



INCREASING ENDOMETRIAL THICKNESS IN MANAGEMENT OF INFERTILITY BY USING SILDENAFIL: INTERVENTIONAL STUDY IN WESTERN INDIA.

Dr Anubhooti Trivedi Resident OBG DMIMS Sawangi Wardha

Dr Kiran Borkar (MD) Associate Professor Department of OBG DMIMS Sawangi Wardha

ABSTRACT

Introduction-An important factor in infertility is thin endometrial thickness (ET). Pregnancy rate was higher in endometrial thickness 6-10mm. Also an adequate ET is an important necessity for favorable IVF outcome. Sildenafil a 5- phosphodiesterase type 5 (PDE5) inhibitor increases endometrial thickness when administered intravaginally.

Methods- An experimental interventional design was conducted at Dept of OBG-GYN at JNMC, DMIMS, Wardha from August 2016-June 2017. Females seeking treatment for Assisted Reproductive technique (ART) with less endometrial thickness were included in study.

They were asked to self-administer per vaginal sildenafil & the response was assessed using Trans Vaginal Sonography (TVS). The data was collected using pre-formed pre-tested questionnaire, compiled, analyzed & using MS-Excel 2007. Data was interpreted using proportions & appropriate tests of significance.

Result- In total 107 participants were taken but 03 subjects were lost in follow up. There is no statistically significant association of age with type of infertility. ($p > 0.05$) Prior to use of Sildenafil, in total 39.42% females had endometrial thickness of > 4.1 mm, 33.65% females had endometrial thickness of > 5.1 mm. Following use of Intravaginal Sildenafil, a statistically significant increase in ET by 1.5mm was noted. During the study no significant adverse effect was reported by any participants.

Conclusion- Hence use of intravaginal sildenafil causes statistically significant increase in Endometrial thickness.

KEYWORDS : Endometrial thickness (ET), intravaginal sildenafil, Assisted Reproductive technique (ART), Trans Vaginal Sonography (TVS).

Introduction- Infertility is the failure to conceive (regardless of cause) after 1 year of unprotected intercourse. This condition affects approximately 10-15% of reproductive-aged couples. Infertility is caused by male and/or female factors. ⁽¹⁾ Male and female factors each account for approximately 35% of cases. Often, there is more than one factor, with male and female factors combined causing 20% of infertility. In the remaining 10% of cases, the etiology is unknown. ⁽¹⁾ An important factor in infertility is thin endometrial thickness. ⁽²⁾ It is expected that endometrial thickness reduces with age. But in all age ranges pregnancy rate was higher in endometrial thickness 6-10mm ($p < 0.05$). ⁽³⁾ Hence in order for successful implantation to occur, an adequately prepared endometrium has to be built up during the menstrual cycle which is regulated by steroid hormones and various growth factors and cytokines. Sufficient uterine blood supply is required for these factors to reach the endometrium. ⁽³⁾ It is observed that endometrial thickness was significantly associated with in vitro fertilization (IVF) outcome. In addition, pregnancy rates were higher when the endometrium was thicker than 10 mm. ^(4,5)

Sildenafil causes vascular relaxation and increase blood flow that increases the endometrial thickness ⁽⁶⁾.

This study was taken up to observe response of intra-vaginal sildenafil in infertile patients with Endometrial Thickness < 7 mm.

Methodology- Hence an experimental interventional design was conducted at Dept of OBG-GYN at JNMC, DMIMS, Wardha. Ethical clearance was taken from department & institute before initiating study. The study was conducted from August 2016-June 2017. All females taking treatment for primary & secondary infertility from Gynecology OPD with less endometrial thickness were included in study. A written valid informed consent was taken from all participants & their spouses. A thorough infertility workup was done for all participants & those with low ET were included.

All eligible participants were asked to self-administer per vaginal sildenafil 50 mg HS from day 6 of menstrual cycle till the day on which single ovarian follicle measures > 18 mm. The response was assessed using Trans Vaginal Sonography (TVS). That endometrial thickness (ET) was measured from day 7 and day 11. The data was collected using pre formed pilot tested questionnaire. The data collected was compiled & analyzed using Ms-EXCEL-2007. The data

was presented using percentages & proportions.

Result- In total 107 participants were taken but 03 subjects were lost in follow up. Hence in total 104 subjects were taken in study. Table-1 shows that maximum i.e. 37.5% participants were in age group of 26-30 yrs. In total 57.69% subjects suffered from primary & 42.3% participants had secondary infertility. There is no statistically significant association of age with type of infertility. ($p > 0.05$). (Table-2).

Prior to use of Sildenafil, in total 39.42% females had endometrial thickness of > 4.1 mm, 33.65% females had endometrial thickness of > 5.1 mm, furthermore 19.23 % females had endometrial thickness > 6.1 mm thus were in need of active intervention. (Table-3)

Following use of Intravaginal Sildenafil, almost 95.2 % participants had ET > 6 mm. This is statistically significant increase in ET ($P < 0.0147$). (Table-3) During the study no significant adverse effect was reported by any participants. The minor discomfort did not compelled discontinuation of its use by participants.

Discussion-The finding of age distribution of participants in study are similar to Ali Fassadi et al that 71.4% of patients were in age group from 20-40 years, while > 40 yrs were 21.4 %. ⁽⁷⁾ There was no statistically significant association was observed between age & type of infertility but these findings were different from that of Abha Maheshwari & et al that proved that women over 35 years of age are nearly twice as likely to present with primary infertility. ⁽⁸⁾

Following use of Intravaginal Sildenafil average ET was 8.39 ± 1.55 mm. The positive correlation has also been shown by Ali Assadi (Tikrit Medical Journal 2012)-) 35.7% of patients in their study developed endometrial thickness to > 7 mm after the use of sildenafil. ⁽⁷⁾ This findings were similar to findings of Dr. Suchika Mangal et al (IJRCOG JUNE 2016)- Compared use of sildenafil and estradiol in increasing endometrial thickness. 64% females of sildenafil group and 48% of estradiol group showed increase post administration. ⁽⁹⁾

Conclusion- Hence use of intravaginal sildenafil causes statistically significant increase in Endometrial thickness without causing significant adverse effects demanding cessation of its use.

Limitations-03 subjects were lost in follow up.

infertile women undergoing intrauterine insemination. Int J Reprod Contracept Obstet Gynecol 2016;5:2274-

Table-1-Distribution of subjects on the basis of age & type of infertility

Age(yrs.)	N	%
Under 25	28	26.92
26-30	39	37.50
31-35	23	22.11
36-40	10	09.61
>40	04	03.86
Total	104	100
Type of infertility		
Type	N	%
Primary	60	57.69
Secondary	44	42.3
Total	104	100

Table-2- Distribution of subjects on the basis of correlation of type of infertility with age-

Age (yrs)	Primary infertility	Secondary infertility	Total
<30	38 (63.33%)	25 (56.81%)	63
30-40	19 (31.66%)	18 (40.90%)	37
>40	3 (5%)	1 (2.72%)	4
Total	60	44	104

Chi sq-1.28 df-2 P-0.52

Table-3-Distribution of subjects on basis of pre & Post sildenafil use ET thickness-

Prior to use of sildenafil		
ET(mm)	N	%
<3 mm	01	0.96
3.0-4.0 mm	41	39.42
4.1-5.0 mm	35	33.65
5.1-6.0 mm	20	19.23
>6 mm	07	06.73
Total	104	100
Post Intra- vaginal Sildenafil use		
ET(mm)	N	%
4.1-5.0	1	0.96
5.1-6	4	3.85
6.1-7.0	18	17.31
7.1-8	26	25.00
8.1-9.0	23	22.12
9.1-10	14	13.46
>10	18	17.31
Total	104	100.00

Average post intervention ET-8.39+1.55mm
 Mean difference i.e. increase in ET post intervention-3.75+1.55mm.
 Mean Pre-post-(-1.801)T-(-9.16) DF-206 P-0.0147 F-1.54

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