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Title:

A ROBUST PROGESTERONE (P_4) RISE POST-SURGE IS INDICATIVE OF ADEQUATE LUTEINIZATION AND CONFERS IMPROVED PREGNANCY OUTCOMES EVEN IN THE PRESENCE OF A POST-TRIGGER FALL IN ESTRADIOL (E_2)

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Background:

After ovulation, primary production of estradiol (E_2) by granulosa cells cease and secondary secretion of progesterone (P_4), a LH-mediated activity, begins. A decrease in E_2 at post-ovulation trigger (Day +1) can signify poor oocyte quality after retrieval and may prompt cancellation of the cycle.

Objective:

The study evaluated the effect of an unpredictable drop in serum E_2 after surge on pregnancy outcomes. A secondary aim of the study was to assess whether degree of luteinization, particularly a high post-ovulation trigger P_4, impacted outcomes in the setting of a decrease in E_2.

Materials and Methods:

This retrospective study includes patients undergoing IVF between 2005-2015 who had a decrease in E2 on Day+1 and had a measured P_4 at surge. Patients were segregated according to percentage E_2 decrease on Day+1: A) ≤10%; B) >10%≤25%; C) >25≤40%; D) >40. Using these cohorts, secondary analysis included degree of luteinization, and patients were segregated accordingly (≤3ng/mL; >3ng/mL). Main outcome measures were pregnancy rate (PR), clinical PR, early pregnancy loss rate and live birth rate (LBR). Bivariate associations were examined using Pearson's Chi-square test and independent samples t-test, as appropriate. All statistical tests were two-sided and p-value<0.05 was considered statistically significant.

Result(s):

Of cycles analyzed, 1432 met the study's inclusion criteria [Table 1]. Age, day 3 FSH, basal AFC and endometrial thickness were similar between groups. Peak E_2 level at surge, E_2 level at Day+1, oocytes retrieved, number of embryos ongoing on day 1 and the number of embryos transferred were also similar between groups except for Group E, as there were no oocytes retrieved. PR, clinical PR and LBR decreased, while miscarriage rates increased with incremental drop of E_2. When P_4 on Day+1 was >3 ng/mL, higher PR, clinical PR and LBR were observed regardless of decrease in E2.

Conclusion(s):

As previously reported, an E_2 decrease on Day+1 is associated with lower pregnancy rates in fresh IVF cycles. Adequate or robust luteinization, as evident by a post-surge two-fold or greater P_4 increase, was associated with higher PR and clinical PR in each cohort. The rise in P_4 may serve as a surrogate marker for documenting the adequacy of ovarian response to trigger and controlled ovarian stimulation. This data provides clinicians with a deeper understanding of the dynamics of successful luteinization, enabling them to better counsel patients and to maximize cycle success.

Table 1: Cycle Parameters and Outcomes based on Percentage Decrease in E_2

	<10% (n=1240)	<25% (n=526)	<40% (n=66)	>40% (n=9)
Age (years)	37.3±4.5	37.6±4.5	37.2±5.1	37.3±6.4
Peak E_2 (pg/mL)	2059.7±1090.7	2092.0±1192.0	2156.2±1177.9	2133.8±1246.7
PR (P_4<3 ng/mL)	39.5% (227/575)	37.2% (86/231)	21.7% (5/23)	20.0% (1/5)
PR (P_4≥3 ng/mL)	50.8% (338/665)	46.4% (137/295)	51.2% (22/43)	50.0% (2/4)
Clinical PR (P_4<3 ng/mL)	30.6% (176/575)	31.6% (73/231)	13.0% (3/23)	20.0% (1/5)
Clinical PR (P_4≥3 ng/mL)	41.4% (275/665)	35.6% (105/295)	39.5% (17/43)	25.0% (1/4)
Loss rate (P_4<3 ng/mL)	15.7% (90/575)	14.7% (34/231)	17.4% (4/23)	0% (0/5)
Loss rate (P_4≥3 ng/mL)	17.3% (115/665)	19.0% (56/295)	18.6% (8/43)	25.0% (1/4)
LBR (P_4<3 ng/mL)	22.9% (130/568)	21.8% (179/229)	4.3% (1/22)	25.0% (1/4)
LBR (P_4≥3 ng/mL)	32.9% (442/659)	26.0% (214/289)	30.2% (30/43)	25.0% (1/4)