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Title:

IN PATIENTS WITH SUB-OPTIMAL ENDOMETRIAL LINING, DOES THE ROUTE OF ADMINISTRATION OF SUPPLEMENTAL ESTROGEN CORRELATE WITH FROZEN EMBRYO TRANSFER OUTCOMES?

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Objective:

Patients routinely receive supplemental oral estrogen in preparation of the endometrial lining prior to a frozen embryo transfer (FET). In patients with suboptimal growth, additional vaginal or transdermal estrogen supplementation may be prescribed in attempt to increase estrogen absorption and optimize uterine lining thickness. To date, there are limited data analyzing the clinical utility of either route. This study aims to evaluate the correlation of vaginal or transdermal estradiol supplementation with patient FET cycle outcomes.

Design:

Retrospective cohort analysis

Materials and Methods:

The study included patients who underwent an autologous or donor egg FET cycle with an endometrial thickness of <7mm on cycle day 10-15 from November 2005-April 2019. Patients were separated into groups by route of additional E2 supplementation (vaginal estradiol tablets (E2 PV group); transdermal estrogen patch (E2 TD group)). Baseline demographics and cycle



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characteristics were collected. Outcomes included endometrial stripe (EMS) at embryo transfer, chemical pregnancy rate, clinical pregnancy rate, and live birth rate. A sub-analysis of euploid FET was performed. A sub-analysis was performed in patients with a structural uterine factor (as identified by an initial hysterosalpingogram (HSG) or saline infusion sonohysterography (SIS)). Statistical significance was calculated using chi-square test and t-test. A p value of 0.05 was set for statistical significance.

Results:

A total of 414 patients underwent 461 FET cycles within the study, including 396 E2 T2 cycles and 65 E2 PV cycles. Baseline demographics were similar between the two groups. A statistically significant increase in EMS at transfer was seen in the E2 PV group compared to the E2 TD group, however, the absolute difference was 0.01 mm (E2 TD 8.34 (4.6-15.5, SD \pm 1.57 vs E2 PV 8.35 (5.1-15.63, SD \pm 2.23), $p=0.0002$). No statistically significant differences in chemical pregnancy, clinical pregnancy, or live birth rates were seen. In the sub-analysis of euploid FETs, EMS at transfer was significantly greater in the E2 PV compared to E2 TD group (8.66 (5.1-15.6, SD 2.06) vs. 8.32 (5.3-13.7, SD 1.53), $p=0.0062$). A significant increase in chemical pregnancy rate was seen in the E2 PV compared to E2 TD group (75% vs. 59.4%, $p=0.05$). However, clinical pregnancy rates and live birth rates were similar. In the sub-analysis of patients with an initially abnormal SIS or HSG, EMS at transfer was significantly lower in the E2 PV compared to E2 TD group (7.05 (5.2-9.0, SD \pm 1.13) vs. 8.11 (5.12-12.46, SD \pm 1.65), $p=0.049$). No significant differences were seen in clinical pregnancy, chemical pregnancy, and live birth rates.

Conclusion:

Supplemental vaginal and transdermal estradiol were equally effective in achieving endometrial thickness >7 mm, and both methods resulted in similar pregnancy outcomes. Patients can be comforted in knowing that both routes of estrogen supplementation are effective in supporting the endometrial lining prior to FET, and choice of method may be based on patient and provider preference.