IMPROVED OUTCOMES WITH PROGRAMMED VS NATURAL CYCLES FOR FROZEN EMBRYO TRANSFER (FET) IN PATIENTS WITH ENDOMETRIOSIS

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Background:

Research on IVF outcomes in patients with endometriosis has shown conflicting results, with some studies reporting diminished outcomes and others reporting no impact. Endometriosis may impair fertility by reducing oocyte quality, altering follicular fluid composition, and compromising endometrial receptivity. For FET, endometrial preparation can be performed using natural (NC) or programmed cycles (PR). Programmed cycles include luteal suppression, which may mitigate the effects of endometriosis. We hypothesized that PR would yield improved outcomes vs NC cycles in patients with endometriosis.

Objective

To compare the outcomes of programmed versus modified natural FET cycles in patients with endometriosis.

Materials and Methods

This retrospective cohort study included patients with a SART diagnosis of endometriosis, who underwent FET between 2016 and 2023 at a single academic fertility center. Patients were grouped according to their endometrial preparation protocol, PR or NC. Primary outcomes were clinical pregnancy (CP) and live birth (LB), while secondary outcomes included positive hCG, spontaneous abortion (SAB), and biochemical pregnancy (BP). Unadjusted comparisons were conducted using chi-squared and t-tests. Generalized estimating equations were applied to control for potential confounders [age, body mass index (BMI), number of embryos transferred, use of donor oocytes, and multiple transfers per patient]. A sub-analysis was performed for transfer of euploid embryos by preimplantation genetic testing for aneuploidy (PGT-A) only.

Results

159 FETs were included from 110 patients, 49 (31%) NC and 110 (69%) PR. Both groups were comparable in age, BMI, AMH, number of embryos transferred, and use of PGT-A. In the unadjusted analysis, PR cycles demonstrated higher CP (63% vs 36%, p=0.002) and LB rates (44% vs. 30%, p=0.098) vs NC. PR cycles also had a significantly higher rate of positive hCG (72% vs. 44%, p=0.001) and SAB (14% vs. 2%, p=0.018), while BP rates were similar (9% vs. 8%, p=0.849).

After adjusting for confounders, PR cycles remained associated with improved odds of CP (adjOR 1.3 [95% CI 1.11, 1.54]) and positive hCG (adjOR 1.45 [95% CI 1.25, 1.69]), with no significant difference in LB (adjOR 1.13 [95% CI 0.96, 1.43]) or BP (adjOR 1.0 [95% CI 0.91, 1.1]). Although SAB rates were higher with PR cycles, the adjusted OR (adjOR 1.15 [95% CI 1.03, 1.29]) suggests a mild increase.

In the sub-analysis limited to euploid embryo transfers, PR cycles were associated with improved odds of CP (adjOR 1.54 [95% CI 1.19, 1.98]) and LB (adjOR 1.43 [95% CI 1.07, 1.78]). Similarly, the odds of positive hCG were higher with PR cycles (adjOR 1.43 [95% CI 1.15, 1.63]). However, there was no significant difference in SAB (adjOR 1.12 [95% CI 0.96, 1.28]) or BP rates (adjOR 1.0 [95% CI 0.89, 1.28]).

Conclusion

Programmed cycles were associated with improved outcomes vs modified natural in patients with endometriosis. PR cycles resulted in higher rates of positive hCG and CP. When limiting to euploid FET, LB rates were higher in PR cycles. These findings suggest that PR may mitigate the adverse effects of endometriosis and improve fertility outcomes. If confirmed by larger studies, these results could guide clinical decision-making and patient counseling to optimize outcomes.

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References: None