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Vaginal sildenafil's effect on cycles of assisted reproductive technologies

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ABSTRACT

Background: In this research, the effect of sildenafil on endometrial blood flow and successful IVF pregnancies in surrogate mothers was evaluated.

Methods: Surrogate moms were involved in this investigation. Thirty individuals were randomly assigned to receive 25 mg of sildenafil vaginally three times a day in addition to normal medications and method, whereas another thirty patients did not get sildenafil.

Findings: The two research groups' mean age, anthropometry, length of infertility, and pre-treatment endometrial thickness were comparable. Following the conclusion of therapy, it was found that the two research groups' endometrial patterns on ultrasonography were comparable (p value=0.58). 6.7% of sildenafil patients and 3.3% of control patients had heterogenic endometrial patterns, while 10% of sildenafil patients and 6.7% of control patients had echogenic patterns. Similarly, the sildenafil group's endometrial thickness was 10.2 ± 1.7 mm, whereas the control group's was 9.7 ± 1.8 mm, with a p-value of 0.62. those in the Sildenafil group had substantially lower uterine artery PI using Doppler ultrasonography than those in the control group. In a similar vein, we discovered that patients in the Sildenafil group had considerably lower uterine artery RI than patients in the control group. Following the patients, we discovered that the clinical pregnancy rate was considerably greater in the Sildenafil group (60%) than in the control group (26.6%), with a p-value of less than 0.05.

Conclusions: In our research population, vaginal sildenafil led to noticeably greater conception rates. Patients on sildenafil had considerably decreased uterine artery PI and RI.

Keywords: Sildenafil citrate, outcome

INTRODUCTION

A healthy embryo, a receptive endometrium, and synchronisation between the endometrium and the embryo are all necessary for successful implantation. One By stopping the breakdown of cGMP, the 5-phosphodiesterase inhibitor sildenafil citrate promotes vasodilation and smooth muscle relaxation. When oestrogen is present, sildenafil citrate causes the endometrium to proliferate due to increased blood flow in the uterine artery. Two When administered vaginally, sildenafil is thought to drastically reduce peripheral natural killer cell (NK-cell) activity and increase the likelihood of successful pregnancies in women who have had repeated losses. Numerous investigations have been carried out in an effort to provide proof about the impact of sildenafil citrate on the results of antiretroviral therapy. Nevertheless, the matter is still up for debate and no firm resolution has been reached. 3 The purpose of the current research was to evaluate the impact of sildenafil on endometrial proliferation in individuals who had unsuccessful efforts at intracytoplasmic sperm injection (ICSI) or in vitro fertilisation.

METHODS

The International Institute of Reproduction and Fertility Training (IIRFT) in New Delhi was the site of the current prospective, randomised investigation. After explaining the study's objectives to the patients, their informed written agreement was acquired. The faculty and head of IIRFT authorised the research. We included surrogates participating in the center's surrogacy program from June to August of 2020. They underwent the embryo transfer procedure just after their uterus endometrial lining had been prepared. They were not subjected to oocyte retrieval. Thus, they were contacted throughout the menstrual cycle and began receiving therapy just for the transfer of

embryos. There were two research groups formed: Group I was the Sildenafil group, where women received 25 mg vaginally three times a day in addition to conventional medications and ICSI method; Group II was the control group, which received just standard medications and ICSI technique without Sildenafil. Surrogate moms between the ages of 18 and 35 who had a regular menstrual history and normal uterine architecture on transvaginal ultrasonography were eligible. Patients with severe renal, hepatic, or cardiorespiratory conditions were not included. The sample size was determined using the formula $n = (Z\alpha/2 + Z\beta) \times PQ \times 2 / d^2$, where d is permitted error (0.3), $Z\alpha/2$ is type I error at 1% (2.56), $Z\beta$ is type II error at 5% (1.64), and $Q = 1 - P$. According to Yahia et al., the clinical pregnancy rate was 20% in the control group and 51.4% in the sildenafil group. P is therefore equal to $(0.514 + 0.84) / 2 = 0.35$. Thus, the sample size for each group was determined to be 22. We enrolled 30 patients in each trial group to account for anticipated attrition.

Data collection and data analysis

Following informed permission, each patient received a vaginal dosage of 25 mg of sildenafil citrate three times a day until the 21st day of the same cycle, following the administration of supplements containing ecospirin, antibiotics, oestrogen, and folic acid. Every patient had anthropometric, obstetrical, and demographic data recorded. Endometrial thickness was measured using transvaginal ultrasonography (TVS), and uterine artery blood flow was measured using Doppler. A measure of the variability of blood velocity in the uterine artery, the pulsatility index (PI) was computed by dividing the mean velocity throughout the cardiac cycle by the difference between the peak systolic and end-diastolic velocities. The resistance index, a measure of the uterine artery's resistance to perfusion, was computed by dividing the difference between the peak systolic and end-diastolic velocities by the peak systolic velocity. Pregnancy rate, endometrial thickness, and uterine artery blood flow on Doppler were the outcome measurements. Ultrasonography visualisation of one or more gestational sacs or conclusive clinical symptoms of pregnancy were used to confirm a clinical pregnancy.

SPSS version 23 (IBM, New York) was used to examine the data. Both quantitative (means and standard deviation) and qualitative (proportions) data were subjected to descriptive analysis. The student's t test was used to compare quantitative data between the two research groups, while chi-square was used to examine qualitative data.

A p value less than 0.05 was considered as statistically significant.

RESULTS

Each research group included thirty patients throughout the study period. The research groups' mean patient ages were 32.5 and 31.7 years, respectively; the p-value was 0.76. The patients in the two research groups had comparable anthropometric measurements, including height, weight, and BMI. Prior to beginning therapy, the sildenafil group's mean endometrial thickness was 8.01 ± 1.7 mm, whereas the control group's was 8.5 ± 1.9 mm (p-value = 0.51). Following the conclusion of therapy, it was found that the two research groups' endometrial patterns on ultrasonography were comparable (p-value=0.58).

Table 1: Baseline characteristics of the patients included in the two study groups.

Baseline characteristics of the patients	Sildenafil group (n=30)	Control group (n=30)	P-value
Mean age (years)	32.5±7.3	31.7±8.18	0.76
Weight (kg)	66.54±10.93	64.75±11.05	0.47
Height (cm)	154.4±8.33	156.37±9.15	0.36
Body Mass Index (kg/m ²)	28.56±4.3	27.64±4.9	0.18
Infertility duration (years)	4.5±1.7	4.9±1.2	0.08
Endometrial thickness (mm)	8.01±1.7	8.5±1.9	0.51

Table 2: Comparing outcomes in the Sildenafil and control group after treatment.

Outcome variables	Sildenafil group (n=30)	Control group (n=30)	P value
Endometrial pattern			
Normal	25 (83.3%)	27 90%)	0.58
Heterogenic	2 (6.7%)	1 (3.3%)	
Echogenic	3 (10%)	2 (6.7%)	
Endometrial thickness (mm)	10.2±1.7	9.7±1.8	0.62
Uterine artery Pulsatility Index (PI)			
Right	2.5±0.6	3.6±0.3	<0.05
Left	2.4±0.8	3.9±0.2	<0.05
Uterine artery Resistance Index (RI)			
Right	0.66±0.1	0.9±0.05	<0.05
Left	0.62±0.2	0.86±0.08	<0.05
Clinical pregnancy	18 (60%)	8 (26.6%)	<0.05

6.7% of Sildenafil patients and 3.3% of control patients had heterogenic endometrial patterns, while 10% of Sildenafil patients and 6.7% of control patients had echogenic patterns. Similarly, the endometrial thickness was 9.7±1.8 mm in the control group and 10.2±1.7 mm in the sildenafil group, with a p-value of 0.62. those in the Sildenafil group had substantially lower uterine artery PI using Doppler ultrasonography than those in the control group. In a similar vein, we discovered that patients in the Sildenafil group had considerably lower uterine artery RI than patients in the control group. Following the patients, we discovered that the clinical pregnancy rate was considerably greater in the Sildenafil group (60%) than in the control group (26.6%), with a p-value of less than 0.05.

DISCUSSION

In the current investigation, we discovered that both research groups' endometrial thickness and ultrasonography pattern were comparable. Since successful implantation also relies on endometrial quality, the significance of the endometrial pattern as a predictor of treatment cycle outcome in IVF-treated patients has been previously studied^{4,5} Pregnancy rates have been shown to increase as endometrial thickness increases. Previous research has shown that oral and vaginal sildenafil citrate, either by itself or in combination with oestradiol, considerably increases endometrial thickness. Six Vaginal sildenafil (25 mg, 4 times daily) improved endometrial thickness (≥ 9 mm) in 70% of patients, according to another research by Sher et al.⁷ Fetih et al. found that sildenafil vaginal gel markedly improved uterine blood flow and endometrial thickness.⁸ According to Chanona et al.'s findings, vaginal sildenafil usage increased implantation and pregnancy in individuals whose endometrial thickness was equivalent to or less than 7 mm during unsuccessful assisted reproductive technology (ART) cycles.⁹ However, endometrial thickness alone cannot be used to predict a successful pregnancy.¹⁰ This was also shown in our research. Without a concomitant increase in endometrial thickness or echogenicity pattern, we found that patients in the Sildenafil group had substantially greater pregnancy rates than those in the control group.

In comparison to the control group, we found that patients who got sildenafil had considerably reduced uterine artery PI and RI. Malinova et al. observed a substantial reduction in uterine artery PI and RI in the patient group that received 25 mg sildenafil citrate, which is consistent with our findings.¹¹ Additionally, we found that the sildenafil group had a greater clinical pregnancy rate than the placebo group. This would imply that increased rates of implantation and pregnancy are linked to increased uterine blood flow. This would confirm the clinical usefulness of ultrasonography in evaluating the endometrium's basal layer's developing potential. The research by Abdel Kader Fahmy et al. found a 2.5-fold increase in pregnancy in the sildenafil group; however, this difference was not statistically significant, which contrasts with our findings.¹² Similarly, Kim et al. found that using oral oestrogen tablets in addition to vaginal sildenafil during the luteal phase of IVF-ET cycle patients doubled the pregnancy rate, but this increase was not statistically significant.¹³

CONCLUSION

In our research population, vaginal sildenafil led to noticeably greater conception rates. Patients on sildenafil had considerably decreased uterine artery PI and RI. Nonetheless, the ultrasonography pattern and endometrial thickness were comparable to those in the control group. Future vaginal sildenafil clinical studies must be carried out on a greater number of these individuals due to the small sample size.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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