached the cleavage stage were frozen.
- The whole cohort was thawed on the appropriate day, if vitrified, of the developmental stage and selected for transfer as the best-quality embryos according to the morphologic assessment criteria.
- Luteal phase support was initiated on the day of the oocyte pickup procedure for the fresh ET and for the frozen embryo transfer .
- We used readymade solutions available for embryo vitrification and thawing procedures. For vitrification procedure the embryos in the cleavage stage were placed for 10 minutes and the blastocyst for 12-13 minutes in equilibration solution at room temperature.
- Afterwards, the embryos were shifted to vitrification solution for 40 seconds and finally immersed into liquid nitrogen (minus 196 degrees).
- The thawing process was started with the removal of the cryolock or vitrifit(cryo devices) from the liquid nitrogen and keeping the embryos in the first thawing solution at 37 °C for 60 seconds and followed by series of thaw wash steps in second solution for 3 minutes and 6 minutes at room temperature.
- Following this, they were transferred into the priorly made equilibrated culture solution in a petridish and kept for culture inside an incubator until the embryo transfer .

RESULTS

Comparison of outcome hormonal predictions of estradiol values in all parameters

Parameters	Estradiol level of≤75 pg/mL	Estradiol levelof >75 pg/mL
Mean (±SD) age (y)	34.1 ± 4.6	35.0 ± 4.2
Pregnancy rate (%)	*(03/19) 15.7%*	*(52/100) 52%*
Mean (±SD) no. of oocytes retrieved per cycle	5.8 ± 3.0	10.2 ± 3.6
Mean (±SD) no. of embryos transferred per cycle	2.2 ± 1.5	2.2 ± 1.5

CONCLUSION

Although estradiol levels of >75 pg/mL and p4 low values (<1.2 ng/ml) are highly predictive of improved Pregnancy Ratesin cycles using luteal support, no test of ovarian reserve is precise enough to merit total reliance on the results. Setting an estradiol level of 75 pg/mL as a cutoff for allowing patients to proceed with ovulation induction should be viewed cautiously. Because laboratory estradiol levels vary between and within assays, the level of 75 pg/mL should be used only as a guideline. Further study on this subject will be necessary to investigate the proposed range of hormonal values (E2, P4) for optimizing the IVF outcomes.

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