Defining the Luteal Placental Shift in Pregnancy Following Frozen Embryo Transfer

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Introduction

The luteal placental shift is defined as the time period when the placenta overtakes production of progesterone from the corpus luteum (CL). In natural pregnancy, this has previously been shown to occur around 7 weeks. In an FET, without the presence of a CL, only exogenous progesterone is present. Therefore, progesterone levels may be evaluated for a significant increases, indicating the luteal-placental shift has occurred.

The purpose of this study is to attempt to define the timing of the luteal-placental shift using pregnancies resulting from frozen embryo transfer (FET) as a model.

Methods

We identified 262 women who conceived following FET between December, 2013-December, 2016. Patients received oral estradiol (E2) for endometrial stimulation. Once the endometrial thickness exceeded 7mm, they started vaginal progesterone (P4), and blastocyst FET occurred on the 6th day of progesterone. An hCG was performed 9 days after FET, and serum E2 and P4 levels were monitored weekly until patients were weaned off of supplementation based on the serum levels.

E2 and P4 values for all patients were combined and evaluated in 3 day blocks (ranging from 4 weeks to 16 weeks gestation) to determine the timing of a significant increase in E2 and P4 using a multilevel model for change. The proportion of patients who reached a progesterone level >15 ng/mL, indicating that the luteal-placental shift had occurred, was evaluated for each gestational week.

Results

A significant increase in serum P4 level occurred between 6 and 7 weeks' gestation, such that by 7 weeks' gestation, 80% of patients had a serum P4 level over 15. All patients exhibited a serum P4 > 15 ng/mL by 10 weeks' gestation. A similar significant increase in serum E2 occurred between weeks 6 and 7.

Week Gestation	% of patients with P4 >15 ng/mL	Average E2 level per week gestation (pg/mL)
Week 4	40%	381.8
Week 5	47%	461.6
Week 6	56%	614.7
Week 7	80%	918.5
Week 8	91%	1075.8
Week 9	97%	1200.7
Week 10	100%	1331.0

The average progesterone levels were also plotted by gestational week to determine a significant increase in levels which would suggest the luteal-placental shift had occurred. The graphical interpretation shows the steepest slope between weeks 5-6 (m=4.54) followed by weeks 6-7 (m=4.34). The average estrogen levels were also graphically evaluated with the greatest rise between weeks 6-7 (m=303.8).

Conclusions

Frozen embryo transfer provides an excellent model for the assessment of the luteal-placental shift, as pregnant patients produce essentially no endogenous E2 or P4 until that time. By evaluating both absolute E2 and P4 levels as well as the rate of rise, we can surmise the timing of the actual shift. These data suggest that the actual shift occurs around 7 weeks' gestation, and that patients undergoing FET should continue to receive estradiol replacement until at least 7 weeks' gestational age and progesterone replacement until at least 8-9 weeks' gestational age.

References

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