OPTIMIZING FROZEN EMBRYO TRANSFER PROTOCOLS IN PATIENTS WITH ENDOMETRIOSIS: A COMPARISON OF MODIFIED NATURAL AND PROGRAMMED CYCLES

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BACKGROUND

- Despite improvements in fertility treatments, women with endometriosis continue to have poorer outcomes compared to those without, suggesting alterations in endometrial receptivity and progesterone resistance may affect implantation[1].
- The optimal protocol for endometriosis patients remains unclear. Modified Natural cycles (mNC) and Programmed cycles with Progesterone in oil are the protocols most often used for this patient population.

OBJECTIVES

To compare pregnancy outcomes from a euploid single embryo transfer between mNC and programmed FET cycles in patients with endometriosis in a large, multicenter study.

MATERIALS & METHODS

Design: Retrospective cohort (2014–2024) comparing modified natural (mNC) vs programmed cycles for euploid FET in patients with confirmed endometriosis via laparoscopy or imaging.

Inclusion: Age <40, autologous oocytes, first single euploid transfer.

Exclusion: ≥41, untested embryos, uterine factor, RPL, donor/GC cycles, multiple transfer.

Data: Site, age, race/ethnicity, BMI, AMH, endometrial thickness.

Outcomes: Clinical pregnancy, live birth, miscarriage.

Analysis: Modified Poisson with GEE; R v4.3.1; $p<0.05$.

RESULTS

- A total of 763 patients met inclusion criteria; 62 patients who underwent a mNC and 701 who underwent a programmed cycle.
- Maximal endometrial thickness was higher in the programmed cycle compared to the mNC group (p=0.049) (Table 1).
- After adjusting for age, BMI, and clinical site, **there was no difference in clinical pregnancy rate or miscarriage rates, live birth, or miscarriage rates per transfer for a mNC compared to a programmed cycle** (Table 2).
- A total of 116 patients who underwent a programmed FET received pre-treatment GnRH downregulation and this did not alter pregnancy rates (Figure 1).

Table 1: Demographics

Characteristic	Overall (n=763)	Programmed (n=701)	mNC (n=62)	P-value
Age, mean (SD)	34.5 (3.05)	34.4 (3.07)	35.3 (2.76)	0.4
<35 35–37 38–39	351 (46%) 279 (36.6%) 133 (17.4%)	327 (46.6%) 255 (36.4%) 119 (17.0%)	24 (38.7%) 24 (38.7%) 14 (22.6%)	
BMI, mean (SD)	25.4 (5.09)	25.5 (5.14)	24.6 (4.43)	0.2
Race/Ethnicity Asian Black/African American Hispanic/Latino Other Unknown White	 133 (17.4%) 30 (3.9%) 39 (5.1%) 47 (6.2%) 201 (26.3%) 313 (41.0%)	 120 (17.1%) 29 (4.1%) 37 (5.3%) 45 (6.4%) 186 (26.5%) 284 (40.5%)	 13 (21%) 1 (1.6%) 2 (3.2%) 2 (3.2%) 15 (24.2%) 29 (46.8%)	
AMH, mean (SD)	3.24 (3.21)	3.27 (3.29)	2.92 (2.10)	0.7
Endometrial thickness max, mean (SD)	10.33 (2.50)	10.38 (2.54)	9.75 (1.87)	0.049

Table 2: Pregnancy Outcomes

Rates	Overall	Programmed FET	mNC FET	RR (95% CI)
Implantation Rate (biochemical + clinical pregnancy/N transfer)	553 (78.7%)	503 (71.8%)	50 (80.6%)	1.22 (0.88, 1.66)
Clinical Pregnancy Rate (intrauterine pregnancy/N transfer)	485 (63.6%)	438 (62.5%)	47 (75.8%)	1.21 (1.04, 1.41)
Live Birth Rate (N live birth/N transfer)	432 (56.6%)	391 (55.8%)	41 (66.1%)	1.19 (0.84, 1.65)
Miscarriage Rate (N miscarriage/N transfer)	48 (6.3%)	45 (6.4%)	3 (4.8%)	0.64 (0.25, 1.36)

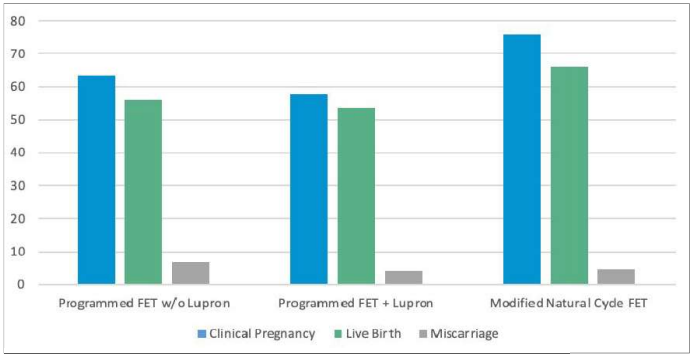

Figure 1: Pregnancy Outcomes of GnRh Agnoist Prior to FET

CONCLUSION

We found no difference in pregnancy outcomes in women with endometriosis based on endometrial preparation, similar to prior retrospective studies from China[2,3]. Furthermore, the addition of a GnRH agonist to reduce inflammation and improve endometrial receptivity prior to transfer did not alter clinical pregnancy or live birth outcomes, although there was a non-significant trend towards reduced miscarriage rates. The findings of this study may provide reassurance to patients and providers on the efficacy of alternative FET protocols for women with endometriosis.

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