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Use of Vaginal Sildenafil Citrate Therapy in Intrauterine Growth Restriction

[1]Dr Kairavi Gokani, MBBS, DNB, MRCOG Obstetrics and Gynaecology, Ankoor Fertility Clinic, Mumbai
[2]Dr. Shraddha Rao, MBBS, MS, DNB Obstetrics and Gynaecology, Ankoor Fertility Clinic, Mumbai
[3]Dr. Priyanka Vora, MBBS, DGO, FCPS, DFP, BIMIE, MICOG, FICOG, Ankoor Fertility Clinic, Mumbai
[4]Dr. Kedar Ganla, MBBS, MD, DNB, Obstetrics and Gynaecology, Ankoor Fertility Clinic, Mumbai
Corresponding Author: Dr. Shraddha Rao, MBBS, MS, DNB Obstetrics and Gynaecology, Ankoor Fertility Clinic, Mumbai.

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Abstract

Purpose: Intrauterine growth restriction (IUGR) is when the fetus has not reached its term growth potential owing to genetic or environmental factors. Presenting a case report where vaginal sildenafil citrate was used in a patient with intra uterine growth restriction (IUGR). Sildenafil citrate, a phosphodiesterase-5 inhibitor that stabilizes cyclic guanosine monophosphate (cGMP) and increases nitric oxide levels, improves placental perfusion by dilation of spiral arteries leading to smooth muscle relaxation, thereby proving to be efficacious in IUGR.

Result: Use of vaginal sildenafil citrate in this patient with IUGR helped us prolong the pregnancy and have a better neonatal outcome with better fetal birth weight and reduced stay in neonatal ICU

Conclusion: Sildenafil citrate helped in converting a pre term IUGR to a term IUGR, thereby reducing neonatal morbidity and reduced burden on health services.

Keywords: Intrauterine growth restriction (IUGR), Sildenafil citrate, colour doppler indices

Introduction

Fetal growth restriction [also called intrauterine growth restriction ([IUGR)] is when the fetus has not reached its growth potential owing to genetic or environmental factors. IUGR occurs as a result of impaired gas exchange and/or if the nutrients delivered to the fetus are not sufficient to allow it to normally thrive in utero. This process can occur owing to any maternal disease leading to decreased oxygen-carrying capacity (e.g. smoking, cyanotic heart disease, or hemoglobinopathy), or by disorders in the oxygen delivery system secondary to maternal vascular diseases [1].

FGR generally refers to a fetus that has failed to reach its biological growth potential because of placental dysfunction [2].

Case Scenario

A 29 year who had been married for 7 years, conceived spontaneously within one year of marriage in 2020, which resulted in an early pregnancy loss. Subsequently she had 2 early pregnancy losses at 6 weeks, all conceived spontaneously. She came to our Out Patient Department in 2021. We evaluated the patient

thoroughly. Husband's semen analysis, sperm dna fragmentation, blood sugars, thyroid profile were within normal limits, ruling out male contribution to infertility. The patient's AMH, antral follicular count, endometrial assessment in natural cycle were done which was normal. APLA screening was also done, which was within normal limits. 3 attempts of IUI were done, all unsuccessful. She opted for IVF, due to secondary infertility. Her fresh embryo transfer was unsuccessful. She conceived after a frozen embryo transfer cycle in 2023. Her antenatal course was uneventful until 27.4 weeks when she started developing gestational hypertension (146/90). She was advised Home BP monitoring. Subsequent BP records were in congruence with diagnosis of gestational hypertension. She was examined in the clinic. Fundal height was lesser than that for gestational age. Her complete hemogram, and liver function tests and renal functional tests were within normal limits. She was started on anti hypertensive, tab Labetolol 100mg thrice a day for the same. Her ultrasound with colour doppler was done. Ultrasound was suggestive of abdominal circumference(AC) less than 5th centile and estimated fetal weight (EFW) was 840 grams. The colour doppler was suggestive of raised resistance in uterine artery. (Ut A PI > 95th centile). She was advised about maintaining adequate hydration, adequate bed rest, a high protein diet, and regular follow up visits. She was started on tab sildenafil citrate 25 mg vaginally thrice a day.

She was further serially monitored. At 29.3 weeks, ultrasound was suggestive of abdominal circumference less than 5th centile and EFW was 994 grams. Colour doppler was suggestive of raised resistance in umbilical artery.

At 33 weeks she had been admitted in view of newly developing pedal edema and albuminuria suggestive of pre eclampsia. Her complete hemogram, liver and renal function tests were within normal limits. Another antihypertensive, Tab Nicardia 10mg twice a day was started. Tab sildenafil was continued. Ultrasound showed that AC continued to be less than the 5th centile while EFW was 1455 grams, liquor was adequate and BPP within normal limits.

At 35.4 weeks, ultrasound showed AC < 5th centile, EFW 1745 grams. The colour doppler was suggestive of CPR < 1.

At 36.3 It was decided to terminate the pregnancy.

LSCS was performed in view of severe pre eclampsia and it being a precious pregnancy. She delivered a female baby weighing 1.9 kg. Baby cried immediately on birth. APGAR 7/10

Baby was in NICU for 3 days in view of preterm IUGR. Post this, baby was discharged.

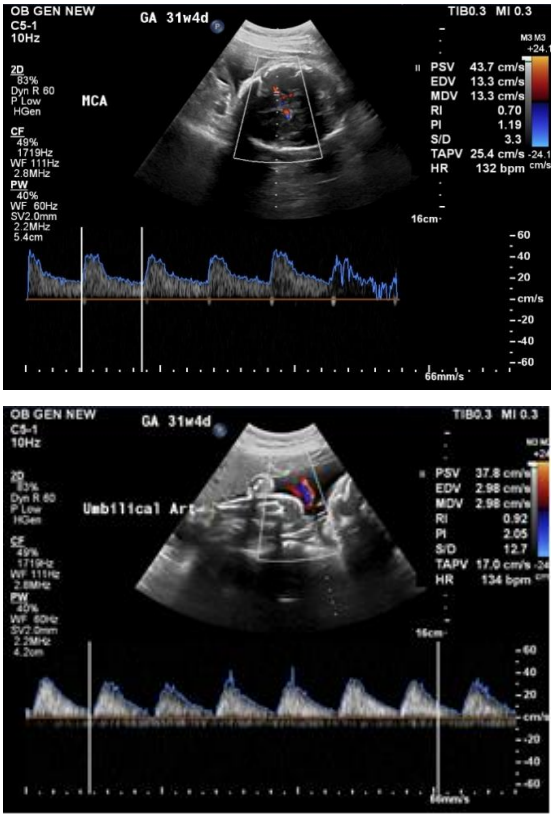

Figure 1 & 2: Colour doppler indicating abnormal cerebro placental ratio indicated by MCA PI and umbilical artery PI

Discussion

In view of its role as the main regulator of the delivery of nutrients for the fetus, and in light of the temporary interface that regulates the connection between maternal and fetal circulation, the placenta is responsible for sustaining fetal growth and development [3]

Decreased placental surface area, overall volume, and diminished vascularization of the terminal villi are associated with fetal growth restriction [4,5]

Failure of cytotrophoblasts to migrate into the maternal spiral artery, and subsequent interaction with natural killer cells, is key for retaining the smooth muscle layer, and internal elastic lamina [5,6]

Consequently, higher blood velocity within the spiral artery results in a decreased lumen, hence negatively affecting perfusion and exchange of nutrients [3].

Doppler studies demonstrated the presence of uterine and umbilical arteries with high-resistance waveforms in intrauterine growth restriction (IUGR) pregnancies and were shown to be related to the disruption of spiral artery invasion by trophoblastic tissue, and failure of the remodeling processes [7]

Sildenafil citrate is a phosphodiesterase 5 inhibitor, and thereby leads to vasodilatation. PDE5 is responsible for the degradation of cGMP to guano-sine monophosphate. Therefore, inhibiting PDE5 delays the breakdown of cGMP and increases vasodilation [8]

Conclusion

IUGR is associated with a myriad of complications. As per Barker's hypothesis, IUGR can pose dire implications in the long term as well. The way that sildenafil citrate can benefit these patients is by converting a pre term IUGR to a term IUGR and thereby reducing complications. It also significantly alleviates the burden on the health sector by reducing NICU stay.

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