



Investigating the effect of endometrial scratch on the success of IUI cycle

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ABSTRACT

Introduction: Because of benefits of IUI than IVF and other methods of treatment of infertility and because infertility with unknown cause and therapeutic intervention are still controversial topics that still embryonic problems and failed implantation are considered its risk factors. Therefore, the objective of this study was to investigate the effect of endometrial scratch on the success of IUI cycle. This investigation evaluated the implantation of embryo in endometrial cavity after injury of endometrium.

Methodology: In this randomized clinical trial study conducted in infertility clinic in the Shahid Ayatollah Beheshti Hospital, 180 women aged 18 to 40 years who suffered from infertility were randomly divided into three groups: 1. control group only IUI (n=60), 2. The treatment group one cycle before IUI under endometrial scratch (n = 60), and 3. Treatment group in IUI cycle endometrial scratch (n = 60). Endometrial scratch was performed by feeding tube and IUI through cutter. For statistical analysis, Kruskal-Wallis test and chi-square test were used.

Results: The prevalence of pregnancy in the third group (in IUI cycle under endometrial scratch) was n = 12, 20.7%, and it was n = 11, 18.00% in the second group (one cycle before IUI under endometrial scratch), which it was higher compared to control group (n=6, 10.2%), but the difference was not statistically significant (P=0.27). Additionally, there was no significant relationship between fertility rate in different groups and patient's age (P=0.88), duration of infertility (p=0.69) and type of infertility (P=0.18).

Discussion and conclusion: The results of this study although were not significant, as the frequency of pregnancy in the two groups under endometrial scratch was higher compared to the control group, it seems that this lack of significance to be due to the small sample size and local mechanical endometrial scratch increased endometrial receptivity and facilitated the embryo implantation.

Keywords: infertility, IUI, endometrial scratch, implantation

INTRODUCTION

Successful implantation depends on quality of blastocyst and endometrium and synchronization between the development and stage of endometrium and embryo.

Infertility prevalence in society has been reported to be about 10% to 15%. While using therapeutic services for their treatment has been increased over the last decades, the infertility prevalence has been remained constant. One of the oldest methods used to treat the infertility is IUI. Intra uterine insemination (IUI) is regarded as one of the most common and known types of artificial insemination, and it is today considered as one of the methods for treatment of infertility with causes, cervical factor, non-ovulation, endometriosis, immunological factor, male infertility, and unknown factor (1). Low levels of unprepared semen fluid was used for intravaginal insemination, but due to the possibility of reaction with proteins, prostaglandins and bacteria available in the semen, and very low success of this method, it is today spoken as historical topic, and washed and prepared sperm rather than semen fluid is nowadays used in IUI (2) and it is used as a non-risky method accepted by majority of physicians and infertility officials (2,3). IUI is affected by various factors. Different studies have indicated that the chance of successful pregnancy in infertile couples, especially infertility with male causes, has been increased by ovulation induction and performing IUI (4). In humans, it is considered as

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implantation window in 19 to 23 menstrual cycles, that is, middle of the secretion phase, which seems that inappropriate receptivity of the uterus accounts for two thirds of pregnancy failures (5). While fertility-assisting methods seem to overcome many infertility issues, embryo implantation failure is still a limiting stage in fertility-assisting methods (6). The uterus receptivity is a process, which is dependent on estrogen and progesterone (7). Animal studies have proven that it has increased trauma to the endometrial decidualization and endometrial receptivity in animals (8). Among different causes of unsuccessful implantation, uterine factors such as thin endometrium, inappropriate endometrial receptivity, and lack of match among immunologic factors have drawn the attention of the most of the researchers in the recent years (9). Thus, one research proved that scratch on the endometrium in days 8, 12, 21, and 26 of the menstrual cycle increased the pregnancy rate following the IUI (10). Given the similar effect of pipe and tube feeding in creating this effect (11), increase in inflammatory protein of macrophage 1B (MIP-1B) can increase endometrial capacity in embryo receptivity (12). Population of decidua leukocytes is increasing at the site of implantation in human and mice, which 65-70% of them belong to intrinsic lethal cells (13). These cells play vital role in the decidua stability (14,15). In the research conducted by Zhou et al, they found that trauma to the endometrium increased the success of infertility treatment cycle in cycles combined with clomiphene (16). While several studies have proven that endometrial scratch increased the success rate of pregnancy following IVF and ICSI, there is a few studies on the outcome of endometrial biopsy on the IUI cycle (11, 12). As successful implantation is an essential prerequisite for continuation of successful pregnancy and embryo interference and endometrial receptivity are considered as two very effective factors in IUI success, and given the similar feedback of IVF and IUI but their significant difference (17, 20) and possibility of IUI in clinic and outpatient in the case of success of this treatment imposes high cost for the infertile patients, the researcher in this research aims to answer the question of whether endoscopic scratch affects the success rate of the IUI cycle In Iranian woman with unknown fertility (19).

METHODOLOGY

This research is a randomized clinical trial study, conducted by a person other than a researcher, assistant performing the IUI (midwife), and data were collected by the same person and announced to the researcher. Moreover, patients were fully aware of the process of procedure, complications, risks, and benefits of treatment by completing the consent form. Endometrial scratch time might be effective in pregnancy outcome. The present research was conducted on 180 patients admitted to the infertility center of Shahid Ayatollah Beheshti Hospital, who met the inclusion criteria of study. Inclusion criteria of research included patients aged 18 to 40 years old, unexplained primary or secondary infertility, having at least one to three 18-20 mm follicle (during the IUI injection), having normal 3-day TSH, PRL, FSH, LH, normal hysterosalpingography and laparoscopy, and sperm count per ml is not less than 15 million, and sperm movement is not less than 40% before washing. The exclusion criteria of the research included any diseases of liver, blood, autoimmune, endocrine and hirsutism, alcohol abuse, smoking, unknown pelvic inflammation disease (PID), endometriosis, or pelvic adhesion, or uterine myoma with a laparoscopy or hysteroscopy three months before IUI. Patients were divided into three groups: 1. control group only IUI (n=60), 2. The treatment group one cycle before IUI under endometrial scratch (n = 60), and 3. Treatment group in IUI cycle endometrial scratch (n = 60). Sampling was performed in the form of triple random blocks. Accordingly, since the first day of study, the first three patients admitted to clinic were randomly assigned to one of the groups so that sample size to reach the sufficient number. Group one is the control group underwent only IUI. The second group is the treatment group underwent endometrial scratch by fixed person in 8 to 9 day cycle before the IUI cycle, and the third group was the treatment group underwent endometrial scratch in 8 to 9 IUI cycle. Endometrial scratch was performed by tube feeding and the patient should not use any hormonal drug in that cycle. All patients in each of the three groups received 100mg of clomiphene citrate for 5 days every day, from 5 days to 9 cycles, and they injected 100 units per day (HMG) from 8 cycles. Vaginal sonography was performed in 11-cycle day based on size and number of follicles, and HMG continued until at least one 18 mm follicle was observed in vaginal sonography. Then 10000 units (Choriomon, IBSA, Switzerland) HCG were injected intramuscularly. IUI in each of the three groups was performed 36 hours after HCG injection. IUI was performed by catheter (BioRad, Berkeley, California). The sperms were separated using Swim-up method (a method in which mobile sperms were separated from at least 10 million sperm washed). HCV beta was checked if the patient had a one-week menstrual delay and the pregnancy was proven with vaginal sonography at 6-7 week. Age of the patient, abortion status, infertility duration, and type of fertility were examined based on the questionnaire. To determine the mean and standard deviation, descriptive statistics were used and distribution of data was evaluated using Kolmogorov-Smirnov test. ANOVA, Kruskal-Wallis and Chi-square were used for analyzing the data. All statistical calculations were performed using

Table 1: Frequency and percentage of frequency of studied variables in groups treated by IUI

groups Variables	Routine IUI (control)	One cycle before IUI+ Endometrial scratch	In IUI cycle+ Endometrial scratch	Significance vale (p)
Pregnancy	Positive	6 (10.2%)	11 (18%)	0.27
	Negative	53 (89.8%)	50 (82%)	
Type of fertility	Primary	39 (66.1%)	40 (65.6%)	0.18
	Secondary	20 (33.91%)	21 (34.4%)	
Embryo abortion status	Positive	0 (0.0%)	1 (1.6%)	0.38
	Negative	59 (100.0%)	60 (98.4%)	

Table 2: The mean and standard deviations of the studied variables in groups treated by IUI

Variables	Groups (n=3)	SD±mean	F ratio	Significance vale (p)
Age (year)	Routine IUI (control)	3.97 ±31.79	0.126	0.88
	One cycle before IUI+ Endometrial scratch	4.45 ±32.13		
	In IUI cycle+ Endometrial scratch	4.58 ±31.77		
Infertility duration (year)	Routine IUI (control)	1.80 ±4.75	0.362	0.69
	One cycle before IUI+ Endometrial scratch	5.34 ±5.25		
	In IUI cycle+ Endometrial scratch	1.66 ±4.84		

SPSS-21 software. The required sample size was estimated by using the sample size estimation formula explained below and considering the confidence level ($Z_{1-\alpha/2}=1.96$) and test power ($\beta-1=0.84$), and OR = 2.2. According to previous studies, P_A is 0.65 and P_B is 0.45 (5,6).

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 [P_A(1 - P_A) + P_B(1 - P_B)]}{(P_A - P_B)^2} = \frac{(1.96 + 0.84)^2 [0.65(1 - 0.65) + 0.45(1 - 0.45)]}{(0.65 - 0.45)^2} \approx 60$$

FINDINGS

Data were analyzed on 178 subjects, cooperated with the researcher until the end of the research. One subject in the first group and 2 subjects in the third group withdrew to continue cooperation, and one subject was added to the second group. The statistical tests findings revealed that the frequency of pregnancy in the third group underwent endometrial scratch was 12 (20.7%), and it was 11 (18.00%) in the second group one cycle before IUI under endometrial scratch, which this number was higher than that in the control group ($n=11$, 10.2%), but this difference was not statistically significant ($P = 0.27$) (Table 1). With regard to infertility type, frequency and percentage of frequency were as follows: in the first group, 39 people (66.1%), in the second group, 40 people (65.6%), and in the third group, 46 people (79.3%) had primary type of infertility. In addition, in the first group, 20 people (33.91%), in the second group, 21 people (34.4%), and in the third group, 12 people (20.7%) had secondary type of infertility. Statistical test revealed that there was no significant relationship between rate of fertility and infertility type ($p=0.18$) (Table 1). Findings also revealed in the second group, only one person (1.6%) had abortion, which was not statistically significant ($P = 0.38$) (Table 1).

Statistical test findings revealed no significant difference between fertility rate in different treatment groups (one, two and three) and patient's age ($F = 0.126$, $P = 0.88$) and duration of infertility ($F=0.362$, $P = 0.69$) (Table 2).

In our research, no side effects such as pain or bleeding in the cases occurred.

DISCUSSION AND CONCLUSION

Findings of current research while were not significant, given the pregnancy frequency in the two groups underwent endometrial scratch compared to that in the control group. In the current research, the success rate of pregnancy in the third group underwent endometrial scratch in the IUI cycle was 20.7% and it was 18.00% in the second group underwent endometrial scratch one cycle before IUI, which it was more in comparison to control group underwent only IUI (10.2%), but this difference was not statistically significant. In addition, no significant relationship was found between the fertility rate in different groups and the age of the patient and the duration of infertility and type of infertility. This research findings were inconsistent with findings of the studies conducted by A. Barash et al (2003), Y. Gnainsky et al. (2010), A. Bhide et al. (2007) (11), and K. Tjon et al. (2015) (17), and A. Badeea et al. (2017) (1). Given the researcher studies and the limited literature of research, it seems that no study consistent with this study has been conducted so far. A successful implantation is a necessary prerequisite for the continued success of pregnancy, and implantation is a complex and multi-factorial process. In the course of IUI, interference between embryo and endometrial receptivity are two very strong

factors in the success of this infertility treatment method, while several studies have shown that endometrial scratch has increased the success rate of pregnancy following IVF and ICSI. However, there is limited number of study on the outcome of endometrial biopsy on IUI cycle (11, 12). In their research, A. Barash et al. (2003) showed that endometrial scratch on days 8, 12, 21, and 26 of the menstrual cycle increased the pregnancy rate following IUI (10). Our results can be a reason for the effectiveness of this method and it seems that this non-significance to be due to the small sample size and local mechanical endometrial scratch increases the endometrial receptivity and facilitates the embryo implantation. This simple and cost-effective method can be effective before complex therapeutic interventions in selected infertile couples, which no certain reason has been specified for their infertility and probably the cause of their infertility is due to problem in embryo implantation. Additionally, this method could reduce the neural tension and treatment costs of these patients. Thus, given the importance of the subject, it is suggested that future studies to be conducted with a larger sample size. It is also recommended that RCT studies to be conducted in future in order to examine the events such as abortion, multiple-pregnancy, and other complications in endometrial scratch. In addition, it is recommended a research to be conducted using higher number of centers and by considering other causes of infertility.

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