

Effect of Endometrial Scratch Injury on Frozen Embryo Transfer Cycles: A Randomized Controlled Trial

Research Article

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Abstract

Aim: To evaluate whether local endometrial scratch injury (ESI) performed during oocyte retrieval improves clinical pregnancy outcomes in frozen embryo transfer (FET) cycles.

Methods: This randomized controlled trial included 333 women under the age of 42, each with at least one prior failed embryo transfer, who underwent FET between March 2015 and May 2024. Patients were assigned to either the ESI group (n = 175) or control group (n = 158). Endometrial scratch was performed once during oocyte retrieval under general anesthesia. Histopathological evaluation of endometrial tissue was also conducted.

Results: No significant differences in baseline characteristics were found. Clinical pregnancy rates were 45 % in the ESI group versus 38 % in controls. Among those with clinical pregnancies, the ongoing pregnancy rate was 43 % in the ESI group and 34 % in the control group.

Conclusion: Endometrial injury during oocyte retrieval may enhance pregnancy outcomes and reduce miscarriage risk in women with prior failed embryo transfers.

Keywords: Embryo transfer, Endometrial injury, Endometrial scratch, Pregnancy rate, Frozen embryo transfer.

Introduction

Repeated implantation failure in assisted reproductive technology (ART) remains a significant challenge, even when high-quality embryos are transferred. One proposed method to improve implantation is endometrial scratch injury (ESI), which may enhance endometrial receptivity through inflammatory and molecular changes. Although some studies report inconsistent results, there is increasing interest in the timing and application of ESI, especially in frozen-thawed embryo transfer (FET) cycles.

Materials and Methods

This randomized controlled trial included 333 patients under 42 years of age with at least one previous failed embryo transfer, who underwent frozen embryo transfer (FET) between March 2015 and May 2024. Patients were randomly assigned to the ESI group (n = 175) or the control group (n = 158) based on the last digit of their clinical record number. The study was conducted at a private IVF center under

the supervision of Assoc. Prof. Dr. Fatma Altıntaşoğlu Horasan.

The endometrial scratch procedure was performed once during oocyte retrieval using an endometrial sampler catheter under general anesthesia. Endometrial tissue samples were sent for histopathological examination. Patients received either hormone replacement therapy (HRT) or were monitored for natural ovulation cycles. Exclusion criteria included uterine anomalies, endometriomas larger than 5cm, and hydrosalpinx.

Ovarian stimulation was performed using a GnRH antagonist protocol, and intracytoplasmic sperm injection (ICSI) was applied to all oocytes. Embryos were cultured to the 2-5days and vitrified. During FET cycles, endometrial thickness and serum hormone levels were monitored, and good-quality embryos were selected for transfer. Luteal phase support was provided. Serum β -hCG was measured 10–12days after transfer, and ultrasound was performed to confirm clinical pregnancy.



Statistical Analysis

Statistical analyses were conducted using Student's t-test and Mann-Whitney U-test for continuous variables. Categorical data were compared using the chi-squared test. P-value < 0.05 was considered statistically significant. Relative risks (RR) with 95% confidence intervals (CI) were calculated for each outcome.

Results

A total of 333 patients were enrolled, with 175 in the ESI group and 155 in the control group. Baseline characteristics, including age, BMI,

duration of infertility, and cause of infertility, were comparable between the groups. (Table 1) summarizes the baseline and cycle characteristics of both groups. The clinical pregnancy rate was 45 % in the ESI group and 38 % in the control group, the ongoing pregnancy rate was significantly higher in the ESI group (43 %) compared to the control group (34 %). (Table 2) shows detailed pregnancy outcomes. There were no statistically significant differences in embryo quality, number of embryos transferred, or endometrial thickness between the groups. Subgroup analysis stratified by number of previous embryo transfers (≥ 1 , ≥ 2 , ≥ 3) and IVF failures did not show statistically significant differences in pregnancy outcomes.

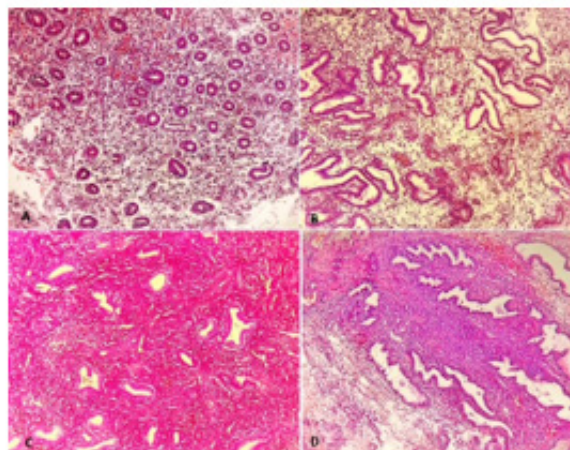


Figure: A- Proliferative endometrium (hematoxylin-eosin, original magnification $\times 100$).

B- Secretory endometrium (hematoxylin-eosin, original magnification $\times 100$).

C- Hyperplastic endometrial polyp (hematoxylin-eosin, original magnification $\times 100$).

D- Functional endometrial polyp (hematoxylin-eosin, original magnification $\times 100$).

Table 1: Baseline and Cycle Characteristics.

Characteristics	ESI Group (n = 175)	Control Group (n = 158)
Age (years)	36.90 \pm 3.32	36.78 \pm 3.45
BMI (kg/m ²)	21.36 \pm 2.81	21.90 \pm 2.81
Infertility duration (years)	4.74 \pm 3.62	4.73 \pm 3.26
Primary infertility (%)	28 (30.1%)	31 (33.3%)
Secondary infertility (%)	65 (69.9%)	62 (66.7%)
Tuboperitoneal factor (%)	45 (48.4%)	46 (49.5%)
Endometriosis (%)	16 (17.2%)	21 (22.6%)
Male factor (%)	42 (45.2%)	44 (47.3%)
Unexplained infertility (%)	5 (5.4%)	3 (3.2%)
1-2 previous IVF attempts	85 (91.4%)	88 (94.6%)
3-4 previous IVF attempts	8 (8.6%)	5 (5.4%)

Table 2: Pregnancy Outcomes per Transfer (Per-Protocol Analysis).

Parameter	ESI Group (n = 175)	Control Group (n = 158)	Relative Risk (95% CI)
Positive HCG rate	85 (48.4%)	69 (43.0%)	1.125 (0.822-1.540)
Biochemical pregnancy rate	6 (6.5%)	5 (5.4%)	1.200 (0.379-3.795)
Clinical pregnancy rate	78 (45.9%)	61 (38.6%)	1.114 (0.782-1.588)
Miscarriage rate	7 (17.9%)	6 (17.1%)	0.946 (0.285-3.142)
Multiple pregnancy rate	4 (10.3%)	4 (11.4%)	0.897 (0.242-3.321)
Ongoing pregnancy/live birth rate	72 (43.4%)	55 (34.2%)	1.158 (0.627-2.137)

Discussion

This randomized controlled trial demonstrated that endometrial scratch injury (ESI), when performed during oocyte retrieval, is associated with improved clinical and ongoing pregnancy rates in women undergoing frozen embryo transfer (FET) cycles. Our findings support the hypothesis that ESI may enhance endometrial receptivity and facilitate embryo implantation, particularly in patients with previous implantation failure [1-6]. The precise mechanisms underlying this improvement remain unclear, but may involve a localized inflammatory response, increased cytokine and growth factor expression, enhanced decidualization, and upregulation of genes associated with uterine receptivity. Previous studies have reported variable results, potentially due to differences in timing, technique, and patient selection [7-9].

Unlike studies that performed endometrial injury during the proliferative or COH phase, our procedure was standardized during oocyte retrieval under general anesthesia, minimizing patient discomfort and allowing histopathological evaluation. The mild nature of the injury, limited to the functional layer, may have contributed to favorable outcomes without adverse effects [1,10-12]. Strengths of our study include a large sample size and consistent timing of the ESI procedure. Limitations include the heterogeneity of patient characteristics and the inability to identify specific subgroups who may benefit most. Although subgroup analysis did not reveal significant differences, larger studies are needed to confirm these findings [13].

Clinical pregnancy rate is defined, as the number of clinical pregnancies (gestational sacs observed ultrasonographically) divided by the number of embryos transfer cycles.

Ongoing pregnancy was defined when the pregnancy had completed ≥ 20 weeks of gestation. The ongoing implantation rate was defined as number of fetuses with heart activity beyond 20 weeks of gestation per transferred embryo.

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