



EFFECT OF SILDENAFIL CITRATE IN PREGNANT WOMEN WITH HIGH RESISTANCE DOPPLER VELOCIMETRY STUDY- A PROSPECTIVE INTERVENTIONAL STUDY.

Obstetrics & Gynaecology

Dr. Srilakshmi MBBS, MS(OBG), FMAS, CIMP

Dr. Zaara Tarannum MBBS, DGO

Dr. M. Tripura Sundari MBBS, MD, DGO, FIMS

ABSTRACT

Placenta regulates the nutrient supply to the growing embryo throughout gestation. Therefore, developmental progression throughout intrauterine life requires adequate placental function¹. Sildenafil citrate is the only PDE5 inhibitor studied in pregnancy. By reducing arterial pressure sildenafil citrate improves arterial perfusion in human placental model⁷

KEYWORDS

Sc- Sildenafil Citrate; UDV= ultrasound Doppler velocitometry

INTRODUCTION :

Placenta regulates the nutrient supply to the growing embryo throughout gestation. Therefore, developmental progression throughout intrauterine life requires adequate placental function¹. During pregnancy, uteroplacental blood flow is responsible for transport of nutrients from the mother to the fetus. Uteroplacental blood flow increases considerably during the second and third trimesters of pregnancy^{2,3}. 29.5% of newborns in India are having low birth weight (less than 2.5kg birth weight)⁴. 18% of pregnancies in India are affected by FGR 5. To augment blood flow to tissues, several new vasodilator drugs have been suggested, and one of these drugs is sildenafil citrate (SC). It is a selective inhibitor of second messenger cyclic guanosine monophosphate formation through inhibition of type-5 phosphodiesterase (PDE5)⁶. There by, resulting in an increased nitric oxide production leading to vascular smooth muscle relaxation and thus causing vasodilation.

Sildenafil citrate is the only PDE5 inhibitor studied in pregnancy. By reducing arterial pressure sildenafil citrate improves arterial perfusion in human placental model⁷. It has been suggested that PDE5 inhibitor may be useful in the treatment of hypertension during pregnancy as well as fetal growth restriction. Sildenafil enhances endothelial function of myometrial vessels in pregnant women with fetal growth restriction and induces vasodilation of chorionic plate arteries in women with uncomplicated pregnancies⁸. Ultrasound doppler velocitometry is a surveillance tool in pregnancies as it depicts fetal perfusion and hence the nutrient availability for the growing fetus. Sildenafil citrate significantly normalizes the ultrasound doppler velocitometry indices⁹. Reduction in blood flow assessed by ultrasound doppler velocitometry (UDV) in uterine artery (Ut A) and umbilical artery (Umb A) is seen in fetal growth restriction¹⁰. This reflects as an increase in UDV indices like RI (Resistance Index), PI (Pulsatility Index). The RCOG prescribes UmbA doppler as the primary surveillance tool in the growth restricted foetuses¹¹. The 'brain sparing effect' causes centralization of blood by compromising systemic circulation and this manifests in the middle cerebral artery (MCA) as decrease in RI, PI and S/D on UDV.

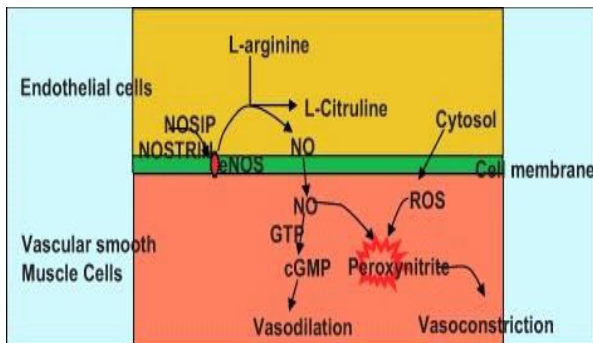


Fig1: NO pathway

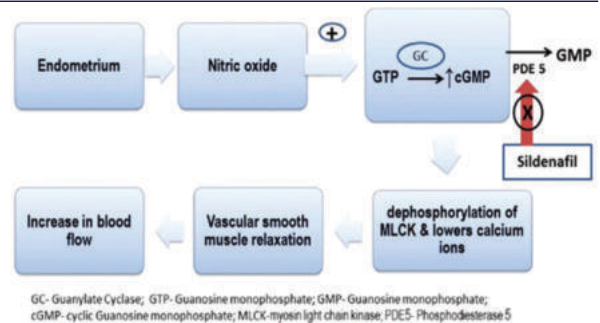


Fig2: An illustration of mechanism of action of sildenafil citrate(8) Oral usage of sildenafil citrate might have several side effects such as headache, flushing, indigestion, sensitivity to light, nasal congestion, back pain, muscle pain, nausea, dizziness, rash. (9) All these can be avoided by vaginal route of administration and also for better local absorption.

Case Study:

AIM:

The aim is to evaluate the effect of sildenafil citrate on uteroplacental perfusion using Doppler indices in pregnant women attending the antenatal clinic with abnormal doppler velocitometry study.

OBJECTIVES:

- Assessment of the effect of sildenafil citrate on
- Umbilical artery doppler indices
- Uterine artery doppler indices
- Middle cerebral artery doppler indices

MATERIALS AND METHODS

Source Of Data:

Study period: 12 months

Study population:

This study was done on Pregnant women of more than 20 weeks of gestation attending the antenatal clinic with abnormal doppler velocitometry study.

Sample size: 40

Inclusion Criteria

- Pregnant women of more than 20 weeks of gestation with abnormal doppler velocitometry study
- any age and any parity.
- BMI between 18 and 35
- singleton pregnancy

Exclusion Criteria

- Anomalous fetus

- multiple gestations
- maternal diseases that contraindicates the use of SC
- women taking medications that interact with sildenafil were the exclusion criteria.⁹² \approx 49
- The minimum required sample is 49.

METHODOLOGY:

Women attending the antenatal clinic with finding of abnormal doppler velocimetry were the subject of interest. The inclusion and exclusion criteria were applied and the women who were eligible to participate and who gave written consent were enrolled in the study. A total of 40 women who met the inclusion criteria were selected and after explaining the procedure, the consent was signed.

A detailed history including obstetric history regarding the duration of pregnancy, any associated comorbidities, previous pregnancy details was taken and thorough clinical examination was done. A relevant medical history of any systemic illness and drug intake which can cross interact with sildenafil citrate was also taken. After the general physical examination, per abdominal examination was done to assess the corresponding fundal height for gestational age and lie of the baby when applicable. Laboratory investigations including CBC, coagulation profile, random blood sugar, liver and kidney function test were done.

All the patients were subjected to obstetric ultrasound and doppler velocimetry parameters such as bilateral uterine artery PI and RI, umbilical artery PI and RI, MCA PI and RI, estimated fetal weight and amniotic fluid index were noted.

The patients were advised to insert tablet Sildenafil citrate 25mg per vaginally twice a day for four weeks. At the end of fourth week a repeat obstetric ultrasound and doppler velocimetry was done and the parameters of bilateral uterine artery PI and RI, umbilical artery PI and RI, MCA PI and RI, estimated fetal weight and amniotic fluid index were noted and compared with the previous obstetric ultrasound and doppler velocimetry results.

RESULTS:

40 Pregnant women attending the antenatal clinic with abnormal doppler velocimetry study were selected for the study. The results were as follows

Age Distribution

In the present study the average age of the study population was 27.61 \pm 3.820 years.

Mean gestational age before intervention was 26.76 weeks with standard deviation of 2.973. the mean gestational age after intervention was 30.76 weeks with standard deviation of 2.973.

Table 1. Distribution of study subjects based on Mean Gestational Age before and after intervention

Variables	Mean \pm SD
Age	27.61 \pm 3.820
Gestational Age Before intervention	26.76 \pm 2.973
Gestational Age After intervention	30.76 \pm 2.973

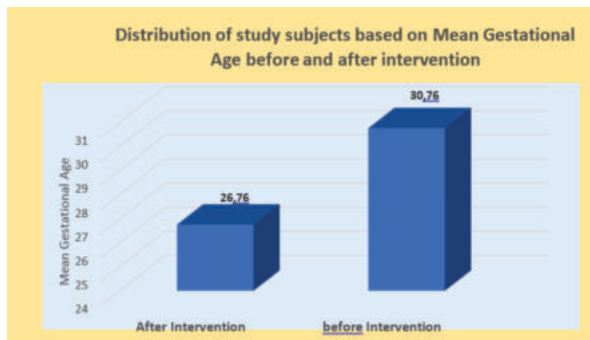


Figure 3. Distribution of study subjects based on Mean Gestational Age before and after intervention:

Table 2. Comparison of doppler velocimetry studies before and after treatment with sildenafil citrate :

Variables	After Intervention	Before Intervention	t-test	p Value
R UT/A PI	0.90 \pm 0.17	1.43 \pm 0.04	-18.27	<0.001*
R UT/A RI	0.54 \pm 0.05	0.65 \pm 0.03	-11.438	<0.001*
L UT/A PI	0.84 \pm 0.10	1.43 \pm 0.05	-36.521	<0.001*
L UT/A RI	0.53 \pm 0.05	0.61 \pm 0.03	-8.541	<0.001*
Umb/A PI	1.14 \pm 0.12	1.23 \pm 0.13	-3.174	0.003*
Umb/A RI	0.64 \pm 0.04	0.72 \pm 0.02	-10.409	<0.001*
MCA PI	2.10 \pm 0.10	2.09 \pm 0.17	0.251	0.803
MCA RI	0.84 \pm 0.01	0.84 \pm 0.02	0.086	0.932
EFW (gm)	1036.5 \pm 373.1	1752.2 \pm 600.5	-18.129	<0.001*
AFI(cm)	13.61 \pm 0.86	18.84 \pm 0.99	-23.041	<0.001*

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Note: * P value <0.05 is considered to be statistically significant.

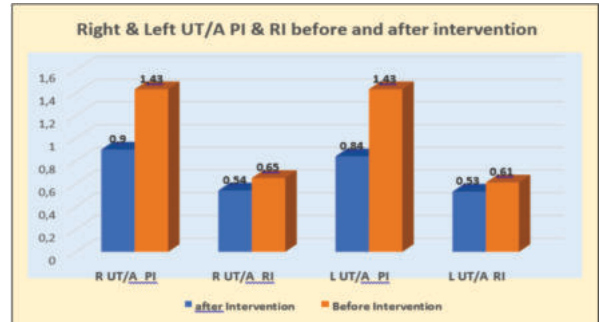


Figure 4. Right & Left UT/A PI & RI before and after intervention

Table 3: EFW before and after intervention In our study, gain in EFW was statistically significant after administration of sildenafil citrate.

Variables	Before Intervention	After Intervention	t-test	p Value
EFW (gm)	1036.5 \pm 373.1	1752.2 \pm 600.5	-18.129	<0.001*

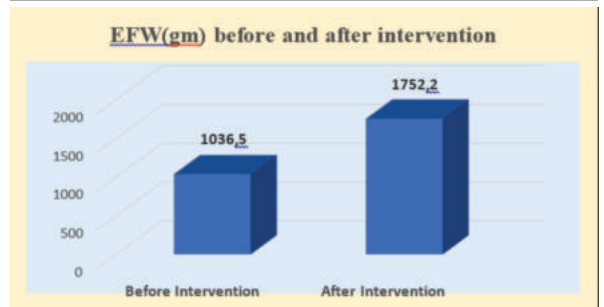


Figure 5. EFW before and after intervention

Table 4: AFI before and after intervention

Variables	Before Intervention	After Intervention	t-test	p Value
AFI (cm)	13.61 \pm 0.86	18.84 \pm 0.99	-23.041	<0.001*

After administration of sildenafil citrate gain in AFI was statistically significant.

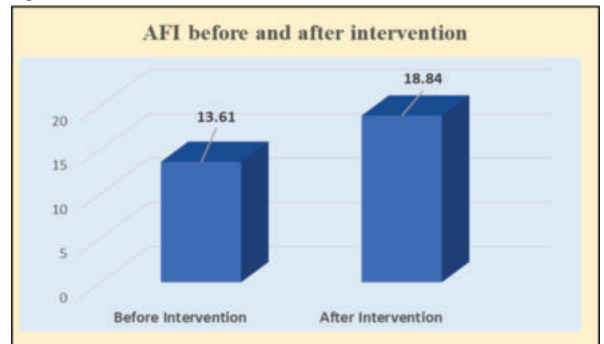


Figure 6: AFI before and after intervention

CONCLUSION:

- We conducted this study to assess the effect of Sildenafil citrate in pregnant women with high resistance doppler velocimetry study indices.
- Our study reported statistically significant improvements in uterine artery and umbilical artery doppler indices with gain in EFW and the volume of AFI in the study population.
- Hence it is implied that Sildenafil significantly improves uteroplacental circulation and normalizes blood flow in foetus, when used in pregnant women with high resistance doppler velocimetry study indices.
- Further, more number of studies with large sample size are needed for confirming the effectiveness of sildenafil citrate in improving doppler velocimetry study parameters and Regarding the effective dose and administration regimen of sildenafil in pregnancy.

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