

ROLE OF VAGINAL SILDENAFIL CITRATE IN CASES OF INFERTILITY PATIENTS WITH POOR ENDOMETRIUM

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INTRODUCTION

Background

- Endometrial thickness is the important factor in management of infertility.
- Endometrial thickness > 8 mm results in increased fertilization rate and pregnancy rate.
- Implantation is the most vital part of reproduction
- Implantation depends on Endometrial receptivity, thickness, endometrial and subendometrial blood flow.
- Aim of the study is improving endometrial thickness and receptivity using sildenafil and thereby improving fertility rates.

MATERIALS AND METHODS

A total of 50 pts who failed with ovulation induction, with good follicle but with thin endometrium are supplemented with sildenafil citrate from D5 and endometrial thickness and fertility rates are measured in these people.

Inclusion criteria

- younger than 40 years
- unexplained infertility
- endometrial thickness less than 8mm in previous cycles

Exclusion criteria included

- Patients with history of hysteroscopic surgeries.
- cardiovascular, renal and liver diseases.
- Male factor infertility.

Treatment protocols: Group was given sildenafil citrate tablets (50 mg) daily in addition to the above treatment protocol from the fifth day of the cycle until the day of starting progesterone. On the thirteenth day of the menstrual cycle, the endometrial thickness was estimated by transvaginal ultrasonography (arranged in a series every other day). The evaluations were performed by a single investigator. If the endometrial thickness was more than 8mm, 100 mg of progesterone was injected intramuscularly.

RESULTS

The endometrial thickness was significantly higher in the sildenafil citrate group ($p < 0.001$), with increase in overall fertility rates of the patients

DISCUSSION

- For successful implantation to occur, an adequately prepared endometrium has to be built up during the menstrual cycle. Endometrial development is regulated by steroid hormones and various growth factors and cytokines.
- Pregnancy rates were higher when the endometrium was thicker than 10 mm. [1]
- Sildenafil is a selective inhibitor of the type V cGMP-specific phosphodiesterase. With the use of sildenafil,

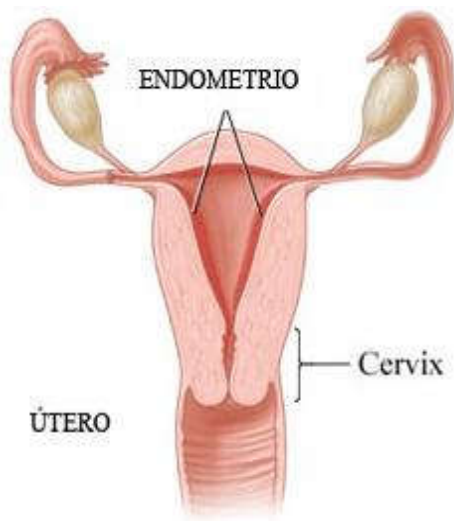
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cGMP levels remain elevated, which leads to vascular relaxation and increased blood flow.

- A positive linear correlation between endometrial thickness measured on the hCG day and pregnancy rate (PR) was identified (2).
- A good correlation has been found between endometrial thickness and the prevalence of conception. An endometrial thickness of ≥ 9 mm in the late proliferative phase, as determined by vaginal ultrasound, correlates well with the chance of pregnancy after ovulation induction, whereas a thinner endometrium is associated with poorer prognosis for success (3).
- However, no attainment of pregnancy was predicted by endometrial thickness alone.
- In our study, sildenafil citrate clearly increased endometrial thickness (9.8 mm vs. 8 mm), and the chemical pregnancy rates were higher in the sildenafil citrate group but not significantly.
- Endometrial and subendometrial blood flows measured by vaginal color Doppler ultrasound are a good predictor of pregnancy during IVF treatment (6),
- A combined analysis of endometrial thickness and pattern on the day of hCG administration proved to be a better predictor of the outcome of IVF/ICSI-ET and may be more helpful for patient counselling than a separate analysis. Elevated estrogen concentrations may increase sensitivity to progesterone action and, thus, lead to secretory advancement. Estrogen/progesterone ratios, which are also associated with the impairment of endometrial receptivity, are the main factors affecting receptivity.
- In this study, sildenafil citrate significantly decreased the estrogen, progesterone and estrogen/ progesterone ratio on the progesterone day.

Endometrial thickness is a Critical Factor in Infertility Management

Endometrial thickness <8mm



Endometrial Thickness >8mm results into.....

- Increased fertilization rate & Pregnancy Rate

Sildenafil Citrate is potential & emerging treatment for increasing Endometrial Thickness >8mm

Sildenafil citrate is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) that prevents the breakdown of cGMP and potentiates the effect of nitric oxide on vascular smooth muscles (17). Sildenafil citrate could lead to an improvement in uterine blood flow and, in conjunction with estrogen, led to the estrogen-induced proliferation of the endometrial lining (16). Sildenafil citrate enhances uterine blood flow and increases endometrial thickening

Sildenafil Citrate enhances uterine blood flow & increases endometrial thickness.

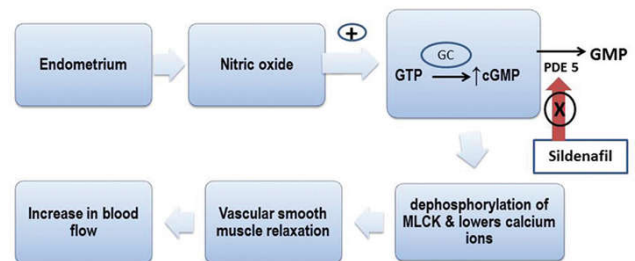


Sildenafil citrate in conjugation with estrogen, led to the estrogen induced proliferation of the endometrial lining

Review Article

An overview on sildenafil and female infertility

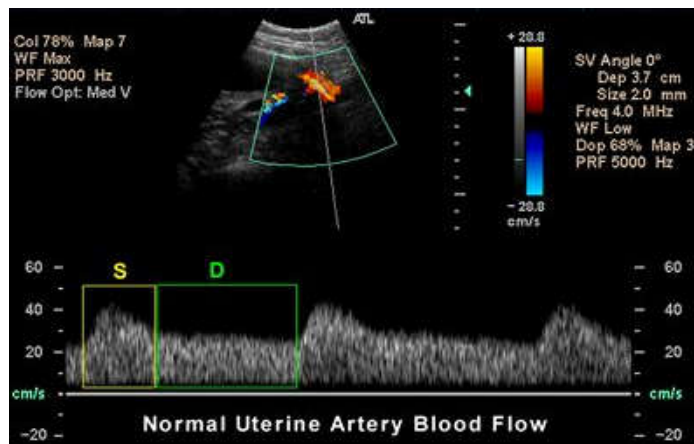
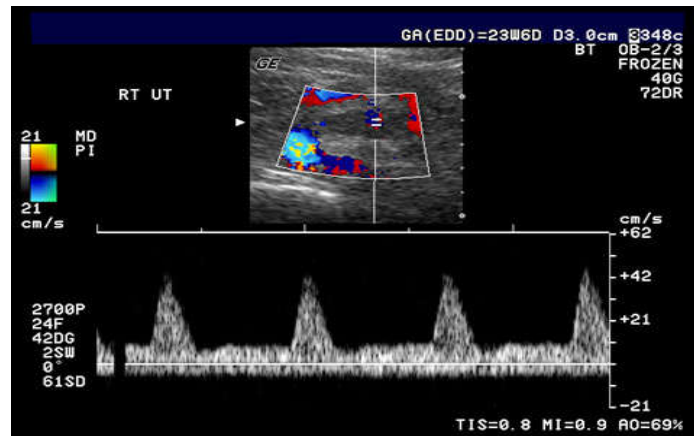
Jyoti M. Benni, Paragouda A. Patil



GC- Guanylate Cyclase; GTP- Guanosine monophosphate; GMP- Guanosine monophosphate; cGMP- cyclic Guanosine monophosphate; MLCK-myosin light chain kinase; PDE5- Phosphodiesterase 5

Sildenafil Citrate – Mechanism of Action





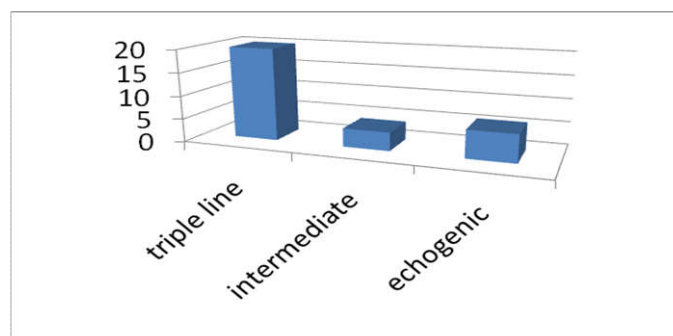
Vaginal Sildenafil increased uterine blood flow thereby increasing endometrial thickness which in turn enhances endometrial receptivity giving a better conception rate

Characteristics of the patients at the start of study

variables	Mean
age	28 yrs
Duration of infertility	72 mths
Basal Fsh(u/l)	5.4
Basal Lh(u/l)	8.76
Basal Fsh/Lh	0.7
Basal progesterone	0.64ng/ml

Effect of sildenafil on progesterone levels, Fsh, Lh, endometrium, implantation rate

variables	Mean
Estrogen/ progesterone on day 13	0.7
Progesterone on day 13	1.12
LH day 13	1.1
Endometrial thickness	9.8
Implantation rate	14.6
Duration of cycle	12.125



Patterns of endometrium & their percentages noted on day 13

Conclusion: As our study shows, the vaginal use of sildenafil citrate is a good way to improve the endometrial receptivity. We recommend the routine use of vaginal sildenafil citrate in patients with a previous failure of ovulation induction cycles due to poor endometrial thickness. Vaginal sildenafil seems to be an effective drug for increasing endometrial thickness & pregnancy rate in infertility patients.

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