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The impact of betamethasone administration on color Doppler ultrasound parameters and neonatal outcomes in fetuses with intrauterine growth restriction

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Abstract

Betamethasone administration increases placental vascular resistance, restoring diastolic flow. This study evaluated changes in the umbilical artery's flow velocity waveform (FVW) after betamethasone treatment in pregnancies with fetal growth restriction (FGR). This descriptive-analytical study examined all pregnant women with FGR who were between 28 and 34 weeks of gestation. These patients were referred to Sanandaj Besat Hospital, where they received betamethasone treatment. Following this administration, color Doppler ultrasound findings were compared to those obtained before the betamethasone treatment. Before betamethasone administration, the mean umbilical artery pulsatility index (U PI) was 0.23 ± 1.31 , significantly higher than 0.20 ± 1.19 after administration. The mean umbilical Resistance Index (U RI) also showed a similar trend, decreasing from 0.07 ± 0.74 to 0.08 ± 0.68 . In contrast, the mean middle cerebral artery pulsatility index (M PI) increased from 0.62 ± 2.28 before administration to 0.80 ± 2.68 after. The mean middle cerebral artery's Resistance Index (M RI) rose from 0.10 ± 0.89 to 0.24 ± 1.06 after administration. Fetal growth restriction can lead to negative outcomes for mothers and fetuses. Administering betamethasone improves umbilical artery resistance, allowing for prolonged pregnancies and reducing the risk of preterm labor. This ultimately lowers costs for families and the healthcare system.

Keywords: betamethasone, color Doppler ultrasound, neonatal outcomes, intrauterine growth restriction

Introduction

Fetal growth restriction (FGR) is a common complication during pregnancy where the fetus does not achieve its optimal growth potential in the uterus. It is diagnosed when the estimated fetal weight (EFW) from an ultrasound falls below the 10th percentile for the corresponding gestational age, and there are also impairments in color Doppler ultrasound parameters. FGR affects approximately 20.5% of all pregnancies worldwide each year [1,2]. The prevalence of FGR is six times higher in underdeveloped and developing countries compared to developed nations. Reports indicate that Asian countries account for 75% of all affected infants. FGR is classified into two categories - symmetric and asymmetric - based on additional biometric parameters related to the fetus, such as head circumference, abdominal circumference, femur length, and intertemporal diameter. In symmetric FGR, all growth parameters are proportionally reduced. In contrast, asymmetric FGR is characterized by a significant reduction in abdominal circumference on ultrasound, which falls below the third percentile for gestational age, while other measurements may remain relatively preserved or even within normal limits [3,4].

FGR is associated with adverse pregnancy outcomes such as stillbirth, preterm delivery, and increased neonatal mortality. While most cases are diagnosed after 32 weeks of gestation, 20-30% occurs before this time, with higher risks of complications for premature cases. FGR's causes are diverse, involving fetal, maternal, and placental factors, with placental insufficiency identified as the most significant contributor. To reduce fetal mortality risk, particularly in high-risk pregnancies, regular prenatal screenings with Doppler ultrasound and amniotic fluid evaluations are essential, as decreased fluid volume may indicate placental issues [1,5,6].

Almost 3% of pregnancies and 5% of high-risk pregnancies are affected by issues related to placental vascular resistance. This condition is diagnosed using color Doppler ultrasound of the umbilical artery, specifically by identifying absent end-diastolic flow (AEDF). In high-risk pregnancies with AEDF, the FVW assessed through color Doppler ultrasound can lead to a 30% reduction in perinatal mortality and improved neonatal survival [7-9].

Corticosteroids are a valuable treatment for women experiencing preterm labor, particularly those who are less than 34 weeks pregnant. Administering a course of corticosteroids before delivery can help with lung development and decrease the likelihood of respiratory distress syndrome [10-12]. Additionally, corticosteroid treatment reduces perinatal mortality and lowers the risk of other complications associated with preterm labor, such as intraventricular hemorrhage and necrotizing enterocolitis [13]. Some evidence indicates that steroids can lead to vasodilation, which in turn increases cardiac output in fetuses with FGR and contributes to improved hemodynamics. Both in vitro and in vivo studies have demonstrated a reduction in vascular resistance in the umbilical cord and placenta following corticosteroid treatment. Additionally, Doppler ultrasound findings in small groups of pregnant women with FGR fetuses have shown that administering betamethasone results in a temporary decrease in the pulsatility index (PI) of the umbilical artery and the reappearance of end-diastolic flow in that artery [14-16]. Some studies have not found changes in vascular resistance and umbilical artery Doppler parameters in fetuses with FGR after corticosteroid treatment [17,18].

Due to the conflicting reports surrounding the effects of betamethasone on umbilical artery Doppler parameters in fetuses with FGR, this study aimed to investigate how betamethasone administration impacts Doppler ultrasound indices and neonatal outcomes in FGR fetuses.

Methods

Study Design and Participants

This descriptive-analytical study focused on pregnant women referred to Sanandaj Besat Hospital, a center specializing in high-risk pregnancies in northwestern Iran. The study evaluated all pregnant

women with fetal growth restrictions who were referred from April 2022 to March 2024.

Sampling

The current study examined all pregnant women with FGR who were between 28 weeks to 34 weeks gestation and had impaired umbilical artery Doppler results. These women were registered at the high-risk clinic of Sanandaj Besat Hospital.

The inclusion criteria for this study were patients who were between 28 and 34 weeks of gestational age and aged between 18 and 42 years. The exclusion criteria included multiple pregnancies, congenital anomalies, chromosomal abnormalities, genetic disorders of the fetus, intrauterine infections, severe preeclampsia or eclampsia, fetal distress that necessitated early termination of pregnancy, and any contraindications to corticosteroid use.

After the university ethics committee approved the proposal and the necessary ethical permits were obtained, pregnant mothers diagnosed with intrauterine growth restriction through color Doppler ultrasound and biometric ultrasound were considered for the study. These mothers were selected if their perinatologist had decided to terminate their pregnancy within the next seven days, provided they met the inclusion criteria and did not meet the exclusion criteria. After obtaining written consent and explaining the study objectives, participants in this group received 12 mg of betamethasone intramuscularly in two doses, administered 24 hours apart.

The patients were admitted to Besat Hospital, where their demographic and clinical information was collected using checklists. 96 hours after the first dose of betamethasone, a perinatologist evaluated the patients again using color Doppler ultrasound to assess umbilical artery flow, middle cerebral artery flow, and ductus venosus. The patients were followed until delivery, and data were recorded on the type of delivery and neonatal outcomes. These outcomes included Apgar score, umbilical cord arterial blood gas pH, newborn weight at birth, perinatal and postnatal mortality rates, and duration of NICU stay.

Statistical analysis

The data obtained were analyzed using SPSS version 26 software. Descriptive statistics are presented as means $\pm$ SD or percentages. A paired P-analysis was conducted to compare the results of the color Doppler ultrasound data, with a significance level set at p less than 0.05.

Results

The demographic information of the patients includes the following: the mean age of the mothers was 29.17 $\pm$ 5.90 years, the mean BMI was 26.23 $\pm$ 3.95, and the mean gestational age at administration was reported to be 32.70 $\pm$ 1.58 weeks (**Table 1**).

Table 1. Descriptive data related to demographic and obstetric characteristics.

Variables	Mean $\pm$ SD	Median	Minimum	Maximum
Maternal age (yr)	29.17 $\pm$ 5.90	29.50	18	40
Body mass index (BMI)	26.23 $\pm$ 3.95	26	19	34
Gestational age (wk)	32.70 $\pm$ 1.58	33	28	34

Neonatal outcomes were as follows: the Apgar score at 1 minute was 8.58 ± 0.64 and 5 minute was 9.00 ± 0.05 and the cord arterial blood gas pH was 7.28 ± 0.07 . No drug-related adverse events or mortality were reported in this study. The length of hospital stay averaged 2.11 ± 0.8 days (**Table 2**).

Table 2. Neonatal outcomes.

Variables	Mean $\pm$ SD	Median	Minimum	Maximum
Apgar 1	8.58 ± 0.64	9	7	9
Apgar 5	9.00 ± 0.05	9	7	9
pH of umbilical cord arterial gases	7.28 ± 0.07	7.3	7.1	7.4
Mortality	0 ± 0.00	0	0	0
Hospitalization duration (days)	0.8 ± 2.11	0	0	8

In this study, at the administration the estimated fetal weight averaged 303.0 ± 16.84 grams. The femur length was reported as 3.88 ± 61.13 mm. The mean head circumference was 292 ± 15.57 mm. The diameter between the two temporal bones measured 79.06 ± 5.08 mm. The abdominal circumference was recorded at 258.3 ± 19.11 mm. Additionally; the base excess was reported as 3.02 ± 6.8 mmol/L. The observed amniotic fluid volume was 2.88 ± 10.05 cm³. The rate of vaginal delivery was 58.34%, while the cesarean section rate was 41.66% (**Table 3**).

Table 3. Clinical findings.

Variables	Mean $\pm$ SD N(%)	Median	Minimum	Maximum
Estimated fetal weight	1684 ± 303.0	1739	1056	2100
Femur length	61.13 ± 3.88	61.87	50.66	67.00
Head circum	292 ± 15.57	295.9	250	310.3
Biparietal diameter	79.06 ± 5.08	80.03	65.58	86.34
Abdominal circum	258.3 ± 19.11	259.6	222.2	306.1
Base execs	6.8 ± 3.02			
Amniotic fluid volume	10.05 ± 2.88	4.5	10	22.7
Normal vaginal delivery	35 (58.34)			
Cesarean section	25 (41.66)			

In this study, the mean U PI (umbilical artery pulsatility index) before dexamethasone administration was 0.23 ± 1.31 , significantly higher than the mean U PI after administration, which was 0.20 ± 1.19 . Additionally, the mean U RI before dexamethasone administration was 0.07 ± 0.74 , also significantly higher than the mean U RI after administration, recorded at 0.08 ± 0.68 (**Table 4**).

Table 4. Changes of Pulsatility Index and Resistance Index of Umbilical Artery.

Indices	Before	After	p-value
U PI	1.31±0.23	1.19±0.20	0.001
U RI	0.74±0.07	0.68±0.08	0.001
M PI	2.28±0.62	2.68±0.80	0.002
M RI	0.89±0.10	1.06±0.24	0.001

Conversely, the mean M PI before dexamethasone administration was 0.62 +/- 2.28, significantly lower than the mean M PI after administration, which increased to 0.80 +/- 2.68. Similarly, the mean M RI before dexamethasone administration was 0.10 +/- 0.89, significantly lower than the mean M RI after administration, which rose to 0.24 +/- 1.06 (**Table 4**).

Discussion

The results of this study indicated that administering betamethasone improved color Doppler indices, including the mean PI and RI of the umbilical artery. The terminal villi of the placenta significantly influence the flow velocity waveform observed in color Doppler imaging and play a crucial role in determining fetal placental vascular resistance. Research suggests that pregnancies exhibiting absent AEDF have fewer third-generation villi in the placental arterioles. Various studies indicate that AEDF in the umbilical artery corresponds to increased resistance to placental blood flow. There is a notable relationship between AEDF in the umbilical artery and abnormal flow velocity waveforms, which can lead to fetal hypoxia, acidemia, and FGR, all of which increase the risk of prenatal mortality. Therefore, using color Doppler ultrasound to detect AEDF in the umbilical artery in high-risk pregnancies could aid in treatment and contribute to improved fetal outcomes [8, 19-22].

In most pregnancies with AEDF in the umbilical artery, diastolic flow often reappears shortly after the administration of corticosteroids. However, this improvement may not last until the end of the pregnancy. To prevent false reassurance from normal fetal vessel waveforms (FVWs), it is advisable to use color Doppler monitoring to address any clinical concerns [9]. Our findings revealed a statistically significant decrease in the mean pulsatility index (PI) and resistance index (RI) of the umbilical artery.

Simchen et al. (2004) conducted a study involving 19 growth-restricted fetuses and six healthy fetuses as a control group to examine the fetal cardiovascular response to corticosteroids. The results indicated that end-diastolic flow returned 24 hours after steroid injection in 10 fetuses with AEDF. However, there was no significant difference in the mean PI between the steroid-treated group and the control group. It was observed that the baseline PI was significantly higher in growth-restricted fetuses compared to healthy fetuses [23]. In our study, we did not include a healthy control group; however, administration of betamethasone improved color Doppler indices, such as the mean PI and RI of the umbilical artery, when compared to measurements taken before the betamethasone treatment. Consequently, betamethasone administration resulted in a decrease in the Umbilical PI and Umbilical RI, while it increased the Mean PI and Mean RI.

In their study, Taghavi et al. (2020) reported that the administration of betamethasone is linked to an increase in placental vascular resistance, which leads to a restoration of diastolic flow. The objective of this study was to evaluate changes in the color Doppler FVW in the umbilical artery following betamethasone administration in pregnancies affected by FGR. After administering betamethasone, there was a statistically significant decrease in the mean PI and RI of the umbilical artery [24].

These findings align with the results observed in our study.

Jain and Bindal (2018) conducted a prospective study with 80 pregnant women experiencing intrauterine growth restriction between 28 and 34 weeks of gestation. They used color Doppler ultrasound to assess blood flow in the umbilical artery, middle cerebral artery, and ductus venosus, along with maternal uterine arteries, before and after betamethasone administration. The results showed significant differences in Doppler indices of the umbilical artery, middle cerebral artery, and ductus venosus before and 24 hours after treatment, but no significant effects were found for the maternal uterine artery. Infants whose mothers showed improvement in umbilical artery PI were less likely to need resuscitation, had better Apgar scores, and required fewer NICU visits. Overall, the study indicated that betamethasone administration could positively impact fetal circulation, though effects varied among cases of intrauterine growth restriction [25].

Ekin et al. (2016) studied the impact of antepartum betamethasone on Doppler parameters in fetal and uteroplacental circulation among seventy-six singleton pregnancies. Doppler measurements of pulse rate indices (PI) in the fetal umbilical artery (UA), middle cerebral artery (MCA), ductus venosus, and maternal uterine arteries were conducted before (0 hours) and at 24, 48, 72, and 96 hours after the first dose of betamethasone. The treatment was administered to women with either positive end-diastolic flow (EDF) or absent/reversed EDF in the UA. Results showed a significant decrease in the PI of the MCA at 24 hours, and 19 fetuses (79.2%) with absent or reversed UA-EDF demonstrated changes in flow within the same timeframe. All changes were transient, lasting up to 72 hours. Therefore, close fetal monitoring with Doppler ultrasound is essential after betamethasone treatment [26].

Fetal growth restriction is linked to negative outcomes for both the mother and fetus in many medical centers. However, administering betamethasone can improve umbilical artery resistance. This improvement allows physicians to prolong the pregnancy, helping to prevent preterm labor and its complications. As a result, this can lead to reduced costs for both the family and the healthcare system.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contribution

All authors contributed equally to this article.

Ethical approval

This study was conducted based on the ethical protocol of the institution where the research was conducted. Informed consent was obtained from the patient and all patient information is protected.

Declaration of competing interest

There are no conflicts of interest.

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