

Progesterone Supplementation Prior to Transfer is Associated with Improved Outcomes in Natural Cycle Frozen Embryo Transfers in Patients with Suboptimal Luteal Progesterone

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BACKGROUND

In natural cycle frozen embryo transfer (NC-FET), the corpus luteum provides endogenous luteal support, however, several studies demonstrate that additional progesterone (P4) supplementation may improve LBR^{1, 2}. Optimal luteal support strategies remain undefined in the literature. Low serum P4 the day prior to transfer in NC-FET is associated with lower LBR³, highlighting the need to evaluate whether earlier P4 initiation improves outcomes.

OBJECTIVE

To compare the effectiveness of P4 supplementation initiated *before* embryo transfer vs standard post-transfer initiation on LBR in individuals undergoing NC-FET with low luteal P4 levels.

MATERIAL & METHODS

- Inclusion Criteria (n=110)**
 - First-ever NC-FET cycle
 - Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine (2017-2022)
 - Underwent serum P4 testing 1-2 days prior to transfer
- Study Design**
 - Comparison of clinical outcomes according to initiation of P4 supplementation before transfer (**Pre-transfer P4 supplementation**) vs after transfer (**Post-transfer P4 supplementation**).
- Statistics**
 - Clinical pregnancy rate (CPR), not pregnant (NP), live birth rate (LBR) were calculated per transfer. +hCG was considered >5mIU/mL
 - Metrics were evaluated for normality and presented as mean ± standard deviation or median (interquartile range)
 - T-test and Chi-square tests were used where applicable.

SUMMARY STATEMENTS

Pre-Transfer P4 supplementation in NC-FET may normalize live birth outcomes in patients with low luteal P4.

This may provide a practical alternative to cycle cancellation or conversion to a programmed cycle.

RESULTS

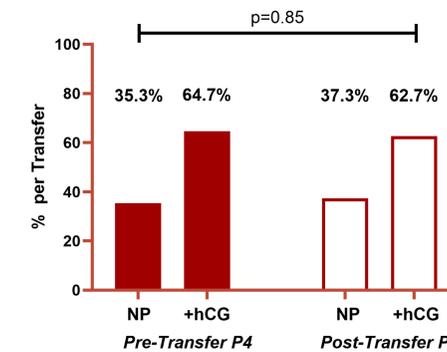
Baseline demographic and clinical characteristics were overall comparable, however, those with pre-transfer P4 supplementation had lower serum P4 1-2d prior to transfer, reflecting pre-transfer intervention.

	Pre-Transfer P4 Supplementation N=51	Post-Transfer P4 Supplementation N=59	P Value
Age at Retrieval	34.7 ± 5.1	35.6 ± 4.0	0.25
Age at FET	35.8 ± 5.2	36.4 ± 4.1	0.45
BMI	23.8 (21.2-27.6)	22.5 (8.1-24.6)	0.64
Percent transferring PGT-tested embryo	42.9%	60.3%	0.08
Serum P4 1-2d prior to transfer (ng/mL)	6.5 ± 2.0	11.3 ± 3.3	<0.0001

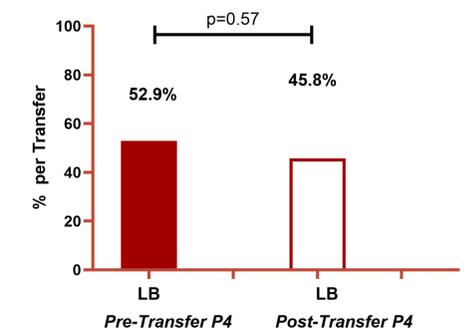
RESULTS

Similar rates of no pregnancy (NP), pregnancy, and live birth (LB) per transfer regardless of timing of P4 initiation.

Rates of no pregnancy and pregnancy per transfer



Rates of LB per transfer



CONCLUSIONS

- Despite significantly lower luteal P4 levels, patients undergoing NC-FET who received pre-transfer P4 supplementation achieved pregnancy and LBRs comparable to those with reassuring luteal P4 who proceeded with standard post-transfer P4 supplementation.
- These data support consideration of pre-transfer serum P4 assessment to guide individualized luteal support. Larger prospective studies are needed to validate these findings.

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