IS PROGESTERONE LEVEL ON DAY OF FROZEN EMBRYO TRANSFER WORTH CHECKING?

Simone Elder[1], Bethelhem Shiferaw[2], Laura Katherine Kaizer[2], Mary D. Sammel[2], Cassandra Roeca[1]
[1]Shady Grove Fertility CO (University of Colorado AMC), Greenwood Village, CO
[2] Department of Biostatistics & Informatics, University of Colorado AMC, Aurora, CO

Background: Adequate progesterone (P4) supplementation for luteal support following frozen embryo transfer (FET) has been studied extensively as more clinics adopt the procedure in lieu of fresh embryo transfer. The intramuscular (IM) progesterone formulation has been previously shown to improve live birth rates in programed FET cycles. However, the optimal range of progesterone levels needed during FET cycles in order to sufficiently support implantation and an ongoing pregnancy remains elusive. Our study aims to examine the influence of luteal support during FET on clinical outcomes in the setting of recent IVF advances and improvements.

Objective: Evaluate the association between serum progesterone levels on day of transfer and subsequent pregnancy outcomes in women undergoing frozen embryo transfer using IM progesterone.

Materials and Methods: We identified patients who underwent in vitro fertilization followed by programmed FET from March 30, 2018 – September 15, 2023. We selected women who underwent aneuploidy preimplantation genetic testing (PGT-A) and who had a subsequent single embryo transfer. We included data from a clinic within our network which routinely collects P4 levels on all patients on the day of FET. Clinical pregnancy was the primary outcome and live birth was the secondary outcome. For statistical measures, associations between patient characteristics and P4 categories (10-<20, 20-<30, 30-<40, >40 ng/ml) were assessed using Chi-square tests, Fisher's exact tests, or ANOVA. The relationships between progesterone and the outcomes (clinical pregnancy and live birth) were assessed using log-binomial regressions. Unadjusted models and models adjusted for variables significantly associated with P4 were included. Risk ratios and their 95% confidence intervals were estimated for comparisons across groups of P4, using 10-<20 ng/ml as the reference group. These categories were used due to overall limited sample size.

Result(s): 178 subjects with known pregnancy outcomes were included of which 108 (60.67%) had a clinical pregnancy. Thus far, 61 (34.27%) had a live birth and an additional 24 (13%) subjects have on-going pregnancies. For patient demographics, only BMI was significantly different by P4 group with lower BMI having significantly higher values of P4. Categories of P4 were not significantly associated with clinical pregnancy in either unadjusted or adjusted models (p=0.392 and p=0.342, respectively after adjusting for BMI). Similarly, categories of P4 were not significantly associated with live birth in the unadjusted and adjusted models (p=0.444 and p=0.453, respectively; Table).

Conclusion: In our cohort, P4 level on day of programmed FET was not associated with clinical outcomes. Checking P4 level on day of FET may increase patient burden and negatively impact the workflow in clinics without significant improvement in cycle outcomes. Larger studies examining this relationship between P4 at the time of FET and pregnancy outcomes should be performed.

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Table. Risk Ratios from log binomial regression models

Outcome Variables	*Comparison*	*Unadjusted RR*	*p-value*	*Adjusted RR*	*p-value*
Clinical Pregnancy	*10-<20***	*1.00*	*0.392**	*1.00*	*0.342**
	20-<30	0.79 (0.60, 1.05)	0.111	0.79 (0.59, 1.04)	0.098
	30-<40	0.98 (0.74, 1.29)	0.872	0.99 (0.75, 1.30)	0.922
	40+	0.95 (0.66, 1.35)	0.762	0.97 (0.67, 1.40)	0.870
Live Birth	*10-<20*	*1.00*	0.444*	*1.00*	0.453*
	20-<30	0.68 (0.41, 1.12)	0.133	0.68 (0.41, 1.12)	0.127
	30-<40	0.82 (0.49, 1.38)	0.463	0.84 (0.50, 1.43)	0.530
	40+	0.66 (0.31, 1.41)	0.285	0.69 (0.32, 1.49)	0.344

Model adjusted for BMI. Age and endometrial thickness were not associated with either outcome and did not demonstrate a confounding effect.

*The type 3 analysis p-values are included, which test if, overall, there is a significant association between P4 groups and the outcome.

**Of note, two patients had P4 < 10 and were included in the 10-20 group.