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Fetal hemodynamic changes following maternal betamethasone administration in pregnancies with fetal growth restriction and absent end-diastolic flow of the umbilical artery

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Abstract: Objectives: To evaluate the effects of antenatal betamethasone administration on umbilical artery (UA), middle cerebral artery (MCA) and ductus venosus (DV) Doppler flow. **Design**: Longitudinal prospective study. **Setting:** Department of Obstetrics and Gynecology, Elsayed Galal University Hospital. **Population:** 50 singleton pregnancies complicated by fetal growth restriction with absent end-diastolic flow in the UA. **Methods:** Doppler indices of the UA, MCA and DV were measured from 28 to 34 weeks prior to and within 24 or 48 hours after starting betamethasone treatment course. Analysis of variance for repeated measures was used to determine the changes in the fetal hemodynamic Doppler flow following maternal corticosteroid administration. **Main outcome measures:** Improvement of UA-PI within 24 hours and DV-PIV (venous pulsatility) within 48 hours from the first betamethasone dose. **Results:** Mean gestational age at delivery was 31.38 weeks and birth weight was 1137.20 g. A reduction in the UA-PI was observed in 46 (92%) cases, with return of end-diastolic flow in 34/50 (68%). The mean UA-PI were 2.08 before corticosteroid administration, 1.75 within 24 hours and 2.09 after 48 hours, with a significant difference along the evaluations ($p<0.001$). No significant changes in the MCA Doppler were observed. DV-PIV decreased from 1.07 prior corticosteroids administration to 0.72 within 24 hours and 0.69 after 48 hours ($p<0.001$). **Conclusions:** There was reduction in the umbilical artery and in the DV pulsatility indices within 24 hours from betamethasone administration that was maintained up to 48 hours.

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Key words: Betamethasone, fetal growth restriction, Doppler ultrasound, ductus venosus, middle cerebral artery, umbilical artery, absent end-diastolic flow

Introduction

Intrauterine growth restriction (IUGR) is defined as a fetus that is at or below the 10th percentile in weight for its gestational age as adopted by the ACOG and the RCOG ***(ACOG,2015).***

Maternal causes of IUGR are usually related to reduced utero-placental blood flow, reduced maternal blood volume, reduced oxygen-carrying capacity, or decreased nutrition to the fetus. Often the etiology is associated with more than one of these mechanisms ***(Hanson et al., 2015).***

Suboptimal fetal growth is linked to adverse short and long term outcomes. Neonatal complications include haematological and metabolic problems and impaired thermoregulation. In addition, intraventricular haemorrhage, necrotizing enterocolitis, seizures, sepsis, respiratory distress syndrome, retinopathy of prematurity and neonatal death contribute to the perinatal morbidity.

Together with the profound perinatal impact of FGR, consequences may continue into adult life in the form of metabolic disease as a result of prenatal reprogramming and postnatal compensatory catch-up growth. It is now well established, that an adverse intrauterine environment increases disease risk in adulthood leading to metabolic syndrome, hypertension, insulin resistance and type 2 diabetes mellitus, coronary heart disease and stroke ***(Alsaied et al., 2017).***

The etiology of fetal growth restriction can be broadly categorized into maternal, fetal, and placental. Although the primary pathophysiologic mechanisms underlying these conditions are different, they often have the same final common pathway: suboptimal uterine–placental perfusion and fetal nutrition ***(Nardozza et al., 2017).***

Aim:

The aim of the present study is to evaluate the effects of antenatal betamethasone administration on umbilical artery (UA), middle cerebral artery (MCA) and ductus venosus (DV) Doppler flow in singleton

pregnancies complicated by fetal growth restriction with absence of end-diastolic flow (AEDF).

2. Patients and Methods:

This study will be a longitudinal prospective study which will be carried out to evaluate the effects of antenatal betamethasone administration on UA, MCA and DV Doppler flow in singleton pregnancies complicated by fetal growth restriction with absent end-diastolic flow of the umbilical artery (AEDF). This study will be carried out on pregnant women attending Elsayed Galal University Hospital in their third trimester of pregnancy with gestational age between 28 and 34 weeks. A total of 50 pregnant women will be included in the study. All the women will receive antenatal betamethasone for fetal lung maturation and will fulfill the following inclusion criteria.

Inclusion criteria:

1- Singleton pregnancies in which no fetal anomalies will be detected by ultrasonography, and complicated by fetal growth restriction with absent end-diastolic flow of the umbilical artery (AEDF).

2- Age from 18-35 years.

3- Gestational age between 28-34 wks.

4- Absence of regular uterine contractions.

5- Doppler examinations directly prior to and within 24 hours and 48 hours after administration of the first dose betamethasone (including two doses repeated at 24-hour apart).

Exclusion criteria:

1- Patients less than 28 gestational weeks or more than 34 weeks.

2- Patients with multiple pregnancies.

3- Patient with anomalous fetuses.

4- Presence of active uterine contractions or precipitation of preterm labor.

5- Presence of any amount of vaginal bleeding.

6- Patient with medical disease (hypertensive, diabetic, renal or cardiac).

Study Procedures:

Informed consent for study procedure will be taken. History taking for (last menstrual period, present history, family history and obstetric history). General examination (blood pressure, pulse and temperature). Ultrasonographic examination for gestational age determination and amniotic fluid index (AFI) calculation. Color/pulsed Doppler studies will be performed a 3.5-MHz curved-array probe using ultrasound apparatuses of similar technology. The high-pass filter will be set at 50-100 Hz. The Doppler image will be frozen when at least five consecutive uniform flow velocity waveforms with a high signal-to-noise ratio are obtained during a period of fetal rest and apnea ***(Nozaki, et al., 2009)***.

Sample Collection:

Pregnant women at high risk for placental insufficiency will be referred by the Prenatal Care Units for assessment of fetal well-being. After absent end-diastolic flow of the umbilical artery (AEDF) is diagnosed, the patient will be hospitalized for bed rest and clinical monitoring until delivery. Placental and fetal evaluation consists of arterial Doppler (UA and MCA) and venous Doppler (DV) will be performed at maximum intervals of 24 hours in all cases. The pulsatility index (PI) and the pulsatility index for veins (PIV) will be used for evaluation of the arterial circulation and DV, respectively. The MCA will be identified at its bifurcation from the internal carotid artery, and the PI will be measured in the proximal one-third of the vessel. The DV will be examined at the inlet portion. The amniotic fluid index (AFI) measurement will be also evaluated daily. Each patient will be examined until a reason for delivery, preceded by a complete cycle of antenatal betamethasone (12 mg per day for two consecutive days), will be observed. The presence of at least one of the following indications will be required to interrupt the pregnancy: AFI lower than 5.0, and DV PIV between 1.0 and 1.5. Doppler flow measurements in the UA, MCA and DV will be obtained immediately before (first doppler), 24 hours (second doppler) and 48 hours (third doppler) after the first betamethasone dose. All newborns will be delivered by cesarean section 24-36 hours after the end of the betamethasone cycle. After delivery, the following immediate neonatal outcomes of interest will be obtained: gestational age at the time of delivery by Ballard scoring system, one- and five- minute Apgar scores, and birth weight.

Statistics:

Recorded data will be analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data will be expressed as mean± standard deviation (SD). Qualitative data will be expressed as frequency and percentage. A total sample size of 50 pregnant women achieves 80% power to detect a change in sensitivity of 0.5 to 0.8 using a two sided binomial test. The target significance level is 0.05.

The following tests will be done:

- Independent-samples t-test of significance will be used when comparing between two means.
- Paired sample t-test of significance will be used when comparing between related samples.
- Chi-square (x^2) test of significance will be used in order to compare proportions between qualitative parameters.
- The confidence interval will be set to 95% and the margin of error accepted will be set to 5%. So, the p-value will be considered significant as the following:

- Probability (P-value): P-value <0.05 will be considered significant while P-value >0.05 will be considered insignificant.

3. Results:

This study was longitudinal Prospective study conducted at the Department of Obstetrics and Gynecology, Elsayed Galal University Hospital on 50 pregnant females diagnosed with fetal growth restriction with absent end-diastolic flow of the umbilical artery (AEDF) selected from the attendees of Elsayed Galal University Hospital from January 2019 to June 2019. The age of the study group was between 18-35(year) with the mean of age (years) 26.76±5.00, gestational age by history was between 28-34 (week) with the mean of 30.54±3.67 (week), gestational age by U/S was between 25-32 (week) with the mean of 28.32±2.01 (week). Past history of IUGR 19 (38.0%). History of smoking 4 (8.0%) as shown in table 1.

Table (1): Baseline characteristics descriptive of the study group.

Baseline characteristics	Total (n=50)
Age (years)	18-35 [26.76±5.00]
Gestational Age/Lmp	28-34 [31.38±2.02]
Gestational age /U/S	25-32 [28.32±2.01]
Past history of IUGR	19 (38.0%)
Smoking	4 (8.0%)

The mean and standard deviation UA and MCA PI and DV PIV at first, second and third are shown in Table 2. A reduction in UA PI within the first 24 hours after steroid administration was observed in46 (92%) cases, with return of positive diastolic flow in 34/50 (68%) cases with AEDF at first Doppler. Significant changes in UA PI were observed along the evaluations (p<0.001), with this difference being significant between first and second Doppler (p<0.001), between first and third doppler (p=0.743) (Figure 1). Regarding MCA PI, analysis of variance for repeated measures showed no significant differences along the evaluations (p=0.159) (Figure 2). Analysis of variance for repeated measures showed significant differences in DV (ductus venosus) PIV along the evaluations (p<0.001). A significant reduction of PIV was observed within the first 24 hours (first doppler versus second doppler, p<0.001). A significant difference was observed between first and second doppler (p<0.001) (Figure 3).

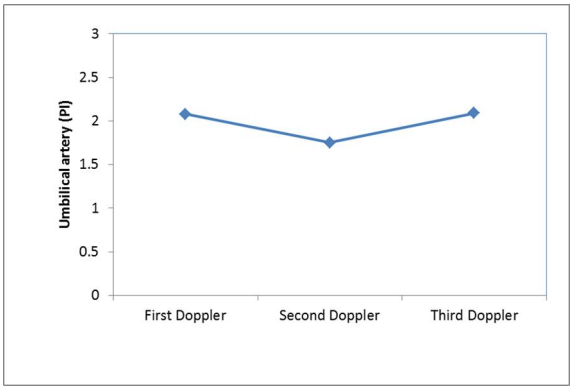

Fig. (1): Comparison between first, second and third Doppler according to umbilical artery (PI).

Table (2): Mean and standard deviation of Doppler values at first, second and third Doppler according to umbilical artery (PI), middle cerebral artery (PI) and ductus venosus (PIV).

Umbilical artery (PI)	Range	Mean±SD	Mean Diff.	t-test	p-value
First Doppler	1.2-2.5	2.08±0.30			
Second Doppler	1.2-2.2	1.75±0.28	0.330	16.583	<0.001**
Third Doppler	1.5-2.5	2.09±0.25	-0.010	-0.330	0.743
Middle cerebral artery (PI)					
First Doppler	0.2-0.8	0.53±0.18			
Second Doppler	0.2-0.8	0.54±0.18	-0.010	-1.429	0.159
Third Doppler	0.3-0.9	0.55±0.15	-0.020	-0.844	0.403
Ductus venosus (PIV)					
First Doppler	0.8-1.3	1.07±0.16			
Second Doppler	0.67-0.75	0.72±0.02	0.350	16.804	<0.001**
Third Doppler	0.65-0.71	0.69±0.01	0.380	16.932	<0.001**

*-Paired Sample t-test; **p-value <0.001 HS, PI=pulsatility index; PIV=pulsatility index for veins;; DV=ductus venosus; First Doppler=pre-betamethasone; Second Doppler =24 hour after first dose; Third Doppler=48 hours after first dose.*

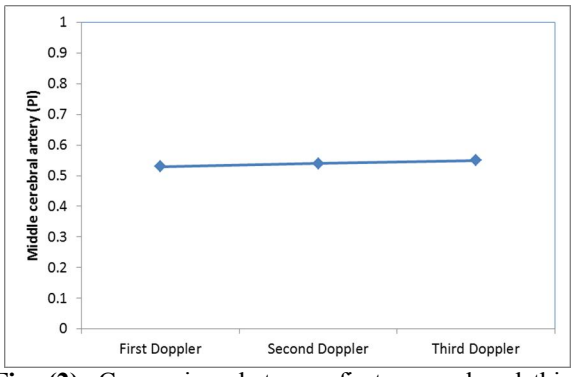

Fig. (2): Comparison between first, second and third Doppler according to middle cerebral artery (PI).

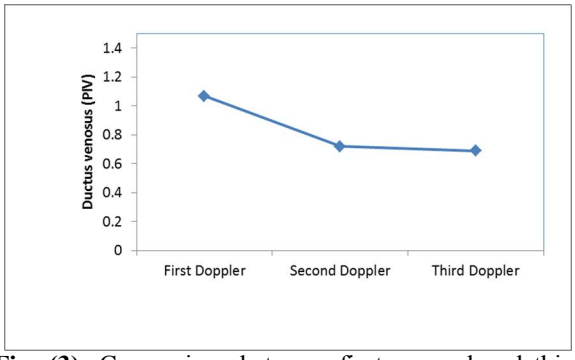

Fig. (3): Comparison between first, second and third Doppler according to ductus venosus (PIV).

4. Discussion:

This study was longitudinal Prospective study conducted at the Department of Obstetrics and Gynecology, Elsayed Galal University Hospital on 50 pregnant females diagnosed with fetal growth restriction with absent end-diastolic flow of the umbilical artery (AEDF) selected from the attendees of Elsayed Galal University Hospital from January 2019 to June 2019. The aim of the present study was to evaluate the effects of antenatal betamethasone administration on umbilical artery (UA), middle cerebral artery (MCA) and ductus venosus (DV) Doppler flow in singleton pregnancies complicated by fetal growth restriction with absence of end-diastolic flow (AEDF). We excluded from our study patients with multiple pregnancies, fetal congenital anomalies and maternal medical diseases (hypertensive, diabetic, renal or cardiac). All patients underwent ultrasonography to determine gestational age and presence of IUGR and we measured the biophysical profile. Umbilical artery and middle cerebral artery ductus venosus Doppler ultrasonographic examination was done. The cases were 50 pregnant women complicated by fetal growth restriction with absent end-diastolic flow of the umbilical artery (AEDF) who were offered Betamethasone 12mg intramuscular every day for two consecutive days.

The results of present study show significant statistical difference between UA indices before & after betamethasone administration. Mean umbilical artery pulsatility index (UA PI) significantly decreased 24 hours after betamethasone ($p<0.001$) with this difference being significant between first and second doppler ($p<0.001$), between first and third ($p=0.743$). A reduction in UA PI within the first 24 hours after steroid administration was observed in 46 (92%) cases. This was similar to the reduction reported by ***Shojaei and Mohammadi, 2015***, who compared the effects of antenatal betamethasone on doppler velocimetry between intrauterine growth restriction with and without preeclampsia. Study was conducted in 2013 on the 40 singleton pregnant women with IUGR fetuses and concerned over maternal or fetal well-being. Women of our study were complicated with intrauterine growth-restriction). Patients were hospitalized at the Department of Obstetrics and Gynecology, Imam Khomeini Hospital, Women Hospital, and Shariati Hospital, Tehran, Iran, for fetal surveillance and delivery. They were treated with two doses of 12 mg betamethasone intramuscularly 24 h apart to enhance fetal lung maturity. Three Doppler measurements absolutely before betamethasone, one day after betamethasone and 5 days after betamethasone administration were performed. They found that betamethasone therapy had significant effects on UA-PI, UM-PI, UM-RI, UM-S/D, MCA-RI, and MCA-UM-RI over 5-day follow up time period in each group (P value for each artery in each group was <0.0001). In addition, findings showed decreased level of UM-PI during five days after betamethasone initiation. But this reduction was transient. Actually, at the end of five-day follow up time, its value returned to baseline level. Pattern of decreasing between IUGR with preeclampsia and without preeclampsia was similar (P value =0.1).

This decrease of the umbilical artery pulsatility index (UA PI) is different from that observed by **Ekin et al., 2016**, who study were about Seventy-six singleton pregnancies that received betamethasone therapy were prospectively evaluated. Doppler measurements of pulsatility indices (PI) in fetal umbilical artery (UA), middle cerebral artery (MCA), ductus venosus and maternal uterine arteries were performed before (0 h) and 24, 48, 72 and 96 h after the first dose of betamethasone. The PI of MCA showed a statistically significant decrease on 24 h compared with PI of MCA of 0 h. This decrease continued on 48 h and 72 h and returned to levels observed before betamethasone administration. In fetuses with absent or reversed EDF in UA, ductus venosus and uterine artery PI values showed no statistically significant differences before and after antenatal glucocorticoid treatment. In contrast,

significant decreases in PI were found in both MCA and UA at 24, 48 and 72 h when compared to the levels at 0 h. Additionally, the administration of maternal betamethasone was followed by a change from absent to positive, reversed to absent or from reversed to positive diastolic flow within 24 h in 19 (79.2%) fetuses with absent or reversed UA EDF.

The results of present study show return of end-diastolic flow was observed in two thirds of cases, as demonstrated previously with similar results by ***Shojaei and Mohammadi, 2015.***

Regarding MCA Doppler study our results show no significant statistical difference were observed over the 48 hours after betamethasone administration. These findings agree with those reported by ***Niroomanesh et al., 2015,*** conducted a prospective, longitudinal, multicenter study at three university-affiliated hospitals in Tehran, Iran, between January 1 and November 30, 2013. The inclusion criteria were FGR, a gestational age of 24–34 weeks, no fetal anomalies, and no previous betamethasone therapy. Doppler blood flow was measured in uterine, umbilical, and middle cerebral arteries before treatment, and 24 hours and 5 days after completion of betamethasone therapy (two 12 mg doses at a 24 hour interval). Overall, 40 women were enrolled. Doppler blood flow through the uterine and umbilical arteries showed significant but transient changes across the three time points ($P < 0.001$), whereas the middle cerebral artery showed no changes. Prenatal betamethasone led to transient improvements in blood flow in the uterine and umbilical arteries among pregnancies affected by FGR.

In both studies, MCA-PI values were low, suggesting a higher proportion of cases with centralization of fetal circulation.

In contrast to the present study, ***Ekinetal., 2016,*** observed a significant reduction in MCA-PI values. However, it is important to emphasize that in the last study mean MCA-PI was higher, suggesting fetal hemodynamic involvement distinct from that observed in the current study in which the mean PI ranged from 0.2 to 0.9. This find could explain the difference between these studies.

Analysis of the venous compartment after antenatal corticotherapy showed a significant reduction in DV PIV within the first 24 hours after betamethasone administration and maintenance of PIV at second and third doppler (first doppler versus second doppler, $p<0.001$). A significant difference was observed between first and second doppler ($p<0.001$). These findings differ from those reported by ***Ekin et al., 2016,*** found no changes in DV PIV after betamethasone administration.

Raghuraman et al., 2018, study Of the 222 FGR pregnancies with abnormal umbilical artery doppler, 94 received betamethasone and had follow up ultrasounds. Umbilical artery doppler improved in 48 (51.1%), with 27 (56.3%) having sustained improvement which is contrast the present study. Lack of umbilical artery doppler improvement was associated with shorter latency and earlier gestational age at delivery, but no difference in composite neonatal morbidity. Umbilical artery doppler response to betamethasone may be useful to further risk stratify FGR pregnancies.

Thuring et al., 2011, evaluated the effects of maternal betamethasone on fetal and uteroplacental circulation in pregnancies at risk of preterm delivery. The study comprised 33 women with singleton pregnancies and severe fetal growth restriction and/or pre-eclampsia during a period of 5 years (2004–2008). Patients were hospitalized at the Department of Obstetrics and Gynecology, Lund University Hospital, Sweden, for fetal surveillance and delivery.

They were treated with two doses of 12 mg betamethasone intramuscularly 24 h apart to enhance fetal lung maturity. Flow velocity waveforms were recorded with Doppler ultrasound from the umbilical artery, the fetal middle cerebral artery, the ductus venosus and both maternal uterine arteries, once before and twice after betamethasone administration.

Two days after betamethasone, a decrease in pulsatility index was found in the umbilical artery ($P = 0.0002$) and ductus venosus ($P = 0.003$). Changes in the umbilical artery waveform from reversed to absent, and from absent to positive diastolic flow, were noted in 12 of 15 cases ($P < 0.01$).

After 4 days, umbilical artery and ductus venosus velocity waveforms in the undelivered fetuses either returned to the type of waveform observed before treatment or showed further deterioration.

Maternal antenatal betamethasone resulted in a significant transient change in the velocity waveform and a decrease in the pulsatility index in the umbilical artery and ductus venosus, but did not influence uteroplacental circulation. These findings indicate a direct effect of betamethasone on fetal circulation. These results are similar to the present study.

According to ***Nozaki et al., 2009***, betamethasone therapy led to a reduction in the UmA and ductus venosus PI after 24 hours; this reduction continued until 48 hours after treatment. These results are similar the present study.

In a study in Australia, ***Robertson et al., 2009,*** observed that betamethasone therapy was associated with a transient reduction in the end-diastolic flow of the UmA for two-thirds of fetuses with FGR. They suggested that a subgroup of fetuses with persistent absent end-diastolic flow in the Um. A. has a higher prenatal risk. These results are similar the present study.

Elsnosy et al.,2018, A prospectively registered study was conducted in Women Health Hospital, Assiut, Egypt, included 50 pregnant women with singleton pregnancies. Doppler studies were performed on the umbilical artery, fetal middle cerebral artery (MCA), fetal descending aorta and maternal uterine arteries just before dexamethasone administration and repeated 24 h after completion of the dexamethasone course.

The mean age of the study group was 27.7±4.5 years. There was a statistically significant difference between all Doppler indices in umbilical artery, fetal MCA and aorta in comparison before and 24 h after maternal dexamethasone administration. Also uterine artery Pulsatility index was significantly different (p=0.001).

Maternal dexamethasone administration to pregnant women at risk of preterm labor improves the blood flow of the maternal uterine artery, fetal MCA, descending aorta and umbilical artery 24 h after its administration. The results of this study is similar to the present study about Doppler indicies of umbilical artery, but differs about MCA indicies as the results of the current study show on statistically significant difference of MCA PI before and after betamethasone administration.

Conclusions:

The present study concluded that betamethasone use in cases of IUGR is associated with significant improvement in the form of decrease in umbilical artery mean pulsatility index. Betamethasone was associated with no significant improvement in MCA pulsatility index in the studied group. Also, antenatal corticotherapy showed a significant reduction in DV PIV at end of the study in studied group.

Recommendations

Doppler is important for the adequate care of patients with severe placental insufficiency. However, further studies are necessary to evaluate fetal acid-base status over 48 hours after betamethasone administration, which will certainly influence therapeutic approaches aimed at the reduction of neonatal morbidity and mortality in these extremely severe cases.

References:

1. Alsaied, T., Omar, K., James, J. F., Hinton, R. B., Crombleholme, T. M., & Habli, M. (2017). *Fetal origins of adult cardiac disease: a novel approach to prevent fetal growth restriction induced cardiac dysfunction using insulin like growth factor. Pediatric Research, 81(6), 919–925.*
2. American College of Obstetricians and Gynaecologists, ACOG (2015) Obstetric Care Consensus No. 3 Summary. (2015). *Obstetrics & Gynecology, 126(5), 1123–1125.*
3. Ekin, A., Gezer, C., Solmaz, U., Taner, C. E., Ozeren, M., Dogan, A., & Uyar, I. (2016). Effect of antenatal betamethasone administration on Doppler velocimetry of fetal and uteroplacental vessels: a prospective study. Journal of Perinatal Medicine, 44(2).
4. Elwani Elsnosy, Omar M. Shaaban, Ahmed M. Abbas, Heba H. Gaber & Atef Darwish (2017). Effects of antenatal dexamethasone administration on fetal and uteroplacental Doppler waveforms in women at risk for spontaneous preterm birth. Middle East Fertility Society Journal.; 22: 13–17.
5. Hanson, M., Kiserud, T., Visser, G. H. A., Brocklehurst, P., & Schneider, E. B. (2015). Optimal fetal growth: a misconception? American Journal of Obstetrics and Gynecology, 213(3), 332. e1–332. e4.
6. Nandini Raghuraman, Bree Porcelli, Lorene Temming, George Macones, Alison Cahill, Methodius Tuuli & Jeffrey M Dicke (2018): Clinical implications of umbilical artery Doppler changes after betamethasone administration, The Journal of Maternal-Fetal & Neonatal Medicine.
7. Nardozza, L. M. M., Caetano, A. C. R., Zamarian, A. C. P., Mazzola, J. B., Silva, C. P., Marçal, V. M. G., Araujo Júnior, E. (2017). Fetal growth restriction: current knowledge. Archives of Gynecology and Obstetrics, 295(5), 1061–1077.
8. Nozaki, A. M., Francisco, R. P. V., Fonseca, E. S. V. B., Miyadahira, S., & Zugaib, M. (2009). Fetal hemodynamic changes following maternal betamethasone administration in pregnancies with fetal growth restriction and absent end-diastolic flow in the umbilical artery. Acta Obstetricia et Gynecologica Scandinavica, 88(3), 350–354.
9. Robertson MC, Murila F, Tong S, Baker LS, Yu VY, Wallace EM. (2009). Predicting perinatal outcome through changes in umbilical artery Doppler studies after antenatal corticosteroids in the growth-restricted fetus. Obstet Gynecol 2009;113(3):636,40.
10. Shojaei, K., & Mohammadi, N. (2015). Comparing the Effects of Antenatal Betamethasone on Doppler Velocimetry between Intrauterine Growth Restriction With and Without Preeclampsia. Global Journal of Health Science, 7(2).
11. Thuring A, Malcus P, Maršál K. (2011). Effect of maternal betamethasone on fetal and uteroplacental blood flow velocity waveforms. Ultrasound Obstet Gynecol;37(6):66-72.

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