

The Effect of Endometrial Scratching before Embryo Transfer in Woman with History of Implantation Failure in Previous Intracytoplasmic Sperm Injection Cycle; Clinical and Biological Study

Abstract

Background: The gain of endometrial scratching in people has been offered with the aid of clinicians as a potential of growing endometrial receptivity was once at the beginning stated as a serendipitous discovering because a high pregnancy price was once located in IVF female who had undergone repeated endometrial biopsies at some stage in their preceding herbal menstrual cycle. The goal of this work used to be to consider the impact of endometrial scratching earlier than fresh or frozen embryo switch on clinical pregnancy fee in girls with records of implantation failure after one or more Intracytoplasmic sperm injection cycle(s) and to predict its cost based on measuring the level of peripheral Natural Killer Cells (cd56).

Methods: This potential randomized learn about was carried out on 60 ladies with records of one or more implantation failure of ICSI cycle, and regular uterine cavity. Patients were divided into two equal groups: an experimental group A and a manage group B. All sufferers were subjected to history taking, clinical examination, investigations for infertility, serum Natural killer cells CD56 measure and hormonal profile.

Results: There was once giant difference in CD56 size between girls who obtained pregnant (decreased CD56) and those who now not got pregnant (increased CD56) in team A .Clinical Pregnancy rate was higher in group A after endometrial scratching was done.

Conclusions: Performing harm profiling at the time of implantation window (CD56 measurement) ought to assist in deciding on sub-groups of infertile patients who would gain from a targeted intervention.

Keywords: Endometrial scratching, Embryo transfer, implantation failure, Intracytoplasmic

sperm injection

Introduction: “The gain of endometrial scratching in human beings which is additionally called endometrial biopsy, endometrial injury, and endometrial trauma, has been supplied through clinicians as a ability of growing endometrial receptivity was once at the start pronounced as a serendipitous finding because a excessive pregnancy rate used to be determined in IVF women who had undergone repeated endometrial biopsies at some point of their preceding herbal menstrual cycle” [1] .

“Barash et al. [1] had been the first to take a look at the speculation that endometrial damage in the natural cycle prior to controlled ovarian hyperstimulation (COH) may want to expand the danger of being pregnant and observed a two-fold expand in stay start price after more than one endometrial scratches in contrast to no scratch. (48.9% vs 22.5 %). Subsequently, a range of research have indicated a conceivable scientific cost of this intervention, mainly in repeated implantation failure (RIF) patients”.

“Endometrial scratching upregulated the expression of seasoned inflammatory cytokines worried in the recruitment of monocytes and their differentiation into macrophages and Dendritic Cells (DCs). These cells are known to trigger the expression of pro-implantation genes in endometrial epithelium and stroma, enabling the apposition and adhesion of the blastocyst” [2].

“DCs and macrophages had been proven to secrete an array of cytokines and enzymes allowing tissue remodelling and angiogenesis, required for the endometrial decidualization and legislation of trophoblast invasion” [3].

“This differentiation of stromal cells inside the decidualization manner is an crucial step for a successful implantation. The scratching induced amplify of VEGF (Vascular Endothelial Growth Factor), a central increase element involved in nearby angiogenesis and placentation” [4].

“The uterine Natural Killer cells (uNK) are every other imperative immune cell population in the human endometrium. Described as CD56bright CD16dim, uNKs are found in the endometrium at the beginning of each menstrual cycle as small agranular cells” [4].

“The aim of this work used to be to consider the effect of endometrial scratching earlier than clean or frozen embryo switch on scientific being pregnant rate in female with history of implantation failure after one or more Intracytoplasmic sperm injection cycle(s) and to predict its value based on measuring the degree of peripheral Natural Killer Cells”.

Patients and Methods:

This potential randomized medical study was once carried out on 60 ladies aged from 18 to 40 years historic at time of embryo transfer, with records of one or greater implantation failure of ICSI cycle, and ordinary uterine cavity (assessed via transvaginal sonography at reserving and no endometrial abnormalities such as, suspected intrauterine adhesions, uterine septa, submucosal fibroids or intramural fibroids exceeding 4 cm in diameter as assessed through the investigator that would require cure to facilitate pregnancy). Exclusion standards had been previous trauma/surgery to the endometrium (e.g., resection of submucous fibroid, intrauterine adhesions), body mass index (BMI) of 35 kg/m² or greater, regarded grade 4 (severe) endometriosis or any degree of adenomyosis and currently taking part in any different fertility study involving medical/surgical intervention.

The patients were divided into two equal groups: an experimental group A (before endometrial scratching, peripheral blood sample was once taken for the measurement of stage of the natural killer cells CD56 by flowcytometry) and a manage group B.

All sufferers subjected to: History taking (full personal, present, past, menstrual and obstetric history), medical examination (general, abdominal and gynaecological examination), investigations for infertility (trans vaginal ultrasound, serum Natural killer cells CD56 measure (only for patients of team A) and hormonal profile (basal FSH, LH and E2. TSH and

Prolactin)).

Blood samples have been accumulated from sufferers at time of examination. For immunophenotyping analysis, two mL of blood were accrued in glass tubes containing EDTA and analysed by glide cytometry inside 24 h after series in order to become aware of CD16 , and CD56 lymphocytes.

Patients in team A, underwent endometrial scratching once between days 20 and 22 of menstrual cycle in the cycle prior to the deliberate ICSI cycle or Embryo Transfer. After applying the cusco speculum in the vagina for disinfection of the uterine cervix with betadine, an endometrial curette (Novac Curette) will be added thru the cervix up to the uterine fundus, after which the examiner slowly retracts the curette while rotating over countless tiers of 360° during 1–2 min.

Endometrial thickness and blood flow had been measured by means of TVS ultrasonography on the day of HCG administration. Oocyte retrieval was carried out 34–36 h after the HCG injection the use of cook's ovum pick out up needle (17 Fr) with the aid of TVS route under ultrasound preparation beneath established anaesthesia. Retrieved oocytes have been inseminated or injected with sperms (intracytoplasmic sperm injection). Fertilization test was finished after 18 h of insemination and embryos were cultured in sequential medium (Vitrolife, Sweden).

Embryo Transfer (ET) used to be done on day 2–5 using ET catheter (Cook, Ecotip). Luteal phase aid in the shape of injection progesterone one hundred mg intramuscular every day or vaginal pessary 400 mg twice day by day was once administered to each the groups.

The outcome measure: medical pregnancy rate (calculated as the number of patients with medical being pregnant (by the detection of foetal heartbeat with an ultrasound scan) divided by the wide variety of patients who underwent ET), between the find out about organizations and its correlation to Natural Killer (NK) cells measurement.

Statistical analysis

Data was computerized using excel sheet. All data analysis was carried out using Statistical Package for the Social SPSS IBM version 19.0. Descriptive statistics, such as mean, median, standard deviation, and range value were calculated for continuous variables. After testing for normality assumptions, using appropriate statistics, mean value was compared between two groups using Student's t independent test. Frequency distributions of categorical variables were compared using Chi Square/Fisher's exact test as appropriate. For all statistical tests, the probability of $P < 0.05$ was considered for statistical significance.

Results:

Age, LH, FSH and E2 were insignificantly different between two groups while BMI was significant higher in group B than group A ($p = 0.001$). **Table 1**

Table 1: Comparison of age, BMI and hormonal profile (LH, FSH, E2) between the two groups

	Group A	Group B	p. value
Age	32.00 ± 3.58	31.93 ± 3.72	0.944
BMI	20.16 ± 1.03	21.34 ± 1.46	0.001*
LH	4.53 ± 2.31	4.19 ± 2.20	0.563
FSH	7.01 ± 1.69	7.32 ± 1.75	0.490
E2	122.01 ± 62.31	149.67 ± 70.84	0.114

Data represented in mean ± standard deviation, *: statistically significant p value, BMI: body mass index LH: luteinizing hormone, FSH: follicle stimulating hormone, E2: estradiol

TSH was insignificantly different between two groups while prolactin was significant higher in group B than group A ($p = 0.030$). **Table 2**

Table 2: Comparison of TSH and Prolactin hormone between the two groups.

	Group A	Group B	p. value
TSH	2.40 ± 1.04	2.27 ± 0.88	0.585

Prolactin	16.07 ± 5.09	18.48 ± 3.03	0.030*
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Data represented in mean ± standard deviation, *: statistically significant p value, TSH: thyroid stimulating hormone

There was insignificant difference between the two groups in the number of previous implantation failure after ICSI cycle. **Table 3**

Table 3: The number of previous implantation failure after ICSI cycles, between the two groups

Number of Implantation failure ICSI cycle	Group A	Group B	P-value	X2
1	16 (53.3%)	15 (50.0%)	0.771	0.519
2	12 (40.0%)	14 (46.7%)		
3	2 (6.7%)	1(3.3%)		

Data represented in frequency (%), ICSI: Intracytoplasmic Sperm Injection

Level of peripheral Natural Killer Cells (cd56) was significantly higher in women who not got pregnant than those who got pregnant in patients of group A (p=0.001). **Table 4**

Table 4: Measurement of natural killer cells CD56, between women who got pregnant and women who not got pregnant in patients of group A.

	Pregnant	Non pregnant	t. test	p. value
Natural killer cells (cd56)	77.47 ± 9.29	215.4 ± 91.16	5.830	0.001*

Data represented in mean ± standard deviation, *: statistically significant p value

Pregnancy rate was insignificantly different between two groups. **Table 5**

Table 5: difference in Clinical pregnancy rate between the two groups

	Group A	Group B	P-value
Pregnancy rate	15 (50.0%)	10 (33.3%)	0.190

Data represented in frequency (%)

Discussion:

“Intentional endometrial injury is frequently being carried out in female present process IVF besides conclusive scientific evidence on its really helpful effects.

Multiple studies have been carried out to look into the effect of endometrial

scratching in girls undergoing ART cycles, but the technique of scratching, the population being scratch, and the find out about pleasant varies extensively” [8].

“The results of the existing study suggest that implantation fee is drastically improved after nearby injury to the endometrium. In this method we measured the level of peripheral Natural Killer Cells CD56 in mid-luteal section to understand the relation between it and the impact of endometrial scratching. The endometrial scratching used to be encouraged solely if the affected person was once diagnosed with a lack of peripheral Natural Killer Cells CD56. The endometrial scratching took location during the mid-luteal segment of the preceding cycle to the actual embryo transfer.”

“Barash et al. [1] in 2003, had been first to document that IVF treatment that is preceded by means of endometrial biopsy doubles the danger for a takehome baby. A complete of 134 sufferers have been divided into two groups: An experimental crew (n = 45) that included patients from whom endometrial samples had been accumulated and a manage group (n = 89)”.

“The implantation rate in the biopsytreated sufferers was once 27.7%, which is considerably higher than that in the manipulate group. Moreover, 30 of the 45 patients in the biopsytreated group conceived, exhibiting a doubled charge of pregnancy as compared to that of the manage group. Live births charge in the biopsytreated patients was greater than twofold greater than that in the controls” [1]

“Raziel et al., [9] prospectively studied one hundred twenty couples with highorder implantation failure of >4 unsuccessful ET of fresh embryos. Intervention team (n = 60) underwent endometrial biopsy twice on days 21 and 26 of the preceding ovarian stimulation cycle; manage group had no intervention (n = 57). Implantation charge used to be drastically

higher for the biopsy group, whereas no statistically sizeable difference used to be discovered for the ongoing being pregnant and miscarriage rates. Compared with that of the controls: The respective rates have been 11% versus 4% for implantation, 30% versus 12% for pregnancy, and 2% versus 8% for ongoing pregnancies. The abortion fee was 28% for each group”.

“Shohayeb and El Khayat [10] in 2012 located that the single endometrial biopsy regimen carried out during hysteroscopy has statistically tremendous higher implantation rate, clinical being pregnant rate, and live beginning price than hysteroscopy without endometrial scraping”.

There were statistically full-size variations concerning the implantation rate, the clinical pregnancy rate, and stay beginning rate. The implantation price in Group A was 12% while in Group B it was once 7%, the medical pregnancy rate used to be 32% in Group A whilst it was solely 18% in Group B, and the live beginning price was 28% in Group A whilst it was 14% in Group B. The abortion price used to be 12.5% in Group A whilst it was 22% in Group B, with no statistically substantial distinction ($P = 0.618$).

“However, Karimzade et al., [12] evaluated the effect of nearby harm to the endometrium on the day of oocyte retrieval on implantation and pregnancy costs in assisted reproductive cycles. They concluded that local injury to the endometrium on the day of oocyte retrieval disrupts the receptive endometrium and has a negative affect on implantation and IVF outcomes. Significantly lower implantation rate (7.9 vs. 22.9%, $P = 0.002$) used to be cited in the experimental team in contrast with the controls”.

“Similarly, Safdarian et al., [13] also discovered that endometrial biopsy did not expand the chances to conceive at the following cycle of treatment. Patients were divided to manage groups ($n = 50$) and experimental team ($n = 50$), who underwent endometrial biopsy.

Endometrial biopsy in these sufferers was once taken by using biopsy catheter on day 21 of their preceding menstrual cycle with use of contraceptive capsule earlier than the IVF-ET treatment. The charges of implantation, chemical pregnancy, and scientific being pregnant in the operation team were 4.9% 18.2%, 12.1%, and in the control crew 6.7%, 19.5%, 17.1%, respectively, that had been now not significant differences”.

Conclusions:

Implantation price will increase drastically after endometrial scratching in patients with previous failed ICSI. Endometrial scratching motives modifications within the endometrium, gene expression, and the immune system, main to stronger endometrial receptivity and higher implantation environment. Performing damage in previous cycle is more fantastic as all these approaches require time and are controlled through the hormones. This is a simple and inexpensive process with lot of benefits as in contrast to risks of contamination and conceivable of future subfertility.

Endometrial immune profiling at the time of implantation window; represented in our study by using the level of peripheral Natural Killer Cells CD56, should assist in deciding on sub-groups of infertile patients who would advantage from a centered intervention. In our experience, within a large populace of sufferers having a history of unexplained repeated embryo implantation failure, only 1/2 of them confirmed a low endometrial immune activation, potentially justifying an endometrial scratching

Consent and Ethical Approval:

An informed written consent was acquired from the patient. The learn about used to be finished after ethical approval from the Institute Ethics Committee.

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