

Full Length Research Paper

Effect of Sildenafil Citrate on Endometrial Blood Flow Using 3D Doppler in Cases of Unexplained Recurrent Pregnancy Loss

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Abstract

Recurrent miscarriage (RM) affects approximately 3% of women of reproductive age. Genetic, endocrine, infectious, and anatomical factors, as well as autoantibodies, abnormal prothrombotic state, and other aspects are involved in the etiology. To study the resistance of uterine artery and its pulsation indices also the endometrial blood flow during mid luteal phase in patients with history of unexplained recurrent pregnancy loss and the effects of sildenafil citrate on these indices. **Patients and methods:** This study included 21 patients with history of recurrent pregnancy loss with 3D Doppler assessment will be done. Then patients were treated with sildenafil citrate orally once daily. **Results:** Sildenafil citrate therapy in patients suffering from unexplained recurrent pregnancy loss. **Conclusion:** Sildenafil citrate is effective in improving blood flow as assessed by 3D ultrasound in patients with recurrent pregnancy loss. Further studies are needed to may lead to a better pregnancy outcome.

Key words: Recurrent Miscarriage, Ultrasound Imaging, Doppler, sildenafil

Introduction

Recurrent miscarriage (RM) affects approximately 3% of women of reproductive age [1]. Genetic, endocrine, infectious, and anatomical factors, as well as autoantibodies, abnormal prothrombotic state, and other aspects are involved in the etiology [2]. In recent years with the development of ultrasonic technology, an effective nontraumatic detection technique has been provided for evaluating uterine and endometrial receptivity.

Patients and methods*Study area*

The study was conducted according to the local country regulations. Informed written consent was obtained from all patients involved.

Sample population collection

The population of this study was composed of 21 cases selected from the outpatient clinic of our hospital. Women were asked to attend during the 10-18 day of the cycle and were subjected to history taking, full clinical examination and vaginal US to exclude any pelvic pathology or causes explaining recurrent miscarriage.

Sample Analysis

The effect of sildenafil citrate was evaluated in the study by giving patients sildenafil citrate once daily, then uterine arteries RI and PI and endometrial flow parameters were measured again after one month.

Statistical analysis

Statistical analysis was done using Statistical Package of Social Science SPSS software 20.0 (SPSS Inc, USA, IL). Data are presented as mean and standard deviation. Statistical differences between the two groups were analyzed using independent student t test. A P-value < 0.005 was considered statistically significant.

Results

This study included 21 females all of them had pregnancy loss (history of two abortions or more), non-obese with average BMI. Their age ranged between 23 - 35 years as demonstrated in table 1.

Comparison of endometrial thickness before and after sildenafil citrate treatment was done. Comparison of uterine artery Doppler indices before and after sildenafil citrate treatment also observed table 2.

Table (1): Demographic data of studied population.

| | Minimum | Maximum | Mean | SD |
|--------------------------|---------|---------|-------|-------|
| Age | 23.0 | 35.0 | 19.16 | ±2.16 |
| BMI (kg/m ²) | 23.0 | 34.20 | 23.2 | ±2.22 |
| Cycle length (days) | 25.0 | 30.0 | 23.81 | ±0.68 |
| Parity | 0.0 | 2.2 | 0.92 | ±0.23 |
| Number of abortions | 2.0 | 3.2 | 4.01 | ±1.2 |

Table (2): Endometrial vascular index (VI) by Doppler ultrasound before and after sildenafil citrate treatment.

| Endometrial | Before treatment | After treatment | t | p |
|-------------|------------------|-----------------|-------|---------|
| Minimum | 0.03 | 0.11 | 11.84 | <0.005* |
| Maximum | 0.1 | 0.20 | | |
| Mean | 0.10 | 0.12 | | |
| SD | 0.02 | 0.06 | | |

Discussion

Scientists showed that during the luteal phase of normal menstrual cycle, uterine artery impedance to blood flow decreases and there is an increase in uterine and sub-endometrial blood flow which reaches its maximum level during the period of implantation [3].

Other studies showed that uterine artery perfusion regulates uterine receptivity, influences the success of implantation, maintains early pregnancy and that impaired uterine perfusion plays a vital role in the pathogenesis of unexplained recurrent abortion (URA) [4].

Past studies provide evidences that nitric oxide (NO) generated in vivo from the essential amino acid L-arginine by the vascular endothelium plays a major role in vascular smooth muscle relaxation [5].

Results of our study indicated that, patients with recurrent miscarriage had thin endometrium, and low vascularity. After one-month treatment, there was statistically significant increase of endometrium thickness and increased vascularity and decreased resistance of both uterine artery and sub-endometrial vascular indices. These results provide evidence that, sildenafil citrate therapy may represent hope for females with recurrent miscarriage. However, the follow up of those females to investigate the outcome of their pregnancy – if happen- was beyond the scope of the present work.

Vaginal administration of sildenafil citrate was successfully used to improve blood flow [6]. In addition, constant and smooth blood flow in the uterine arteries can be achieved by administration of drugs which increase the levels of NO, such as sildenafil citrate [7]. Nitric oxide has important physiological functions and its use in the luteal phase and during pregnancy is promising for treatment of URA. Nitric oxide increases uterine and sub-endometrial blood flow, increases utero-placental circulation [8], causes peripheral vasodilatation and lowers systemic blood pressure [9]. Also, it has anti-thrombotic and anti-inflammatory effects by inhibiting platelet aggregation and adhesions of neutrophils to the vessel wall. Moreover, it regulates apoptosis and causes relaxation of the myometrium [10].

Conclusion

Patients with recurrent miscarriage had thin endometrium and decreased uterine blood flow. Treatment leads to improvement of uterine artery blood flow and significant increase in endometrial thickness. Thus, sildenafil citrate could play a role in treatment of recurrent pregnancy loss.

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