Research Article,

The Role of Endometrial Scratching to Improve the Pregnancy Rate Among Infertile Couples

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Abstract:

Background: Different technologies have been used in order to improve the endometrial condition as well as the quality of embryos; however, still the implantation process could fail. Endometrial Scratching (ES) has been proposed by many studies and revealed conflicting results.

Objective: The study Aims to investigate the effect of ES on improving the Clinical Pregnancy Rate (CPR) and Live Birth Rate (LBR).

Methodology: This is a retrospective study was carried out at Libyan National Fertility Centre. 188 Infertile women were included in the study in two different groups. 95 patients who underwent ES and 93 as control group. Cases with male factor infertility, history of surgical sterilization, premature ovarian failure, endometriosis and other hormonal disturbance (thyroid /prolactin) had been excluded from the study.

Results: The CPR was positively affected by scratching procedure among infertile women after perform ES (p value 0.022). The secondary infertile patients have got significant benefit after performing ES by improving the CPR (P value 0.045). The ES has improved the CPR on patients with previous history of failed Intra-Cytoplasmic Semen Injection ICSI (P value 0.043). However, there was no statistically significant difference to the effect of ES on LBR.

Conclusion: The study found that the ES has a positive role to improve the implantation among specific group of infertile couples. It is recommended to perform ES for couples with secondary infertility and previously failed ICSI cycle.

Introduction:

Different technologies of assisted reproductive conception have been used around world in order to improve the CPR among infertile couples [1]. The endometrial receptivity and quality of embryos are considered as important factors affecting the pregnancy rate. The structural anomalies in the uterine cavity such as congenital problems, fibroid, polyp, endometrial adhesion and endometrial thickness are major factors affecting the implantation and so the pregnancy rate [2,3].

Despite, the development in diagnostic and therapeutic technology in order to improve the endometrial condition (Transvaginal Ultrasound Scan and Hysteroscopy) as well as the quality of embryos, still the implantation of embryos could fail (35% of embryo transfer rate) [4,5]. Consequently, the improvement in the pregnancy rate is still under research [6,7].

The implantation window is a process that involves activation of some inflammatory cells as well as its mediators such as macrophages, natural killer cells, interleukin and tumor necrosis factor [8, 9, 10, 11]. During this window, essential coordinated interactions between a healthy embryo and normal uterus take place and ended by pregnancy [12]. So, ES has been projected to stimulate the endometrium to catch the implantation window and so improve CPR [13]. The explanation how ES can improve the implantation is still under debate, however its potential to improve the endometrial implantation is crucial to be investigated [11, 14]. ES could be considered as a cost-effective procedure because it is an outpatient procedure and only requires
simple analgesics. On the other hand, it carries a risk of intra-uterine infection \cite{15, 16}. Also, proven the efficacy of ES could help to apply a policy of single embryo transfer which will reduce the risk of multiple pregnancy as well as the unnecessary assisted conception cycles Intra Uterine Insemination (IUI), ICSI and In-vitro fertilization (IVF). So, is a cost-effective procedure \cite{7, 9}. Various research has been carried out and studied the effect of ES on pregnancy rate before imparking in assisted conception cycles as well as natural conception, however; the results were not conclusive mostly due to heterogeneity in the data included as well as the time of ES had been done during the cycle \cite{1, 4}. This study aims to evaluate the improvement in pregnancy rate and pregnancy outcome among sub-fertile couples after performing the endometrial scratching during the mid-luteal phase of the previous cycle.

**Materials and Methods:**
This is a retrospective study was carried out at Libyan National Fertility Centre. 201 Infertile women were included in the study in two different groups. 95 patients who underwent ES (scratching group) and 93 patients who did not perform ES (control group). Cases with male factor infertility, history of surgical sterilization, premature ovarian failure, endometriosis, poly-cyclic ovaries and other hormonal disturbance (thyroid /prolactin) have been excluded from the study. The endometrial scratching was done during the luteal phase (18, 19, 20 and 21of menstrual cycle). The procedure was under general anesthesia, insertion of the vaginal speculum and the cervix became clear when the normal saline used as a distension media to stimulate the endometrium as well as wash the uterine cavity from any undetected pathology by trans-vaginal sonography that, could be act as an inhibitory factor for implantation process.

Patients from the two groups (study and control groups) went for assisted conception ICSI in steps. Controlled Ovarian Stimulation (COH) was applied on second day of menstrual cycle and the ovarian response was monitored by TVS and Estradiol level and when at least three follicles reach 18mm (mature follicles), Human Chorionic Gonadotrophin (HCG) was injected. Thirty-six hours later follicles collected by transvaginal ultrasonography-guide under general anesthesia and after fertilization of oocytes with sperm in the laboratory, embryos were transferred. Serum \( \beta \)-hCG levels were measured 12-14 days after transfer the embryos.

**Statistical analysis:**
In this study, the statistical analysis for the Data was done by using software SPSS 23.0. The descriptive statistics were either continuous variables which presented by mean ± standard deviation or categorical data which presented by counts (percentage). The comparison of various data between the two groups was done by using chi square. The significant relation is considered when the level of P value achieves <0.05.

**Results:**
This study involves 201 cases (95 cases perform endometrial scratching and 93 without scratching as a control group). The all scratching procedures for the involved cases were done during the luteal phase of the menstrual cycle. There were 13 cases excluded from the study due to different day of scratching (day 12, 13 of menstrual cycle). The descriptive data were shown in table1 which involve age, duration of infertility, ovarian response markers Follicular Stimulating Hormone (FSH), Antra Follicular Count (AFC), Luteinizing Hormone (LH), Thyroid Stimulating Hormone (TSH) and Estradiol E2.

**Table 1: Descriptive Data for both groups Scratching and Control groups.**

| Variable          | Scratching group (n=95) mean±SD | Control group (n=93) mean±SD |
|-------------------|--------------------------------|-------------------------------|
| Age(y)            | 32.34 ± 4.58                   | 32.95 ±4.43                   |
| Infertility time (year) | 4.28 ±2.559                   | 3.96 ±2.738                   |
| FSH (IU/L)        | 6.84 ±1.91                     | 7.17 ±1.72                    |
| LH (IU/L)         | 4.37 ±1.54                     | 4.59 ±1.47                    |
| E2 (pg/mL)        | 35.58 ±15.13                   | 36.47 ±16.26                  |
| TSH (IU/L)        | 2.083 ±0.68                    | 2.14 ±0.79                    |
| AFC               | 4.28 ±2.64                     | 7.78 ±2.57                    |

The study revealed that the clinical pregnancy rate and rate of live birth clearly affected by the scratching procedure and \( p \) value was statistically significant (0.044, 0.042) respectively.
By analysis subgroup analysis among scratching group of patients according to the infertility type, its clear (table 4) that the patients with secondary infertility had got benefit after performing a scratching procedure by improving the clinical pregnancy rate as 62.96% who had negative pregnancy test were with primary infertility and this gives a significant relation (P value 0.045).

Table2: Effect of scratching procedure on the pregnancy rate and outcome.

| Variable          | Scratching Group N=95 | Control Group N=93 | P value |
|-------------------|-----------------------|--------------------|---------|
| CPR               | 54 (56.84%)           | 35 (37.63%)        | 0.044   |
| LBR               | 39 (41.05%)           | 23 (24.70%)        | 0.042   |
| Abortion Rate     | 15 (15.70%)           | 12 (12.90%)        | 0.564   |

There had been some cases with previous history of ICSI and when studied the effect of scratching on those group of people revealed that the scratching procedure has a positive effect in improving the pregnancy rate among patients with previous trials of assisted conception ICSI.

Table3: Compare the effect of scratching procedure on the types of infertility and clinical pregnancy rate

| Positive Pregnancy (n=41) | Negative Pregnancy (n=54) | P value |
|---------------------------|---------------------------|---------|
| Primary infertility       | 21/41 (51.22%)            | 34/54 (62.96%) | 0.045   |
| Secondary infertility     | 20/41 (48.78%)            | 20/54(37.04%)  |         |

Discussion:
The present study has concluded that the endometrial scratching has a role to improve the implantation rate among infertile couples; however, LBR does not changed with the ES procedure. In the recent time, endometrial scratching has been proposed as a process to improve pregnancy rate as it involves superficial injury to the endometrium helping in a process of embryo's implantation by releases growth factors, chemical and gene switching that leaves the endometrium to grow healthy and ready for implantation [17, 18, 19, 20]. Barash et al [1] was first to demonstrate the positive effect of ES by doubling the implantation rates as well as the live birth rates in cases with Recurrent Implantation Failure (RIF) [1, 21, 22]. In addition, Neeta Singh et al [23] revealed that the implantation rate was statistically significant (P =0.028) in cases with RIF who were group1 with ES during the luteal phase 19.4% and group2 who had no ES 8.1%. However, the live birth rate and miscarriage rate were no significant difference between the two groups [22]. Moreover, Milan Reljić et al [24] performed study among cases 429 ICSI cycle with age less than 40 years and had previous failed trials of ICSI and found that the CPR significantly higher among group with ES (P =0.007). Furthermore, Emiko Kanazawa et al [3] studied three groups, group1 with ES, group2 with only hysterectomy and group3 with no treatment received. The clinical pregnancy rate was statistically significant between group1 and 3 (P = 0.03) but with group 2 no statistically significant (P = 0.103).

On the other hand, there has been various studies concluded that the ES has no significant role to improve the CPR. Mahnaz Ashrafi et al [12] studied 169 cases with more than one IUI cycle failure and normal uterine cavity which revealed no significant difference (P = 0.09) in CPR as well as LBR and miscarriage rate [25, 26]. In addition, various research was conducted on cases with RIF and normal uterine cavity before imparking in ICSI cycle and revealed no significant differences in improving the CPR between group with ES and groups with no treatment intervention [4, 13, 27, 28]. Moreover, variety of studies conducted on women who plane for frozen-thawed embryo transfer and applying ES to improve the pregnancy outcome which giving a result with no significant differences study and control group [29, 30, 31].

Table4: Compare the effect of scratching procedure on the cases with previous failed ICSI and no trials before.

| Negative Pregnancy N (%) | Positive Pregnancy N (%) | P value |
|--------------------------|--------------------------|---------|
| History of failed ICSI(51 cases) | 30 (31.58%) | 21 (22.11%) | 0.043   |
| History of no trial (44 cases) | 24 (25.26%) | 20 (21.05%) |         |
Limitations:
The current study has some limitations that because it’s retrospective in nature missed other factors interfering with the embryo's implantation as well as limit the number of cases involved, for that reason, could not generalize the result. It is recommended that, large Randomized Control Trials to examine the role ES among subgroups of patients to prove the improvement in implantation rate and LBR as the question is performing ES will have to achieve a positive statistically significant result.

Conclusion:
The study's findings were in consistent with some previous research which proves that the endometrial scratching has a positive role to improve the implantation among infertile couples. However due to its limitations and the conflict with the results from other studies, it is recommended a multicenter randomized controlled clinical trial in order to identify the exact group of people as candidates who can get benefit from ES procedure and so answering the question about the possibility of performing the ES as a routine procedure for special group of infertile couples.

Abbreviation
Endometrial Scratching (ES), Clinical Pregnancy Rate (CPR), Live Birth Rate (LBR), Intra-Cytoplasmic Semen Injection (ICSI), Controlled Ovarian Stimulation (COH), Recurrent Implantation Failure (RIF), Human Chorionic Gonadotrophin (HCG), Follicular Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), Antra Follicular Count (AFC), Thyroid Stimulating Hormone (TSH). In-vitro fertilization (IVF), Intra Uterine Insemination (IUI)

Ethical Approval:
The approval of the study was obtained from the Research Ethics Committee at Scientific Research and Documentation Department, Libyan National Fertility Center - Misurata, Libya (PR 2021-11), and parental written consent has been collected and preserved by the author(s)

Competing Interests:
Authors have declared that no competing interests exist.

Authors’ contributions:
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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