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THE EFFECT OF ANTENATAL CORTICOSTEROID ADMINISTRATION ON UMBILICAL ARTERY DOPPLER VELOCIMETRY IN PREGNANCIES COMPLICATED WITH FETAL GROWTH RESTRICTION

FETAL BÜYÜME KISITLILIĞI İLE KOMPLİKE OLAN GEBELİKLERDE ANTENATAL KORTİKOSTEROİD UYGULAMASININ UMBİLİKAL ARTER DOPPLER VELOSİMETRİSİ ÜZERİNE ETKİSİ

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ABSTRACT

Objective: To examine the effect of antenatal corticosteroid administration on umbilical artery (UA) Doppler measurements in pregnancies complicated with fetal growth restriction (FGR).

Methods: This cross-sectional study was conducted with 149 pregnant women scheduled for antenatal corticosteroid therapy because of the possibility of preterm birth. UA Doppler measurements (PI, S/D ratio, RI) before antenatal corticosteroid administration and 24 and 48 hours after the last dose of corticosteroid administration were evaluated and compared with each other in pregnant groups complicated with FGR and uncomplicated with FGR.

Results: No statistically significant change was observed in UA Doppler parameters 24 and 48 hours after antenatal corticosteroid treatment in each group with and without FGR. While there was no significant difference between the precorticosteroid UA Doppler parameters (PI, S/D ratio, RI) of the two groups with and without FGR, the values of these parameters 24 hours after the last dose of treatment were statistically higher in the group complicated with FGR than in the uncomplicated group. However, no statistical difference was observed in UA Doppler parameters between the two groups 48 hours after the last dose of treatment.

Conclusion: Antenatal corticosteroid does not permanently affect UA Doppler parameters in the case of FGR. Close monitoring of the fetus for 72 hours after the first dose of antenatal corticosteroid may be helpful in pregnant women complicated by FGR.

Keywords: Antenatal corticosteroid, fetal growth restriction, fetal doppler, umbilical artery

ÖZ

Amaç: Fetal büyüme kısıtlılığı (FBK) ile komplike olan gebeliklerde antenatal kortikosteroid uygulamasının umbilikal arter (UA) Doppler ölçümleri üzerine etkisini incelemek.

Yöntem: Bu kesitsel çalışma, erken doğum olasılığı nedeniyle antenatal kortikosteroid tedavisi planlanan 149 gebe kadın ile gerçekleştirildi. FBK ile komplike olan ve FBK ile komplike olmayan gebe gruplarında, antenatal kortikosteroid uygulamasından önceki ve son doz kortikosteroid uygulamasından 24 ve 48 saat sonraki UA Doppler ölçümleri (PI, S/D oranı, RI) değerlendirildi ve birbirleriyle karşılaştırıldı.

Bulgular: FBK olan ve olmayan her grupta, antenatal kortikosteroid tedavisinden 24 ve 48 saat sonra UA Doppler parametrelerinde istatistiksel olarak anlamlı bir değişiklik gözlenmedi. FBK olan ve olmayan iki grubun prekortikosteroid UA Doppler parametreleri (PI, S/D oranı, RI) arasında anlamlı fark bulunmazken, son tedavi dozundan 24 saat sonra bu parametrelerin değerleri FBK ile komplike olan grupta komplike olmayan gruba göre istatistiksel olarak yüksekti. Ancak son tedavi dozundan 48 saat sonra iki grup arasında UA Doppler parametrelerinde istatistiksel fark gözlenmedi.

Sonuç: Antenatal kortikosteroid, FBK durumunda UA Doppler parametrelerini kalıcı olarak etkilememektedir. Doğum öncesi kortikosteroidin ilk dozundan sonra 72 saat boyunca fetüsün yakından izlenmesi, FBK ile komplike olan gebe kadınlarda faydalı olabilir.

Anahtar kelimeler: Antenatal kortikosteroid, fetal büyüme kısıtlılığı, fetal doppler, umbilikal arter

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Introduction

Fetal growth restriction (FGR), generally means that the estimated fetal weight measured ultrasonographically is below the 10th percentile for gestational age.[1-3] Maternal, fetal or placental causes may play a role in the occurrence of fetal growth restriction. Poor placental perfusion (ie placental insufficiency) is one of the most common pathologies associated with fetal growth restriction.[2,3] Adverse changes in uteroplacental and fetal-placental circulation cause fetal growth restriction. Uteroplacental and fetal placental circulation can be evaluated by ultrasonographic Doppler parameters. These evaluations can generally be made by examining the Doppler indexes of the uterine artery (UtA), umbilical artery (UA), middle cerebral artery (MCA) and ductus venosus (DV) vessels.[2,4]

Perfusion to the fetoplacental unit can be evaluated by Doppler velocimetry of the umbilical artery (UA).[5] In a normal pregnancy, as the pregnancy progresses, a decrease in the commonly used UA Doppler indices systolic:diastolic ratio (S/D ratio), pulsatility index (PI) and resistance index (RI) is observed in parallel with the increase in end-diastolic flow and decrease in vascular resistance in the UA.[6-8] However, in FGR, there is a decrease in diastolic flow in the UA initially due to increased vascular resistance. Depending on this situation, the S/D ratio, PI and RI indices of the UA may increase.[6,9] In the early stages of FGR, the PI of UA increases due to the decrease in the end-diastolic velocity. In later stages of FGR, absence or reversal of end-diastolic flow in UA occurs.[5] Absence or reversal of end-diastolic flow in the UA increases the risk of perinatal mortality.[3] Redistribution of blood flow occurs when fetal hypoxemia is present in fetuses with FGR. In this condition, known as the brain-sparing reflex, increased blood flow to the brain, heart, and adrenal glands and decreased flow to the peripheral circulations occur.[1,4] The increase in blood flow to the brain during end-diastole with this redistribution in fetuses with FGR is marked by a decreased pulsatility index [PI] in the middle cerebral artery (MCA).[4,5] Likewise, various changes can occur in the sonographic Doppler findings of different vessels in fetuses with FGR. However, the UA is the most commonly studied vessel in Doppler velocimetry due to its accessibility and strength of association with fetal outcomes.[5] In addition, it is thought that the use of UA Doppler velocimetry during antepartum evaluation in fetuses with FGR reduces perinatal mortality.[3,4] Given these circumstances, the UA is the preferred vessel in which Doppler flow velocity is evaluated to guide management in pregnancies complicated by suspected FGR.[4]

Antenatal corticosteroid administration is carried out in order to accelerate fetal lung maturation in pregnant women with a possibility of preterm birth for any reason. This practice reduces the risks of fetal and neonatal death and respiratory distress syndrome.[10] However, antenatal corticosteroid administration also places significant physiological and metabolic demands on the fetus.[11] Studies have shown that this practice may cause temporary reductions in fetal heart rate, fetal respiration and trunk movements.[12,13] In addition, animal experiments have shown that this application may cause fetal hypertension with increased vascular resistance[14], decreased cerebral blood flow with decreased oxygen delivery[15], and an increase in fetal lactate levels.[16] Although healthy fetuses can tolerate the physiological and metabolic demands of antenatal corticosteroids, fetuses with FGR may not cope easily with these problems.[11]

The purpose of this study is to evaluate the effect of antenatal corticosteroid administration on umbilical artery Doppler velocimetry measurements in pregnancies complicated by FGR. Thus, we aim to better understand the effects of antenatal corticosteroid administration on the fetus with FGR.

Methods

Study design and participants

This cross-sectional study was carried out with pregnant women who were planned for antenatal corticosteroid treatment between 2018-2019 due to the possibility of preterm delivery. 149 pregnant women who were treated with antenatal corticosteroid were included in the study. FGR was diagnosed in 49 of 149 pregnant women who received antenatal corticosteroid therapy, and the remaining 100 pregnant women who received antenatal corticosteroid therapy were diagnosed to be at risk of preterm delivery for reasons other than FGR (spontaneous preterm contraction, premature rupture of membranes, gestational cholestasis, preeclampsia, placenta previa etc.).

Pregnant women carrying a fetus whose estimated fetal weight was below the 10 percentile for gestational age, with or without a Doppler abnormality such as increased resistance in the umbilical artery, were included in the FGR group. Gestational age was calculated according to the last menstrual period and confirmed according to the crown-rump length, which was the first trimester ultrasonography measurement.

Pregnant women who had complicated pregnancy with fetal anomaly, who had multiple pregnancies, who left their pregnancy follow-up unfinished, and those under 18 years of age were excluded from the study.

The study was approved by the local ethics committee on 02.02.2018. Informed consent was obtained from participants.

Protocols

Demographic characteristics of the patients and ultrasonographic fetal biometric measurements were recorded just before antenatal corticosteroid administration. The data obtained were compared between pregnant women with FGR complicated and FGR uncomplicated.

Before antenatal corticosteroid administration, UA Doppler measurements (PI, S/D ratio, RI) were made and

recorded. As a corticosteroid, 12 mg betamethasone (Celestone chronodose ampul) was administered intramuscularly twice with 24-hour intervals. UA Doppler measurements were repeated 24 and 48 hours after the last dose of corticosteroid administration. The obtained Doppler measurements were evaluated and compared with each other in pregnant groups complicated with FGR and uncomplicated with FGR.

Ultrasound examinations were performed transabdominally with a 5 MHz probe (Toshiba, Aplio 500 device). Examination of the UA was performed when the mother was in the supine and slightly left-leaning position, while there was no significant fetal movement. The insonation angle was adjusted to be parallel to the blood flow. The color Doppler window was set to a minimum size, surrounding the vascular structure to be examined. At least three measurements were made. In each measurement, 10-15 waveforms were taken and the averages measured from three different consecutive cardiac cycles were recorded.

Statistical analysis

Analyzes were performed with IBM© SPSS program version 20. Measurement data were tested with Kolmogrov-Smirnov tests for the assumption of normal distribution. Variables are given as median (interquartile range [IQR]). Mann-Whitney U test and Friedman tests were used in appropriate places for the comparison of measurement data that did not show normal distribution. $p<0.05$ was accepted for statistical significance in all analyzes.

Results

Demographic characteristics and ultrasonographic fetal biometric measurements recorded just before antenatal corticosteroid administration were compared in Table 1 between pregnancies complicated with and uncomplicated with FGR.

In Table 2, UA Doppler parameters (S/D ratio, PI, RI) of pregnant women with and without FGR were evaluated just before the antenatal corticosteroid and 24 and 28 hours after the last dose of antenatal corticosteroid. No statistically significant change was observed in UA Doppler parameters at 24 and 48 hours after antenatal corticosteroid treatment in each group with and without FGR ($p>0.05$ for all). UA Doppler parameters S/D ratio and PI were found to be higher 24 hours after antenatal corticosteroid in the group complicated with FGR than before treatment, but this increase was not statistically significant. While there was no significant difference between the precorticosteroid UA Doppler parameters of the two groups complicated and uncomplicated with FGR ($p>0.05$ for all), the values of these parameters 24 hours after antenatal corticosteroid treatment were found to be statistically higher in the group complicated with FGR than in the group uncomplicated with FGR ($p=0.022$ for UA-S/D ratio, $p=0.001$ for UA PI, $p=0.014$ for UA-RI). No statistical difference was observed between the two groups in UA Doppler parameters 48 hours after antenatal corticosteroid treatment ($p>0.05$ for all).

Discussion

There are few studies in the literature examining the effect of antenatal corticosteroid administered on Doppler parameters in pregnant women with fetal growth restriction and preterm birth risk.[17-20] As in our study, there are almost no studies comparing the effects of antenatal corticosteroid therapy on the Doppler parameters of pregnant women complicated with and uncomplicated with FGR. We determined that antenatal corticosteroids did not statistically affect UA Doppler parameters at 24 and 48 hours for each group with and without growth restriction. In our study, although it was observed that the UA Doppler parameters S/D ratio and PI were higher in the FGR group 24 hours after the last dose than before treatment, this increase was not found to be statistically significant. While there was no significant difference between the precorticosteroid UA Doppler parameters (S/D ratio, PI and RI) of the two groups, complicated with and without FGR, the values of these parameters 24 hours after the last treatment dose were found to be statistically significantly higher (worse) in the group complicated with FGR than in the group uncomplicated with FGR. No such difference was observed between the two groups in parameters after 48 hours. For this reason, we think that although antenatal corticosteroid affects UA Doppler parameters negatively when first applied in fetuses with growth restriction, this situation improves 48 hours after the last dose. Therefore, if growth restriction is detected in the fetus of the mother to whom antenatal corticosteroids will be administered, it may be useful to follow it more closely in the first 72 hours from the beginning of the treatment.

Wijnberger et al.[17] compared the Doppler parameters of 55 patients with growth restriction, which were measured in the last 5 days before betamethasone administration and in the first 5 days after betamethasone administration. If more than one measurement was obtained, the time closest to betamethasone administration was evaluated. The compared Doppler parameters of the study were UA-PI, MCA-PI, DV-PI and the UA-PI/MCA-PI ratio. It was determined that these values did not show a significant difference between the first values before and after betamethasone. In addition, the course of these Doppler parameters over time was also evaluated in the studies of Wijnberger et al. Doppler values measured 5 days before and 9 days after betamethasone administration were compared with the values measured on the day of betamethasone administration. The UA-PI value did not change significantly over time. MCA-PI values showed a significant and gradual decrease over time. At days 5, 6, 8 and 9, MCA-PI values were significantly lower than at day 0. The UA-PI/MCA-PI ratio increased significantly over time. At day 8, the UA-PI/MCA-PI ratio was

Table 1. Comparison of demographic characteristics and ultrasonographic fetal biometric measurements recorded just before antenatal corticosteroid between pregnant women complicated with and uncomplicated with FGR

	With FGR (n=49)	Without FGR (n=100)	P[1]
Age	30 (24-35)	29 (25-35)	0.945
Weight (kg)	74.0 (67.0-82,0)	74.0 (64.0-80.0)	0.630
Height (mm)	159 (157-163)	161 (158-165)	0,060
Body mass index (kg/m²)	29.3 (26.6-31,2)	28.4 (25.0-30.8)	0.215
Gravida	2 (1-3)	2 (1-3)	0.938
Parity	1 (0-1)	1 (0-2)	0.718
Gestational age based on last menstrual period	34.6 (32.2-36)	32.5 (30-34.6)	***<0.001****
Gestational age based on ultrasound measurements	32 (30-33.4)	33 (30.1-34.5)	0.060
Gestational ages based on each ultrasonographic fetal biometric measurement			
Biparietal Diameter	32.1 (30.4-33.4)	33 (30.1-34.5)	0.111
Head Circumference	32.4 (30.4-34.1)	33.1 (29.6-34.3)	0.522
Abdominal circumference	30.4 (29.3-32.5)	32.5 (29.6-34.5)	***0.003****
Femur Length	32 (30.1-34)	32.4 (30.0-34.3)	0.505
Estimated Fetal Weight	1843 (1393-2124)	2076 (1488-2429)	***0.037****

Variables are given as median (interquartile range [IQR]). [1]Mann–Whitney U test.*Signifies statistical significance. FGR, Fetal growth restriction; With FGR, Pregnant women complicated with FGR; Without FGR, Pregnant women uncomplicated with FGR.

Table 2. Evaluation of umbilical artery Doppler parameters of pregnant women with and without FGR just before the antenatal corticosteroid and 24 and 28 hours after the last dose of antenatal corticosteroid

		With FGR (n=49)	Without FGR (n=100)	P[1]
UA-S/D ratio	**Prior**	2.6 (2.3-3.1)	2.4 (2.2-2.9)	0.319
	After 24 hour	2.6 (2,3-3,2)	2.4 (2.1-2.8)	***0.022****
	After 48 hour	2.5 (2,1-3,0)	2.4 (2,1-2.8)	0.364
	p[2]	0.290	0.143	
US-PI	**Prior**	1.0 (0.8-1.1)	0.9 (0.8-1.1)	0.083
	After 24 hour	1.0 (0.9-1.2)	0.9 (0.7-1.0)	***0.001****
	After 48 hour	0.9 (0.7-1.1)	0.9 (0.7-1.0)	0.104
	p[2]	0.092	0.102	
UA-RI	**Prior**	0.6 (0.6-0.7)	0.6 (0.5-0.7)	0.110
	After 24 hour	0.6 (0.6-0.7)	0.6 (0.5-0.7)	***0.014****
	After 48 hour	0.6 (0.5-0.7)	0.6 (0.5-0.6)	0.475
	p[2]	0.082	0.318	

Variables are given as median (interquartile range [IQR]). [1]Mann–Whitney U test. [2]Friedman test. *Signifies statistical significance. FGR, Fetal growth restriction; With FGR, Pregnant women complicated with FGR; Without FGR, Pregnant women uncomplicated with FGR. UA-S/D ratio, The umbilical artery systolic to diastolic ratio; UA-PI, The umbilical artery pulsatility index; UA-RI, The umbilical artery resistance index.

significantly higher than on the day of betamethasone administration. DV-PI values increased gradually over time. The DV-PI values on days 7 and 8 were significantly higher than the values on day 0.[17] In our study, only UA Doppler parameters were evaluated, and the latest evaluation was made 48 hours after corticosterone. In our study, while MCA-PI and DP-PI values were not analyzed as in the Wijnberger study, UA-SD and US-RI parameters were analyzed in addition to the UA-PI value. Senat et al.[18] examined how 40 FGR fetuses were affected by antenatal corticosteroid in terms of Doppler parameters. Betamethasone was used as corticosteroid in the group with 25 fetuses, and dexamethasone was used in the group with 15 fetuses. Doppler measurements were made before the treatment (day 0), 24-48 hours after the mother's first injection of corticosteroid, and 4-7 days later. UA-PI, descending aorta-PI and MCA-PI were evaluated as Doppler parameters. No statistically significant changes were observed over time in the Doppler parameters examined in both groups treated with corticosteroids. However, PI in MCA tended to decrease 24-48 hours and 4-7 days after maternal steroid administration compared to pretreatment values in both groups. In our study, groups were not separated according to the type of corticosteroid administered and only UA Doppler parameters were examined. In our study, UA-PI value after corticosterone in fetuses with FGR did not show statistically significant changes, consistent with the studies of both Senat et al. and Wijnberger et al. However, in our study, unlike the studies of Wijnber et al. and Senat et al., Doppler parameters of fetuses without growth restriction and corticosterone administered were also evaluated as a control group. Accordingly, 24 hours

after the last dose of antenatal corticosteroid, the UA-PI value in the group with FGR was significantly higher, that is, more negative, than the UA-PI value in the group without FGR.

In the study of Niroomanesh et al.[19], published in 2015, some Doppler parameters of the UA, uterine artery and MCA vessels were evaluated in 40 patients with FGR before betamethasone, 24 hours and 5 days after the completion of betamethasone doses. Although a statistically significant decrease was observed in the uterine artery PI value 24 hours after the treatment, it was found that the value returned to the pre-treatment value after 5 days and no significant difference was observed with the value before the treatment. This temporary decrease in the uterine artery may be important, as 16 (40%) of the 40 people included in the study had preeclampsia along with FGR. In the UA-PI value, a significant decrease, or improvement, was observed 24 hours after the completion of betamethasone and 5 days after the completion of betamethasone. The results of this study are not consistent with our study, in which UA-PI in fetuses with FGR did not show significant changes at 24 hours and 48 hours after the last dose of corticosterone.

In the case of FGR, adverse changes in UA dopplers are associated with stillbirth and neurological disorders. Therefore, UA Doppler changes in fetuses with FGR may play a role in determining the time of delivery.[4,21] Absence or reversal of end-diastolic flow in the UA has been associated with severe FGR.[4] In recent studies, the effect of corticosteroids has been started to be investigated in FGR fetuses with UA end-diastolic flow loss or abnormal UA Doppler findings. In the prospective study performed by Nozaki et al.[20], the values of the Doppler parameters (UA, DV and MCA) of 32 fetuses with FGR and end-diastolic flow loss in the UA before and after betamethasone were examined. In their studies, the values immediately before, 24 hours and 48 hours after the first dose of betamethasone were examined. In their study, flow loss in UA Doppler returned in 22 cases after 24 hours. A statistically significant decrease, that is, improvement, was observed after 24 hours in UA PI. Although an increase was observed in UA PI values compared to the values after 24 hours in the evaluation after 48 hours, it was still significantly lower than before betamethasone, that is, it was observed as better. DV value was also lower after 24 hours compared to baseline. There was no significant difference in DV-PI between the evaluations after 24 hours and after 48 hours. For MCA PI, however, no significant differences were observed between repeated measurements.[20] The results of this study are inconsistent with our study in terms of post-corticosteroid UA-PI values in case of FGR. In our study, unlike this study, the UA-PI value in FGR did not change significantly before the corticosteroid administration, 24 hours and 48 hours after the last dose of corticosteroid administration. In fact, in the case of FGR in our study, UA Doppler parameters were observed to be higher (worse) than before treatment 24 hours after the last dose of corticosteroid administration, but this could not be proven statistically. And these parameters are statistically significantly higher, that is, worse, in the FGR group than the UA Doppler parameters of the non-FGR group 24 hours after the last dose of betamethasone. In our study, unlike Nozakinin's study, UA Doppler parameters before the corticosteroid administration, 24 hours and 48 hours after the last dose of corticosteroid were examined in all fetuses with growth restriction with or without end-diastolic flow loss. Only those with end-diastolic flow loss in the UA were not taken into account in our analyses.

In 2004, Simshenet al.[22] evaluated the perinatal outcomes after antenatal corticosteroids in a small sample prospective study of 25 people. Fetuses of 19 patients had end diastolic Doppler flow loss or reverse flow in the UA with FGR. In this group with FGR, they observed that fetuses with return of end-diastolic flow after antenatal corticosteroid had a better perinatal outcome compared with those with permanent loss of end-diastolic flow or reversed end-diastolic flow. In 2009, Robertson et al.[23] published a new study with a larger number of patients similar to the study by Simshen et al. They performed a retrospective cohort study of betamethasone administration in FGR pregnancies without end-diastolic flow of the UA. Transient return of end-diastolic flow after betamethasone was observed in the majority of pregnant women included in the study, approximately two-thirds. Persistent flow loss was present in about one-third. Pre-pregnancy medical disorder was more common in pregnant women with persistent loss of flow. Some perinatal outcomes were better in the group with transient return of UA end-diastolic flow, neonates of this group required less assisted ventilation, assisted ventilation for a shorter duration, and supplemental oxygen for a shorter duration. In other words, they found that fetuses with FGR with permanent loss of diastolic flow in the UA after betamethasone administration were at higher perinatal risk compared to the group with transient return of flow loss. Although the exact cause has not been determined, Robertson et al. stated that this may be due to the loss of the ability of fetuses with permanent end-diastolic flow loss after betamethasone to induce a vascular response to corticosteroids.

Miller et al.[24] demonstrated in a sheep experiment that administration of betamethasone in fetal growth restriction may be associated with impaired neuronal integrity and increased cell death in the brain due to increased cerebral oxidative stress. In the review by Vidaeff et al.[11] published a review examining the benefits and harms of antenatal corticosteroids in fetuses with FGR. In their study, they recommended close fetal monitoring to fetuses with severe FGR until 48-72 hours after antenatal corticosteroids due to the effects of antenatal corticosteroid on umbilical and placental blood flow. In our study, we observed a temporary worsening of UA Doppler parameters in fetuses with FGR compared to fetuses without FGR, 24 hours after the last dose of betamethasone administration, and we found that this situation improved after 48 hours. Therefore, in our

study, similar to Vidaeff et al., we recommend close fetal monitoring for fetuses with FGR during the first 72 hours after antenatal corticosteroid administration.

In our study, the the transiently higher umbilical artery Doppler parameters 24 hours after treatment in the FGR group than in the non-FGR group may be due to the difficulty of fetuses with FGR in meeting the physiological and metabolic demands imposed on the fetus by antenatal corticosteroid treatment. In the fetus group with FGR, all pregnant women whose umbilical artery Doppler parameters were found to be normal, flow loss, and reverse flow before treatment were included in our study. We do not know whether the results of our study would have been different from the present if only pregnant women with loss of flow or reverse flow in the umbilical artery were included.

The strength of our study is its prospective nature and the fact that it evaluated the post-corticosteroid Doppler parameters of the FGR as well as the non-FGR group. An important limitation of our study is that we stopped Doppler measurement after evaluating 48 hours after the last corticosterone dose and did not follow up with long-term Doppler. One of the limitations is that we did not separately evaluate the pregnant women with normal umbilical artery Doppler parameters and flow loss and reverse flow in the umbilical artery before antennal corticosteroid treatment in the FGR group. Another limitation is that we only evaluated the Doppler parameters of the UA and did not evaluate the Doppler parameters of other vessels such as MCA, DV, and descending aorta.

In conclusion, it was observed that antenatal corticosteroid did not permanently affect umbilical artery Doppler parameters in pregnancies complicated with FGR. In pregnancies with FGR, umbilical artery Doppler parameters are transiently higher (i.e., worse) 24 hours after the last corticosteroid dose than in pregnancies uncomplicated with FGR, but this resolves after 48 hours. Therefore, if corticosterone is administered to mothers of fetuses with FGR, close monitoring for 72 hours after the first dose may be beneficial.

Compliance with Ethical Standards

This cross-sectional study was approved by Marmara University Clinical Research Ethics Committee on 02.02.2018 with protocol code 09.2018.161.

Informed Consent

Informed consent was obtained from study subjects.

Conflict of Interest

No conflict of interest is declared by the authors.

Author Contributions

Data Collection or Processing: S.Z., S.S.; Analysis or Interpretation: S.Z., S.S.; Literature Search: Writing: S.Z., M.D.

Financial Disclosure

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References

1. Uquillas KR, Grubbs BH, Prosper AE, Chmait RH, Grant EG, Walker DK. Doppler US in the Evaluation of Fetal Growth and Perinatal Health. *Radiographics.* 2017;37(6):1831-1838. doi:10.1148/rg.2017170020
2. Krishna U, Bhalerao S. Placental insufficiency and fetal growth restriction. *J Obstet Gynaecol India.* 2011;61(5):505-511. doi:10.1007/s13224-011-0092-x
3. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 204: fetal growth restriction. *Obstet Gynecol.* 2019;133(2):e97–e109. doi:10.1097/AOG.0000000000003070
4. Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. *Am J Obstet Gynecol.* 2012;206(4):300–338. doi:10.1016/j.ajog.2012.01.022
5. Aditya I, Tat V, Sawana A, Mohamed A, Tuffner R, Mondal T. Use of Doppler velocimetry in diagnosis and prognosis of intrauterine growth restriction (IUGR): A Review. *J Neonatal Perinatal Med.* 2016;9(2):117-126. doi:10.3233/NPM-16915132
6. Nnamani AO, Ibewuike CU, Okere PC, Obikili EN. Comparative analysis of umbilical artery doppler indices of normal and suspected IUGR fetuses in the third trimester. *Niger J Clin Pract.* 2021;24(12):1793-1799. doi:10.4103/njcp.njcp_46_18
7. Acharya G, Wilsgaard T, Berntsen GK, Maltau JM, Kiserud T. Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy. *Am J Obstet Gynecol.* 2005;192(3):937-344. doi:10.1016/j.ajog.2004.09.019
8. Srikumar S, Debnath J, Ravikumar R, Bandhu HC, Maurya VK. Doppler indices of the umbilical and fetal middle cerebral artery at 18-40 weeks of normal gestation: A pilot study. *Med J Armed Forces India.* 2017;73(3):232-241. doi:10.1016/j.mjafi.2016.12.008
9. Khanduri S, Parashari UC, Bashir S, Bhadury S, Bansal A. Comparison of diagnostic efficacy of umbilical artery and middle cerebral artery waveform with color Doppler study for detection of intrauterine growth restriction. *J Obstet Gynaecol India.* 2013;63(4):249-255. doi:10.1007/s13224-012-0326-6
10. McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev.* 2020;12(12):CD004454. doi:10.1002/14651858.CD004454.pub4
11. Vidaeff AC, Blackwell SC. Potential risks and benefits of antenatal corticosteroid therapy prior to preterm birth in pregnancies complicated by severe fetal growth restriction. *Obstet Gynecol Clin North Am.* 2011;38(2):205-214. doi:10.1016/j.ogc.2011.02.011
12. Rotmensch S, Liberati M, Celentano C et al. The effect of betamethasone on fetal biophysical activities and Doppler velocimetry of umbilical and middle cerebral arteries. *Acta Obstet Gynecol Scand.* 1999;78(9):768-773.
13. Mulder EJ, Derks JB, Zonneveld MF, Bruinse HW, Visser GH. Transient reduction in fetal activity and heart rate variation after maternal betamethasone administration. *Early Hum Dev.* 1994;36(1):49-60. doi:10.1016/0378-3782(94)90032-9

14. Derks JB, Giussani DA, Jenkins SL et al. A comparative study of cardiovascular, endocrine and behavioural effects of betamethasone and dexamethasone administration to fetal sheep. *J Physiol.* 1997;499(Pt 1):217-226. doi:10.1113/jphysiol.1997.sp021922.
15. Schwab M, Roedel M, Anwar MA et al. Effects of betamethasone administration to the fetal sheep in late gestation on fetal cerebral blood flow. *J Physiol.* 2000;528(Pt 3):619-632. doi:10.1111/j.1469-7793.2000.00619.x.
16. Bennet L, Kozuma S, McGarrigle HH, Hanson MA. Temporal changes in fetal cardiovascular, behavioural, metabolic and endocrine responses to maternally administered dexamethasone in the late gestation fetal sheep. *Br J Obstet Gynaecol.* 1999;106(4):331-339. doi:10.1111/j.1471-0528.1999.tb08270.x.
17. Wijnberger LD, Bilardo CM, Hecher K, Stigter RH, Visser GH. Effect of antenatal glucocorticoid therapy on arterial and venous blood flow velocity waveforms in severely growth-restricted fetuses. *Ultrasound Obstet Gynecol.* 2004;23(6):584-589. doi:10.1002/uog.1052.
18. Senat MV, Ville Y. Effect of steroids on arterial Doppler in intrauterine growth retardation fetuses. *Fetal Diagn Ther.* 2000;15(1):36-40. doi:10.1159/000020972
19. Niroomanesh S, Shojaei K, Moghadam SF, Mohammadi N, Rahimi Z, RezaeiKeyhanaei K. Effect of prenatal betamethasone on fetal, uteroplacental, and maternal blood flow velocity in pregnancies complicated by fetal growth restriction. *Int J Gynaecol Obstet.* 2015;130(3):270-273. doi:10.1016/j.ijgo.2015.04.043
20. Nozaki AM, Francisco RP, Fonseca ES, Miyadahira S, Zugaib M. Fetal hemodynamic changes following maternal betamethasone administration in pregnancies with fetal growth restriction and absent end-diastolic flow in the umbilical artery. *Acta Obstet Gynecol Scand.* 2009;88(3):350-354. doi:10.1080/00016340902730334
21. Raghuraman N, Porcelli B, Temming LA et al. Clinical implications of umbilical artery Doppler changes after betamethasone administration. *J Matern Fetal Neonatal Med.* 2020;33(1):42-48. doi:10.1080/14767058.2018.1484095
22. Simchen MJ, Alkazaleh F, Adamson SL et al. The fetal cardiovascular response to antenatal steroids in severe early-onset intrauterine growth restriction. *Am J Obstet Gynecol.* 2004;190(2):296-304. doi:10.1016/j.ajog.2003.08.011
23. Robertson MC, Murila F, Tong S, Baker LS, Yu VY, Wallace EM. Predicting perinatal outcome through changes in umbilical artery Doppler studies after antenatal corticosteroids in the growth-restricted fetus. *Obstet Gynecol.* 2009;113(3):636-640. doi:10.1097/AOG.0b013e318197bf4d
24. Miller SL, Chai M, Loose J et al. The effects of maternal betamethasone administration on the intrauterine growth-restricted fetus. *Endocrinology.* 2007;148(3):1288-1295. doi:10.1210/en.2006-1058