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TO ANALYSE THE EFFECT OF ENDOMETRIAL SCRATCHING ON PREGNANCY RATES IN PREVIOUSLY FAILED IUI CYCLES

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Abstract

Background: To analyse the effect of endometrial scratching on pregnancy rates in previously failed IUI cycles

Methods: Randomized control study conducted on Couples attending the Infertility Clinic, Obstetrics & Gynaecology Department, SMS Medical College, Jaipur and requiring repeat IUI were recruited for the study from Feb 2019 to November 2020.

Results: women in which IUI failed two times positive results after scratching was present in 16.15% cases followed by 6.92% positive results in women who had three times IUI failed and women who had only one-time IUI failed positive results was present in 4.62% cases. In controls we found positive results with 5.38% in women having one-time IUI failed followed by 3.85% in women where two time IUI failed and only in 2.31% women positive results found having three time IUI failed.

Conclusion: In conclusion this study demonstrates 2.5-3 fold increase in pregnancy rates after scratch, endometrial scratching can be a preferred option in patients with previous failed IUI cycles before opting for expensive IVF treatment.

Keywords: IUI, IVF, Inferetility

Introduction

Infertility is the inability of a sexually active non-contracepting couple to achieve pregnancy in one year (WHO ICMART). IUI is one of the most popular Assisted reproductive technique (ART) for treatment of unexplained infertility.[1]

Infertility, a major health problem nowadays, affects around 8–12% of couples worldwide[2]. Unexplained infertility affects up to 15–30% of infertile couples. Management options for unexplained infertility are expectant management, timed intercourse, IUI with or without controlled ovarian stimulation, ART, i.e. IVF/intracytoplasmic sperm injection (ICSI)[1].

Implantation includes apposition, adhesion and invasion phases. For successful implantation there is a complex interaction between maternal endometrium and the conceptus. Factors involved in feto maternal interaction are hormones, growth factors, cytokines, chemokines, adhesion molecules, extracellular matrix components and matrix degrading enzymes. Receptive endometrium is therefore necessary for successful implantation. In humans, uterus becomes receptive during mid-secretory phase of menstrual cycle (day 19–23) known as window of implantation (WOI)[2]. It is considered that poor endometrial receptivity is accountable for approximately sixty percent of implantation failures[3].

It is considered that poor endometrial receptivity can improved by endometrial scratching.

Several mechanisms are believed to play a role in improving the outcome. After endometrial injury, cytokines that are released during the repair process induce endometrial changes favorable for implantation. Endometrial injury also induces decidualization, which favors implantation as well.[4]

The endometrial scratching is a simple, practical, cost-effective procedure which can be done in an OPD (Outpatient Department) setting, if proven effective in improving clinical pregnancy rates in previous 1-3 failed IUI cycles, then it can be offered before more advanced and expensive IVF procedure.

Thus, the present study is planned to analyse the effect of endometrial scratching on pregnancy rates in previously failed IUI cycles.

Material & Methods

Randomised control study.

Prospective study

Infertility clinic, Obstetrics and Gynecology Department of SMS Medical College, Jaipur.

Feb 2019 to November 2020

STUDY GROUP

All previously failed IUI cases

Group-A (Case): patients in whom repeat IUI done with endometrial scratching

Group-B (Control): patients in whom repeat IUI done

Inclusion Criteria

- All previous failed IUI cases
- Women willing to give consent

Exclusion Criteria

- Acute inflammatory condition in both partner
- Age >35 years
- >3 failed IUI cycles
- Women with anovulation in stimulated cycles
- Women not willing to give consent

Methodology

Couples attending the Infertility Clinic, Obstetrics & Gynaecology Department, SMS Medical College, Jaipur and requiring repeat IUI were recruited for the study from Feb 2019 to November 2020.

Written and informed consent was taken from all the participants.

After inclusion and exclusion criteria, 260 women were screened for which 260 women were recruited for study, 130 in each group.

Patients of case group were undergo endometrial scratching on day 20–22 of previous cycle (in women with 28–30 days) cycle or postovulatory day 6–8 (in patients with prolonged cycles) in which ovulation was confirmed by ultrasonography.

Endometrial scratching was performed with Pipelle (endometrial sampling device).

IUI was performed in all patients after controlled ovarian stimulation as per standard protocol.

Statistical Analysis

Quantitative data was described as mean and standard deviation. Qualitative data described as proportion. Appropriate statistical test was used to find out statistically significant. p-value < 0.05 was taken as significant.

Results

Table 1: Distribution of Subjects According to general characteristics

Variable	Case Group	Control Group	p-value
Age (Mean ± SD (in yrs))	27.99 ± 3.46	27.19 ± 3.11	0.932
***Married Life* (Mean ± SD (in yrs))**	4.5 ± 1.4	4.4 ± 1.2	0.5369
BMI(Mean ± SD)	24.8 ± 4.0	24.8 ± 4.0	0.99
Type of infertility (primary : secondary)	124 : 6	125 : 5	0.99
Duration of infertility (Mean ± SD (in yrs))	4.5 ± 1.4	4.4 ± 1.2	

The mean age of women in case group was 27.99 years and that in control group mean age was 27.19 years the difference was not statistically significant. In cases group (56.25%) and control group (67.69%) majority of patients was in age group 26-30 years followed by in 20-25 years. The mean duration of married life in cases group was 4.5 years and that in control group was 4.4 years. Majority of women in cases (60%) had 2-4 years of married life and that in control group 50% had married life of 2-4 years. In 39.23% women in cases had married life on 5-8 years and that in control group 50% had married life of 5-8 years. The difference was not statistically significant. Here, the mean BMI of women in cases was 24.8 kg/m^2 and that in control group mean was 24.8 kg/m^2. In cases, 95.38% had primary infertility and 4.62% had secondary infertility. Similarly, in controls 96.15% had primary and 3.85% had secondary infertility. The difference was not statistically significant (p-value >0.05).

Table 2: Distribution of Subjects According to Failed Attempt of IUI

Failed Attempt of IUI	Case Group		Control Group		p-value
	No.	%	No.	%	
One	7	5.38	35	26.92	<0.0001
Two	48	36.92	63	48.46	0.059
Three	75	57.69	32	24.62	<0.0001
Total	**130**	**100.00**	**130**	**100.00**	

In cases, 57.69% women had three times failed IUI followed by 36.92% had 2 times and 5.38% had one-time failed IUI. Similarly, in controls, 48.46% had two times failed IUI followed by 24.62% had three times failed IUI and 26.92% had one-time failed IUI.
The difference was statistically significant as p-value<0.05.

Table 3: Distribution of Subjects According to 1st Cycle Endometrial Vascularity

1st Cycle Endometrial Vascularity (Ovulatory Phase)	Case Group		Control Group		p-value
	No.	%	No.	%	
Z1	32	24.62	31	23.85	0.8805
Z2	60	46.15	60	46.15	1.000
Z3	26	20.00	27	20.77	0.8731
Z4	12	9.23	12	9.23	1.000
Total	**130**	**100.00**	**130**	**100.00**	

In cases, 46.15% had Z2 ovulatory phase followed by 24.62% had Z1 phase, 20% had Z3 phase and 9.23% had Z4 phase. Similarly, in controls, 46.15% had Z2 ovulatory phase followed by 23.85% had Z1 phase, 20.77% had Z3 phase and 9.23% had Z4 phase.
The difference was not statistically significant as p-value greater than 0.05

Table 4: 1st and 2nd Cycle Endometrial Thickness in Cases and Controls

	Case Group		Control Group		p-value
	Mean	SD	Mean	SD	
1st cycle endometrial thickness	7.08	0.49	7.08	0.49	1.00
2nd cycle endometrial thickness	8.45	0.56	7.11	0.52	<0.0001

The mean 1st endometrial thickness was almost same in both cases and control so the difference was not statistically significant. But mean endometrial thickness in 2nd cycle in cases was 8.45 cm and in controls 7.11 cm. The difference was statistically highly significant (p-value <0.0001).

Table 5: Mean Pre and Post Wash Sperm Count

Count (in million)	Case Group		Control Group		p-value
	Mean	SD	Mean	SD	
Prewash Sperm	34.43	4.55	34.41	4.61	1.000
Postwash Sperm	28.18	3.44	28.17	3.31	

In both cases and control mean pre-wash and post-wash sperm count was almost same so the difference was not statistically significant.

Table 6: Mean Pre and Post Wash Sperm Motility

Motility (in %)	Case Group		Control Group		p-value
	Mean	SD	Mean	SD	
Prewash Sperm	40.28	1.40	40.19	1.40	1.000
Postwash Sperm	53.31	4.71	53.31	4.71	

In both cases and control mean pre-wash and post-wash sperm motility was almost same so the difference was not statistically significant.

Table 7: Distribution of Subjects According to Follicles

Follicles	Case Group		Control Group	
	No.	%	No.	%
One	97	74.62	97	74.62
Two	33	25.38	33	25.38
Total	**130**	**100.00**	**130**	**100.00**

p = 1.000
In both cases and controls majority (74.62%) had one follicle followed by 25.38% had two follicles. The difference was not statistically significant.

Table 8: Distribution of Subjects According to 2nd Cycle Endometrial Vascularity

2nd Cycle Endometrial Vascularity (Ovulatory Phase)	Case Group		Control Group		p-value
	N	%	N	%	
Z1	20	15.38	31	23.85	0.0886
Z2	60	46.15	60	46.15	1.00
Z3	38	29.23	26	20.00	0.0856
Z4	12	9.23	13	10.00	0.8270
Total	**130**	**100.00**	**130**	**100.00**	

Here, in cases 46.15% women had Z2 phase followed by 29.23% had Z3, 15.38% had Z1 and 9.23% had Z4 phase.
In controls 46.15% women had Z2 phase followed by 23.85% had Z1, 20% had Z3 and 10% had Z4 phase.
The difference was not statistically significant as p-value > 0.05.

Table 9: Association of IUI and Positivity (n=130)

Failed Attempt of IUI	Case Group		Control Group		p-value
	Positive	%	Positive	%	
One	6	4.62	7	5.38	0.7677
Two	21	16.15	5	3.88	0.0009
Three	9	6.92	3	2.31	0.077

Here, in women in which IUI failed two times positive results after scratching was present in 16.15% cases followed by 6.92% positive results in women who had three times IUI failed and women who had only one-time IUI failed positive results was present in 4.62% cases.
In controls we found positive results with 5.38% in women having one-time IUI failed followed by 3.85% in women where two time IUI failed and only in 2.31% women positive results found having three time IUI failed.

Discussion

Endometrial scratching which is a simple out-patient procedure has gained importance of late with investigators recommending it as a tool to increase pregnancy rates in failed IVF cycles. Ever since, several studies have reported improved pregnancy rates in previous failed ART cycles, though results however are conflicting. Evaluation of this procedure in failed IUI cycles is even less studied.[5] Abdelhamid AMS et al[6] first reported the beneficial effects of endometrial injury in previous failed IUI cycles in their study published in the year as recent as 2013 almost a decade after the first report in IVF cycle.

In our study both cases and controls majority (74.6%) had one follicle followed by 25.4% had two follicles. The difference was not statistically significant (Table-17). Gupta V et al[5] found number of dominant follicles was significantly higher in the study group compared to control group. Range of dominant follicles in the study and control group was 1–5 and 1–4 respectively (p = 0.015).

The mean 1st endometrial thickness was almost same in both cases and control so the difference was not statistically significant. But mean endometrial thickness in 2nd cycle in cases was 8.45 cm and in controls 7.1 cm. The difference was statistically highly significant (p-value<0.0001). Dogra A et al[7] found that Mean endometrial thickness was comparable in both the cases (9.20 ± 3.37) and controls (9.16 ± 3.20). The difference was not statistically significant (p value=0.532). Zarei A et al[8] mean endometrial thickness was comparable in both the groups in their study. While study by Hamdi K et al[9] showed higher endometrial thickness in control group. Mean endometrial thickness was 8.33 ± 0.97 in cases and 10.5 ± 1.37 in controls in their study. On the other hand, Gupta V et al[5] found higher endometrial thickness in cases (9.18 ± 3.35) as compared to controls (8.53 ±1.88).

In both cases and control mean pre-wash and post-wash sperm count and motility was almost same so the difference was not statistically significant.

Here, in cases 46.2% women had Z2 phase followed by 29.2% had Z3, 15.4% had Z1 and 9.2% had Z4 phase. In controls 46.2% women had Z2 phase followed by 23.8% had Z1, 20% had Z3 and 10% had Z4 phase. The difference was not statistically significant as p-value > 0.05. In cases, 46.2% had Z2 ovulatory phase followed by 24.6% had Z1 phase, 20% had Z3 phase and 9.2% had Z4 phase. Similarly, in controls, 46.2% had Z2 ovulatory phase followed by 23.8% had Z1 phase, 20.8% had Z3 phase and 9.2% had Z4 phase. The difference was not statistically significant as p-value greater than 0.05.

In our study women in which IUI failed two times positive results after scratching was present in 16.2% cases followed by 6.9% positive results in women who had three times IUI failed and women who had only one-time IUI failed positive results was present in 4.6% cases. In controls we found positive results with 5.4% in women having one-time

IUI failed followed by 3.8% in women where two time IUI failed and only in 2.3% women positive results found having three time IUI failed. Mardanian F et al[10] found that the success rate of pregnancy in the study group underwent endometrial scratch in the IUI cycle was 20.7% and it was more in comparison to control group underwent only IUI (10.2%), but this difference was not statistically significant. 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 (Mardanian F et al[10]). Goel T et al[10] found significantly high pregnancy rates in their RCT. They assessed 284 IUI cases and eligible 144 patients were randomised into two groups equally without any dropouts and found 31.9% pregnancy rate in ES group compared to 16.7% pregnancy rate of non ES controls and concluded that ES is beneficial, cost effective and simple method that can be attached in IUI cycles.

Conclusion

Endometrial scratching in the mid proliferative phase of the intervention cycle is useful in increasing biochemical and clinical pregnancy rates in women after failed intra uterine insemination.

Scratching is able to enhance the receptivity of the endometrium, but a number of other pathologies may be responsible for implantation failure. Scratching appears to be a successful measure for enhancing the chances of implantation in women with recurrent implantation failure.

Scratching is convenient, easy to perform, and associated with very little pain. Based on the existing body of data, as mentioned above, scratching could be offered to patients with recurrent implantation failure in order to try to enhance pregnancy and live birth rates, after the women have been informed in detail about the procedure.

In conclusion this study demonstrates 2.5-3 fold increase in pregnancy rates after scratch, endometrial scratching can be a preferred option in patients with previous failed IUI cycles before opting for expensive IVF treatment.

Further studies are recommended evaluating effect of endometrial scratching on IUI outcome and endometrial receptivity on a larger sample size in a multicentric design.

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