

A Study on Sildenafil Citrate in the Treatment of IUGR & Oligohydramnios

Jayati Nath*, Sarita Chaube, Neha Rani and Pahula Verma

Department of Obstetrics and Gynecology, India

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Abstract

Intra Uterine Growth Restriction is a challenge to clinicians all over the world because no definitive treatment is available, and many empirical therapies are tried for treating the same. The present study was a multi-centric hospital based prospective observational study conducted in three tertiary care centers in Northern India on 200 patients with late onset IUGR and oligohydramnios. Sildenafil citrate 25mg 8 hourly was given till delivery. All the outcomes were noted and analyzed. After sildenafil therapy, 87 out of 90 patients with only IUGR, 35 out of 40 cases of oligohydramnios only and 64 out of 70 patients with IUGR & oligohydramnios both had marked improvement & 14 cases showed no improvement. From this study we concluded that adding sildenafil citrate in the treatment of IUGR and oligohydramnios can be a beneficial option.

Keywords: Intrauterine growth restriction; Oligohydramnios; Sildenafil citrate; Placental insufficiency

Abbreviations

IUGR: Intrauterine Growth Restriction; FGR: Fetal Growth Restriction; AC: Abdominal Circumference; AFI: Amniotic Fluid Index; BPP: Biophysical Profile; EFW: Estimated Fetal Weight; MCA: Middle Cerebral Artery; NST: Non-Stress Test; NICU: Neonatal Intensive Care Unit; USG: Ultrasonography

***Corresponding author:** Jayati Nath, Department of Obstetrics and Gynecology, India

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Introduction

Intrauterine Growth Restriction, also called Fetal Growth Restriction, still an enigmatic clinical entity with not many treatment options, is basically because of underlying placental insufficiency which often associated with oligohydramnios, which causes major perinatal morbidity and mortality [1,2]. In developing countries like ours, IUGR poses a big burden on the healthcare sector-accounting for approximately 50 percent of stillbirths & 10 percent of perinatal mortality [1-4]. It is also seen that the survival rate of very remote from term, severely growth restricted babies (< 28 weeks of gestation) is quite dismal [1,5,6]. The main underlying osteopathological process of IUGR is placental insufficiency, attributed to failure of adequate invasion by the placental trophoblasts & transform the spiral arterioles in the maternal placental vasculature in early pregnancy [1,7,8]. Sildenafil citrate, a type 5 Phosphodiesterase Inhibitor (PDE5) is a potent vasodilator which dilates the myometrial arterioles in women with pregnancies complicated with IUGR [1,9]. It also enhances the availability of amino acids important in the conception and fetal growth & thus can have positive impact on pregnancy with fetal growth restriction. In many studies with sildenafil in IUGR, the results have been encouraging as evidenced by better fetal abdominal circumference (AC), increased liquor volume and better Doppler changes with associated decreased NICU admissions and improvement in perinatal outcomes [1,10-12]. The present study was therefore embarked upon simultaneously in 3 different tertiary care centers of North India (2 in Haryana & 1 in UP) to evaluate the effectiveness of sildenafil citrate in treatment of early & late onset IUGR and oligohydramnios.

Materials & Methods

- Study type: Multi-centric, hospital based, prospective, observational study.
- Study population: Antenatal patients with IUGR (early & late onset) & Oligohydramnios
- Study sample size: 200
- Study period: October 2019 to September 2020
- Study duration: One year

Inclusion criteria

- a) Pregnant women with period of gestation 27-36 weeks with IUGR (early/late onset)
- b) Ac and/or EFW<10th centile with/without Doppler changes
- c) AFI < 5cm

Exclusion Criteria:

- a) Patients with fetal congenital anomalies/ congenital infections
- b) Known case of medical disorders eg chronic renal / cardiac diseases

All such antenatal patients fulfilling the inclusion & exclusion criteria were enrolled in the study with proper informed written

consent & were given sildenafil citrate 25mg 8 hourly till delivery with USG & Doppler color flow studies two weekly. All these patients were assessed regularly for weight gain, blood pressure, complete blood count, serum uric acid & creatinine, Liver function tests, albumin. Fetal assessment was done by Doppler USG, AFI, BPP- every two weeks & biweekly NST. Any side effects like headaches, indigestion, palpitations, facial skin flushing, photophobia, visual disturbance, hearing impairment were noted. In Doppler color flow studies, Uterine & Umbilical arteries, Middle Cerebral Artery (MCA), Ductus Venosus (DV) were studied for changes before & after administration of sildenafil citrate.

Amniotic Fluid volume (AFI) & Abdominal Circumference (AC) were assessed 2 weeklies to monitor fetal growth. At delivery, mode and gestation at delivery, birth weight, APGAR score, liquor color (meconium) & NICU admission & duration of stay was noted (Table 1).

Table 1: The demographic and general characteristics of groups.

Gestation @admission (weeks)	Gestation @delivery								
	Early Preterm	32-34	weeks	Late preterm	34-37	weeks	Term	≥ 37	weeks
	n	%	'p' value	n	%	'p'	n	%	'p'
27-30	0	50	0	2	20	0.004	4	40	0.004
30-32	6	10	0.018	29	50	0	28	89	0
32-34	0	0	-	4	20	0.003	64	80	0
34-36	0	0	-	0	0	-	20	100	0

Statistical analysis

All the relevant data were entered into MS Excel-2007 & analyzed using SPSS version 20.0 software. Interpretation of the

data was done with the help of Chi- square test (χ^2 test) & period student 't' test to compare continuous variables. A 'p' value < 0.05 was considered statistically significant (Table 2);[13].

Table 2: Result with sildenafil citrate.

Variable	Before Sildenafil	After Sildenafil	% of improvement
IUGR only	87/90	Mar-90	96.66
Oligohydramnios only	35/40	May-40	87.5
IUGR + Oligo	64/70	Jun-70	91.42
	n= 200		

Results & Observations

Discussion

No specific full proof therapy is available for pregnancy with severe early-onset IUGR. There are 2 ways of going about once the diagnosis is made-(a) Expectant management including maternal lifestyle modification & fetomaternal surveillance & (b) Termination of pregnancy. In our study we observed significant improvement in the fetal outcome in terms of gestational age at delivery, birth weight, APGAR Score with sildenafil citrate treatment. Premalatha et al. [14] in their study from Karnataka, found similar results with 2 stillbirths, with improved perinatal outcomes and reduced NICU admissions. Von Daldeszen (Canada) reported mean gestational age at delivery at 25+ 6 weeks in the control group as opposite to 27+6 weeks in the sildenafil group with increased AC growth (OR 12.9; 95 % CI) [1,9].

A study from Chhattisgarh showed improved Ac in 70% of treated group with sildenafil citrate [1,15]. Panda et al. [15] reported marked improvement in the doppler blood flow indices and better pregnancy outcomes with sildenafil citrate [1,16]. Ferreira et al. [17] from Canada used 20mg sildenafil citrate in severe IUGR pregnancies at average 25+3 weeks gestation until delivery, with average weight gain at birth by 249 grams (558gm versus 807 grams) [1,17].

Conclusion

From our study we have gathered empirical evidence that sildenafil citrate which causes vasodilatation of the myometrial arteries in IUGR, increases utero-placental blood flow and potentiates fetal growth, can offer a promising therapeutic intervention in pregnancies complicated with early onset severe IUGR and oligohydramnios.

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