

Research Article

Comparison between the Uses of Sildenafil Citrate and Nitroderm Patch as Treatment for Intra Uterine Growth Restriction (IUGR)

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Abstract

Objective: Comparison between the use of sildenafil citrate and nitroglycerine transdermal patch as vaso dilator to improve placental blood flow in case of intra uterine growth restriction (IUGR). **Patient and methods:** This prospective study was conducted in Minia University maternity hospital during the period between 1st January 2013 to 31st January 2014. 40 patients had severe IUGR between 28 -34 w singleton pregnancy were recruited in the study. They were allocated into two groups **Group (A):** Included 20 participants who received 25mg Sildenafil citrate daily. **Group (B):** Included 20 participants who received Nitroglycerine 5mg transdermal patch daily. **Results:** Both groups were compared as regard the GA, EFW, UAPI and AFI at time of inclusion in the study and at time of delivery. Mean GA at the beginning of the study was the same in both groups it was 31.7, mean GA at time of delivery was higher in group A (34.35±1.66) than in group B (33.9±1.41). There was no difference in UAPI between two groups either at beginning of the study or at the time of delivery. Mean EFW at the beginning of the study was 1230±155.93 in group A and it was 1320±211.76 in group B, Mean EFW at time of delivery was higher in group A (1520±219) than in group B (1495±198), Mean AFI at the beginning of the study was nearly the same in both groups. Mean AFI at time of delivery was higher in group A (7.8 ± 0.76) than in group B (7.45 ± 0.75). **Conclusion:** Sildenafil as a vasodilator improve GA, EFW, UAPI, AFV more than nitroglycerine but more extended studies is recommended to support these results .

Keywords: Intrauterine growth restriction, sildenafil citrate, Nitroglycerine transdermal patch

Introduction

Small for gestational age fetus (SGA) refers to a fetus that has failed to achieve a specific biometric or estimated weight threshold by a specific gestational age. SGA fetus are at greater risk of stillbirth nearly 40% of stillborn fetuses after exclusion of malformation are caused by IUGR.

Severe early-onset intrauterine growth restriction (IUGR) Complicating approximately 0.2% of pregnancies that increases the risk of perinatal morbidity and mortality, particularly as a result of iatrogenic premature delivery⁽¹⁾

Sildenafil citrate vasodilates the myometrial arteries isolated from women with IUGR-complicated pregnancies⁽¹⁾

Sildenafil treatment was associated with increased fetal AC growth compared with women who received nitroglycerins dermal patch. Sildenafil improves perinatal outcomes for early-onset IUGR-complicated pregnancies⁽²⁾

Transdermal glyceryltrinitrate administration was associated with a significant decrease in uterine artery RI and the UA PI, whereas no significant difference was found in MCA PI.

The hypothesis was that Sildenafil citrate therapy would increase the likelihood of increased growth velocity [measured by abdominal circumference (AC) (ultrasound)] for fetuses of pregnancies complicated by severe early-onset IUGR⁽³⁾.

Aim of the Work

Comparison between the use of sildenafil citrate and nitroglycerine transdermal patch as vaso dilator to improve placental blood flow and perinatal outcome in case of intra uterine growth restriction (IUGR).

Patients & Methods

This study had been conducted at Obstetric and Gynecology department at Minia University Hospital, Egypt in the period between 1st January 2013 to 31st January 2014 aiming to compare between Sildenafil citrate and Nitroglycerine trans derm patch as a vasodilator in cases of IUGR. After being approved by the ethical committee of the department.

Idea of the work was explained to all patients also oral and written consent had been taken. Patients with pregnancies complicated with IUGR according to Hadlock et al 1985 (Estimated fetal weight > 500g & less than 10th centile) attending for

antenatal care in fetomaternal clinics of the maternity university hospital. Gestational age at enrolment ≥ 28 and ≤ 34 weeks of gestation, cases of multiple gestation and structural abnormality were excluded from the study.

40 patients included in the study were allocated into two gp

- **Group (A):** Included 20 participants who received 25mg Sildenafil citrate daily.
- **Group (B):** Included 20 participants who received 5mg Nitroglycerine transdermal patch daily.

All patients were subjected to

History taking, Clinical examination (general, local)

Laboratory investigation, US, Doppler studies of Umbilical artery Fetal monitoring by cardiocography (CTG).

A) Sildenafil citrate: Erec tablets 100 mg 25 mg once per day

B) Nitro glycerine trans dermal patch: nitroterm patch 5mg around the umbilicus per day

Results

Demographic characters of patients recruited in both groups shown in table (1)

	Group A N = 20	Group B N= 20	P value
Age	24.8 ± 5.38	25.25 ± 5.65	0.798
Gravidity	2.55 ± 0.89	2.8 ± 1.47	0.520
Parity	1.6 ± 1.19	1.65 ± 1.31	0.900

Table (2): comparison between both groups as regard GA, UAPI, EFW, AFI at the beginning of the study and at time of delivery, Apgar score and number of neonates admitted to NICU in both groups. GA the study at beginning of was the same it was 31.7, means GA at time of delivery was higher in group A 34.35±1.66 than in group B 33.9±1.41. There was no difference in UAPI between two groups

either at beginning of the study or at the time of delivery. Mean EFW at the beginning of the study was 1230±155.93 in group A and it was 1320 ± 211.76 in group B, Mean EFW at time of delivery was higher in group A (1520±219) than in group B (1495±198). Mean AFI at the beginning of the study was nearly the same. Mean AFI at time of delivery was higher in group A (7.8 ± 0.76) than in group B (7.45 ± 0.75).

Table (2): Comparison GA,UAPI,EFW and AFI at beginning of the study and at time of delivery between both groups

	Group A N = 20	Group B N= 20	P value
Gestational age at beginning of the study	31.75 ± 2.07	31.75 ± 2.07	1.000
Gestational age at delivery	34.35 ± 1.66	33.9 ± 1.41	0.362
P value	< 0.001*	< 0.001*	
UAPI at beginning of the study	0.95 ± 0.05	0.96 ± 0.05	0.355
UAPI at delivery	0.98 ± 0.04	0.98 ± 0.04	1.000
P value	0.005*	0.042*	
EFW at beginning of the study	1230 ± 155.93	1320 ± 211.76	0.134
EFW at delivery	1520 ± 219.09	1495 ± 198.61	0.707
P value	< 0.001*	< 0.001*	
AFI at beginning of the study	6.5 ± 1	6.9 ± 0.91	0.194
AFI at delivery	7.8 ± 0.76	7.45 ± 0.75	0.155
P value	< 0.001*	< 0.001*	

Table (3) Number of neonates admitted to NICU was high in group A than group B despite the APGAR score was higher in the first group.

Table (3): Comparison between Apgar score and NICU admission in both groups

	Group A N = 20	Group B N= 20	P value
Apgar score	7.5± 0.76	7.25± 0.79	0.313
Number of incubation	13 (65%)	10(50%)	0.337

Discussion

Severe early-onset intrauterine growth restriction (IUGR) increases the risk of perinatal morbidity and mortality, particularly as a result of iatrogenic premature delivery.⁽¹⁾

Infants are at increased risk of perinatal complications such as fetal distress, asphyxia, neonatal encephalopathy, hypothermia, hypoglycemia, poor feeding long-term neurological and developmental disorders. Survival rates for severely growth-restricted fetuses very remote from term (<28 weeks of gestation) are dismal^(1,2). In the long term, deficient growth in utero is related to an increased incidence of hypertension, diabetes mellitus, and coronary heart disease in adulthood⁽⁴⁾.

In the present study sildenafil citrate showed more increase in fetal weight than that in nitroglycerine trans dermal patch and that disagree with the results of⁽⁵⁾.

In our our study sildenafil citrate showed decrease in UAPI more than in nitroglycerine group and that disagree with the results of⁽⁶⁾.

In our results number of babies in group A incubated are more than in babies of group B and that disagree with the results of⁽⁷⁾.

Conclusion

Sildenafil as a vasodilator improve GA, EFW, UAPI, AFV, neonatal Apgar score more than nitroglycerine but more extended studies is recommended to support these results and to recommend Sildenafil as a treatment in cases of severe IUGR.

Reference

1. Bilardo CM, Wolf H & Stigter RH (2004): Relationship between monitoring parameters and perinatal outcome in severe, early intrauterine growth restriction. *Ultrasound Obstet Gynecol.* Feb; 23(2): 119-25
2. Petersen SG, Wong SF, UrsP, Gray PH, Gardene GJ. Early onset, severe fetal growth restriction with absent or reversed end-diastolic velocity wave form in the umbilical artery: perinatal and long term outcomes. *Aust NZ J Obstet Gynaecol* 2009; 49:45-51
3. Winer N, Branger B, Azria E, Tsatsaris V, Philippe JH, Roze JC, et al., L – Arginine treatment of severe vascular fetal intrauterine growth restriction : a randomized double blind controlled trial . *clin Nut* 2009; 28:243-8
4. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM 1993 Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X): relation to reduced fetal growth. *Diabetologia* 36:62–67
5. Bruschetti M, Gazzolo D, Di Lorio R 2002: Maternal nitric oxide supplementation decreases cord blood s100B IN IUGR *clinical chemistry April vol.48 no. 4 647-650*
6. Gazzolo D, Vinesi P, Geloso MC, Marcelletti CF, Iorio FS, Marianeschi SM, et al. S100 blood concentrations in children subjected to cardiopulmonary by-pass. *Clin Chem* 1998; 44:1058-1060.
7. Gandullia, *Clinical chemistry* 47, NO. 6, 2001