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Original Research Article

Endometrial Thickness and Embryo Quality in the Implantation in the Natural Cycle in Vitro Fertilization: A Prospective Analysis

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Abstract:

Background and Aim: The challenge of determining thickness at the beginning of growth is one of the major issues in studying change in endometrial thickness. In contrast to a stimulated IVF cycle, one follicle that naturally develops to dominance is the treatment focus in NC-IVF, which leads in the majority of instances with a single embryo being available for transfer. The aim of our study is to assess the effect of endometrial thickness and embryo.

Material and Methods: After Natural Cycle in Vitro Fertilization (NC-IVF) was carried out, 250 cases of ET were included in the study. Based on the results of the -hCG pregnancy test two weeks after ET and confirmation by transvaginal ultrasound at six weeks of gestation, the patients were split into two groups: those who were pregnant and those who were not. At the commencement of monitoring (the first to fourth day of the cycle), the levels of estradiol, progesterone, follicle-stimulating hormone (FSH), and LH in serum were assessed. During subsequent routine control visits, millimeter-level ultrasound measurements of the follicle and endometrial thickness were taken every two days after measuring estradiol, progesterone, and LH. The NC-IVF cycle was stopped by the increasing slope of LH (> 20 mIU/mL), declining estradiol levels, and progesterone levels of 1.5 ng/mL.

Results: When results were compared between the two groups, the pregnant woman group's endometrial thickness was found to be significantly larger. ($p \leq 0.05$) The highest implantation potential and in utero survival were found in embryos with fragmentation less than or equal to 10% in both univariate and multivariate analyses (p 0.01 and p 0.05, respectively). 18.8% of embryos implanted overall after transfer.

Conclusion: Endometrial thickness and embryo quality have a big impact on implantation in NC-IVF. The 8-cell embryos with the lowest or equivalent 10% fragmentation on the third day after oocyte retrieval have the highest implantation potential.

Keywords: Embryo, Endometrial thickness, Human Chorionic Gonadotrophin, Natural Cycle in Vitro Fertilization.

Introduction

It has been said that human reproduction is surprisingly ineffective. This assertion seems justified given that only 40–60% of all conceptions in young, healthy women result in a live birth. Human chorionic gonadotrophin (hCG), which rises in maternal blood and urine once the embryo embeds in the endometrium, enables accurate estimations of the incidence of pregnancy loss. Numerous studies have found striking consistency in the finding that one in three embryos die after implantation.[1,2] In 1993, a study on the relationship between high progesterone levels and the calibre of embryos was published for the first time. According to several reports, PL has little impact on the viability of embryos. Additionally, donor/recipient cycles and freeze-thaw cycles don't

appear to be affected negatively by PL. However, Huang et al. showed that in gonadotropin-releasing hormone (GnRH) antagonist cycles, the rates of high-quality blastocyst formation are adversely associated to P4 levels on the day of oocyte maturation.[3,4] Mammal endometrium is necessary for the beginning and upkeep of pregnancy. In order to retain its function, the endometrium in females grows and disappears frequently throughout the menstrual cycle. Infertility may therefore be indicated by endometrial thickness, which is commonly measured by ultrasonography (USG).[5,6]

The challenge of determining thickness at the beginning of growth is one of the major issues in studying change in endometrial thickness. While a woman is still shedding endometrium from the previous cycle, basal layer endometrial growth begins. In most situations, it won't be possible to assess new endometrial growth until the fifth day of the cycle, making any assessment of new endometrial growth by ultrasonography during menstruation erroneous. Endometrial proliferation can be started after menstruation during assisted conception cycles, which can help to lessen this issue.[7,8]

In contrast to a stimulated IVF cycle, one follicle that naturally develops to dominance is the treatment focus in NC-IVF, which leads in the majority of instances with a single embryo being available for transfer. Three NC-IVF treatments are equivalent to three conventional IVF-ET treatments in terms of cumulative pregnancy rate, however NC-IVF is 15% less expensive per pregnancy overall.9 In addition, when compared to traditional IVF, the embryo quality appears to be better with NC-IVF. Thin endometrium was identified as an independent unfavorable prognostic factor in NC-IVF in a 2018 study by von Wolff et al.[10] Without any bias or selection, NC-IVF offers a singular opportunity to examine and relate embryonic traits to their probability for implantation. The aim of our study is to assess the effect of endometrial thickness and embryo.

Material and Methods

The gynecology department of a hospital and medical school conducted the current investigation. After NC-IVF was carried out, 250 cases of ET were included in the study. The one year study term was in place from April 2022 to April 2023. Prior to the study's launch, the institutional ethical committee was made aware of it and an ethical clearance certificate was obtained. Patients who met the following inclusion and exclusion criteria were included in the study: patients with an age of less than 38 years, a BMI of less than 25, and patients with one available embryo for transfer in a non-stimulated cycle where only human chorionic gonadotropin was used to trigger ovulation. Patients who underwent hysteroscopy or an HSG and had an abnormal uterine cavity were not included in this study.

The study included every woman who met the inclusion requirements. Based on the results of the -hCG pregnancy test two weeks after ET and confirmation by transvaginal ultrasound at six weeks of gestation, the patients were split into two groups: those who were pregnant and those who were not. No medication was given to stop an early luteinizing hormone (LH) rise and potential follicule rupture. At the commencement of monitoring (the first to fourth day of the cycle), the levels of estradiol, progesterone, follicle-stimulating hormone (FSH), and LH in serum were assessed. During subsequent routine control visits, millimeter-level ultrasound measurements of the follicle and endometrial thickness were taken every two days after measuring estradiol, progesterone, and LH. The NC-IVF cycle was stopped by the increasing slope of LH (> 20 mIU/mL), declining estradiol levels, and progesterone levels of 1.5 ng/mL. The aspiration procedure was carried out 36 hours after the application of hCG, and the oocyte was inseminated with motile spermatozoa about 2–5 hours afterwards. By counting the amount of pronuclei, fertilisation was evaluated 20 hours later. Embryos scored 48 and 72 hours after insemination had a fertilisation rate of 82.4%, and the overall percentage of NC-IVF cycles with recovered oocytes was 77.2%.

From one endometrial-myometrium interphase to the matching interphase, the highest endometrial thickness in the longitudinal plane of the uterus was assessed using transvaginal ultrasound. In this study, the measurement taken the day hCG was administered served as the reference value. Two weeks following the oocyte retrieval, a positive hCG test was used to determine whether or not a woman was pregnant. Six weeks later, ultrasound imaging of the intrauterine gestational sac revealed an embryo with a heartbeat.

Statistical analysis

SPSS 18.0 was used for the statistical analysis (SPSS, Inc., Chicago, IL). The difference in endometrial thickness on the day of hCG administration between pregnant and non-pregnant women was compared using a 2 test to evaluate patient and cycle variables. Statistics were deemed significant at p 0.05.

Results

The patients included in the study were divided into two groups. One group consists of pregnant women and other with non-pregnant groups. The patient’s history, cycle characteristics, body mass index were recorded and tabulated for the statistical analysis.

The numbers of transplanted embryos, retrieved oocytes, and serum estradiol levels used as hCG triggers were compared between the two groups. When results were compared between the two groups, similar findings were made.

When compared to the other non-pregnant women group (7.5 1.2 mm), the pregnant woman group's endometrial thickness was found to be larger (12.5 3.8 mm). Table 1 displays the pregnancy rate and endometrial thickness on the hCG injection day. Only one pregnancy, which ended in an early miscarriage, was established with endometrial thickness less than 7 mm. Miscarriage rates were 10.8% overall. Until a plateau of 10 mm is attained, our results show a statistically significant difference in successful implantation (p = 0.0012). The endometrial thickness difference between pregnant and non-pregnant women was not statistically significant after the threshold value of 10 mm. The 8-cell embryos on day 3 with less than 10% fragmentation, symmetrical blastomeres, and no multinucleated blastomeres—i.e., so-called "top quality embryos"—had the highest implantation rate according to the embryo quality. The highest implantation potential and in utero survival were found in embryos with fragmentation less than or equal to 10% in both univariate and multivariate analyses (p 0.01 and p 0.05, respectively).18.8% of embryos implanted overall after transfer. When examined by multiple regression analysis, the influence of endometrial thickness and embryo quality on implantation potential supports their separate effects on pregnancy rate.

Table 1: Pregnancy rate and endometrial thickness on day of hCG application

Endometrial thickness	Pregnant women group	Non pregnant women group
< 6 mm	1	35
7 mm	1	30
8 mm	3	46
9 mm	5	30
10 mm	8	24
11 mm	8	11
12 mm	10	12
13 mm	7	6
> 14 mm	9	4

Discussion

One of the key problems in examining changes in endometrial thickness is the difficulty of determining thickness at the start of growth. Basal layer endometrial development starts while a woman is still shedding endometrium from the prior cycle. Any assessment of new endometrial growth by ultrasonography, while a woman is menstruating, is incorrect since, in the majority of cases, it won't be possible to assess new endometrial growth until the fifth day of the cycle. During cycles of assisted conception, endometrial expansion can begin following menstruation, which may help to mitigate this problem.[11,12]

Successful implantation requires enough secretory and proliferative changes. Although offered as indicators of endometrial receptivity, triple-layer endometrial patterns and endometrial thickness larger than 7 mm have a significant rate of false-positive outcomes. Under hormonal replacement therapy, blood flow rises, this enhances uterine receptivity. The absence of a triple layer pattern can indicate early secretary alterations, which would mean that the peak receptivity time may have passed.[13] The effects of a "thin" endometrial lining on clinical outcomes, including as live birth rates, are still largely unknown. Iatrogenic causes, including as hysteroscopic treatments that damage the endometrium, aggressive uterine curettage, and infections, are known risk factors for a portion of individuals' eventual thinner endometria, but idiopathic causes are far less well understood. Additionally, patients who had a thin endometrium (6 or 7 mm) at the time of progesterone injection for FET might have more compaction in the days leading up to the actual ET. There is still much to learn about the potential factors that contribute to poor implantation following ET, including as individual variations in uterine architecture, endometrial vascularity, and the steroidal microenvironment.[14,15]

One of the most crucial elements in predicting pregnancy following in-vitro fertilisation and embryo transfer is endometrial receptivity. Transvaginal ultrasound is a believed to be a non-traumatic and straightforward approach for measuring endometrial thickness, which has been used as an individual indicator for endometrial receptivity. The endometrial thickness determined the day hCG was administered is often used.[16]

Ovarian hyperstimulation may have a negative impact on the endometrium's receptivity, causing the embryo and endometrium to develop at different rates and perhaps preventing successful implantation. With the embryo itself only accounting for about 30% of implantation failures and insufficient uterine receptivity accounting for roughly 70% of implantation failures, in vitro

investigations have revealed new roles for the decidualized endometrium as a biosensor of embryo quality. Furthermore, a more mature endometrium that favours embryos with a higher number of blastomeres, or in a later stage of development, may be the cause of the higher endometrial thickness seen in stimulated cycles.[17] In natural cycle IVF, endometrial features differ significantly from those in medically induced cycles. Day 2 NC-IVF two cell embryos were shown to have good implantation potential in the absence of any additional defects. According to our research, an endometrial margin of at least 7 mm is necessary for an NC-IVF implantation to be successful. There are conflicting findings about the potential link between endometrial thickness and treatment success following IVF. The bulk of earlier research either employed various ovarian stimulation methods or reported limited series (less than 200 cycles). Although constrained by the heterogeneity of study data, systematic review and meta-analysis demonstrated that pregnancy rates increased as endometrial thickness increased, but that pregnancy rates remained significantly lower up to an endometrial thickness value of 10 mm. The differences that induction protocols and/or multiple embryos may bring are overcome in NCIVF, which may serve as the best model for investigating the possible link between embryo quality, endometrial thickness,and implantation success.

Conclusion

Endometrial thickness and embryo quality have a big impact on implantation in NC-IVF. The 8-cell embryos with the lowest or equivalent 10% fragmentation on the third day after oocyte retrieval have the highest implantation potential. The ideal threshold for a viable pregnancy appears to be endometrial thickness of at least 7 mm.

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