Role of Antenatal Dexamethasone Administration on Fetal Doppler Velocimetry

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Abstract

Aim: The aim of this study was assess the change in fetal and uteroplacental circulation following antenatal dexamethasone administration to high-risk of preterm labor pregnant women.

Patients and Methods: Prospective study was conducted between January and May 2021 in Tikrit city at Salahadeen General Hospital /genecology and obstetrics department The study included 30 pregnant women with high risk of preterm labor with gestational age from 24 to 34 weeks. Doppler Study were performed just before dexamethasone administration and will be repeated 24 h after completion of the dexamethasone course.

Results: The study showed the highest means of Fetal MCA pulsitility index. levels were recorded in women who at risk of preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups at 24 hour after dexamethasone administration ($P<0.05$). The study showed the highest means of Fetal MCA resistive index levels were recorded in women with preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration ($P<0.05$). The study showed the highest means of Uterine artery pulsitility index. levels were observed in women with preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration.

Keywords*: dexamethasone, fetal Doppler velocimetry, antenatal administration*

Introduction

Preterm birth is the delivery of a baby before 37 completed weeks' gestation. Most mortality and morbidity affects "very preterm" infants (those born before 32 weeks' gestation), and especially "extremely preterm" infants (those born before 28 weeks of gestation) [(1)]. Doppler assessment of the placental circulation plays an important role in screening for impaired placentation and its complications of pre-eclampsia, intrauterine growth restriction and perinatal death[(2)]. Assessment of the fetal circulation is essential in the better understanding of the pathophysiology of a wide range of pathological pregnancies and their clinical management[(3)]. Doppler ultrasound provides a non-invasive method for the study of fetal hemodynamics. Investigation of the uterine and umbilical arteries gives information on the perfusion of the uteroplacental and fetoplacental circulations, respectively, while Doppler studies of selected fetal organs are valuable in detecting the hemodynamic rearrangements that occur in response to fetal hypoxemia[(4)]. Doppler velocimetry is used to assess small-for-gestational-age (SGA) fetuses at risk of adverse perinatal outcome. Doppler abnormalities in the umbilical artery (UA) are related closely to placental disease. On the other hand, changes in

the fetal middle cerebral artery (MCA) reflect fetal cardiovascular adaptations to hypoxia or blood flow redistribution[5]. Thus, decreased pulsatility index (PI) has been considered a compensatory phenomenon to protect the fetal brain in the context of intrauterine growth restriction (IUGR). Poor uterine artery blood flow is associated with biochemical and cellular evidence of impaired placental development and function[6]. Uterine artery Doppler assessment appears effective in screening populations at high-risk for preeclampsia.[1] Poor uterine artery blood flow is also associated with adverse pregnancy outcome from other placental syndromes such as fetal growth restriction, abruption, and stillbirth[7]. Maternal administration of synthetic corticosteroids (dexamethasone), by accelerating the maturity of the fetal lung, reduces neonatal mortality, respiratory distress syndrome, intraventricular hemorrhage and necrotising enterocolitis in preterm infants. Previous studies have shown that steroids have an effect on fetal behaviour and fetal heart rate variability[8,9]. In fact, conflicting results concerning the effects of betamethasone and dexamethasone on fetal heart pattern have been reported. Dexamethasone was associated with an increase in long term and short term variability and decreased fetal movements on the first day after steroid administration followed by a decline in fetal heart rate variability on the second day [10]. Different studies found that betamethasone treatment is associated with significant reduction of the middle cerebral pulsatility index, especially at gestation before 32 weeks[11-13]. The aim of this study was assess the change in fetal and uteroplacental circulation following antenatal dexamethasone administration to high-risk of preterm labor pregnant women.

Patients and Methods

Prospective study was conducted between January and May 2021 in Tikrit city at Salahadeen General Hospital /genecology and obstetrics department. The study included 30 pregnant women with high risk of preterm labor with gestational age from 24 to 34 weeks.

Inclusion criteria :

1) Women with singleton uncomplicated pregnancy.

2) Women with risk of preterm labor

3) Women with normal utero-placental vascular resistance at the time of initial scanning (umbilical artery flow-velocity waveforms values above the fifth centile according to the reference limits as published by Arduini and colleagues); and

Exclusion criteria

1- Women who were unfit for conservative management patient actually in labor and fetal demise.

2- women with infants with known major structural malformation, complicated pregnancy, preterm, rupture of the membranes (PROM), vaginal bleeding as in (placenta previa and abruption placentae), .

3- suspected chorioamnionitis

3- maternal medical conditions e.g. PET, autoimmune diseases, DM.

4- maternal obstetrical conditions e.g. Polyhydramnios and oligohydramnios

5- non-reassuring fetal wellbeing e.g. presence of fetal bradycardia (FHR<120bp) or tachycardia (FHR>160bp) detected by sonicaide.

Doses of 12 mg dexamethasone intramuscularly 12 hours apart

1-Standrized questionnaire: designed by researcher

2- Doppler Study were performed just before dexamethasone administration and will be repeated 24 h after completion of the dexamethasone course. Blood flow velocity waveforms were obtained from the umbilical artery, fetal middle cerebral artery (MCA), and maternal uterine arteries.

Eligible participants were evaluated through full history taking and detailed anatomical scan by level II sonographer before inclusion to confirm their gestational age and exclude any structural anomalies.

Each woman received the recommended course of corticosteroids to induce fetal lung maturity consisting of two doses of 12 mg dexamethasone (Dexamethazone 8 ml, Sigma Pharam, Egypt) intramuscularly 12 hours apart.

Doppler studies were performed just before dexamethasone administration and repeated 24 hours after completion of the dexamethasone course using a SonoAce X6 machine (Medison, Korea) with 3.75 MHz transabdominal probe. All patients underwent Doppler examination by 2 different level II sonographers.

Doppler examination was done with the fetus in a quiet state, in absent of fetal movements and fetal breathing movements. The angle of insonation was optimized to be as low as possible, never exceeding 45°. The sweep speed was 2.5 cm /s and the pulse repetition frequency ranged from 3.5 - 5.5 Khz. The Doppler spectrum was recorded during maternal voluntary apnea.

Blood flow velocity waveforms were obtained from the umbilical artery, fetal middle cerebral artery (MCA), fetal descending aorta and maternal uterine arteries. Spectral pulsed wave Doppler analysis was done after that; RI and PI were calculated for each vessel. The formulas used for PI and RI were PI = (S-D)/mean and RI = (S-D)/S respectively, when S is the peak Doppler frequency shift and D is the minimum. At least 5 uniform waves forms of the spectrum were recorded and analyzed. Blood flow velocity waveforms were recorded from the umbilical artery in the free floating mid-portion of the umbilical cord[13]. Doppler signals registered from the fetal MCA in its proximal third. The MCA vessels were located with color Doppler ultrasound overlying the anterior wing of the sphenoid bone near the base of the skull[(14)]. Doppler signals obtained from the uterine arteries in the region of the lower uterine segment. Insonation of the uterine artery was done at its crossover the iliac artery[(15)]. Velocity waveforms from the fetal descending aorta were recorded at the lower thoracic level just above the diaphragm, keeping the angle of insonation of the Doppler beam below 45°.

Results

The study included 30 women with risk of preterm birth. We anticipated the risk of preterm birth on the basis of; preterm uterine contractions (n=17), placenta previa (n=9) and pre-eclampsia (n=4). The demographic data are presented in Table 4.1. The mean age of the study group was 28.4 ± 3.9 years. At the time of dexamethasone administration, mean gestational age was 30.6 ± 3.1 weeks.

Table 1: Maternal and neonatal characteristics of the studied cases

Maternal characteristics	
Age (years); mean ±SD	28.4 ± 3.9
Parity; median (Range)	4 (0 – 7)
Gestational age (weeks+days)	
At examination; mean ± SD (Range)	30.6 ± 3.1
At delivery; mean ± SD (Range)	31.1 ± 2.6
Neonatal characteristics	
Birth weight (gm); mean ± SD	1142.4 ± 640.4
PCU recommended; n (%)	17 (56.67%)
Apgar score (1 minutes) < 7; n (%)	20 (66.67%)
Apgar score (5 minutes) < 7; n (%)	13 (43.33%)
Gender (Female); n (%)	19 (63.33%)

The study showed significant differences among studied women with risk of preterm uterine contractions, placenta previa and pre-eclampsia regarding the average of Umbilical artery pulsitility index., where the highest averages recorded in the three groups before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration (P<0.05), more details in Table 2 below.

Table 2: Umbilical artery pulsitility index.

Studied cases (Before and 24 after hours of Dexamethasone)		Umbilical artery pulsitility index.		P. value	
		Mean	SD		
Threatened preterm labor (n:17)	Before	1.24	0.23	0.038	0.031
	24 hour after	1.02	0.16		
Preeclampsia (n:8)	Before	1.21	0.37	0.039	
	24 hour after	1.01	0.41		
Placenta previa (n:5)	Before	1.12	0.32	0.042	
	24 hour after	1.01	0.31		

The study showed significant differences among studied women with risk of preterm uterine contractions, placenta previa and pre-eclampsia regarding the average of Umbilical artery resistive index, where the highest averages recorded in the three groups before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration (P<0.05), Table 3.

Table 3: Umbilical artery resistive index

Studied cases (Before and 24 after hours of Dexamethasone)		Umbilical artery resistive index		P. value	
		Mean	SD		
Threatened preterm labor (n:17)	Before	0.66	0.21	0.031	0.028
	24 hour after	0.62	0.17		
Preeclampsia (n:8)	Before	0.71	0.13	0.034	
	24 hour after	0.68	0.11		
Placenta previa (n:5)	Before	0.65	0.14	0.044	
	24 hour after	0.61	0.21		

The study showed the highest means of Fetal MCA pulsitility index. levels were recorded in women who at risk of preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups at 24 hour after dexamethasone administration (P<0.05), more details in Table 4 below.

Table 4: Fetal MCA pulsitility index.

Studied cases (Before and 24 after hours of Dexamethasone)		Fetal MCA pulsitility index.		P. value	
		Mean	SD		
Threatened preterm labor (n:17)	Before	2.21	0.71	0.022	0.028
	24 hour after	2.17	0.51		
Preeclampsia (n:8)	Before	2.18	0.54	0.016	
	24 hour after	2.15	0.53		
Placenta previa (n:5)	Before	2.21	0.13	0.019	
	24 hour after	2.01	0.26		

MCA: middle cerebral artery

The study showed the highest means of Fetal MCA resistive index levels were recorded in women with preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration (P<0.05), more details in Table 5 below.

Table 5: Fetal MCA resistive index

Studied cases (Before and 24 after hours of Dexamethasone)		Fetal MCA resistive index		P. value	
		Mean	SD		
Threatened preterm labor (n:17)	Before	0.91	0.45	0.039	0.032
	24 hour after	0.85	0.43		
Preeclampsia (n:8)	Before	0.88	0.34	0.034	
	24 hour after	0.82	0.55		
Placenta previa (n:5)	Before	0.86	0.25	0.028	
	24 hour after	0.80	0.31		

The study showed the highest means of Uterine artery pulsitility index. levels were observed in women with preterm uterine contractions, placenta previa and pre-eclampsia respectively before dexamethasone administration as compared with the same groups 24 hour after dexamethasone administration (P<0.05), more details in Table 6 below.

Table 6: Uterine artery pulsitility index.

Studied cases (Before and 24 after hours of Dexamethasone)		Uterine artery pulsitility index.		P. value	
		Mean	SD		
Threatened preterm labor (n:17)	Before	0.96	0.45	0.039	0.032
	24 hour after	0.87	0.43		
Preeclampsia (n:8)	Before	0.94	0.34	0.034	
	24 hour after	0.86	0.55		
Placenta previa (n:5)	Before	0.90	0.25	0.028	
	24 hour after	0.85	0.23		

The study showed significant differences among studied women with risk of of preterm uterine contractions, placenta previa and pre-eclampsia regarding the average of Uterine artery resistive index, before and 24 hour after dexamethasone administration (P>0.05), Table 4.7.

Discussion

Fetal biophysical profile and Doppler ultrasonography have been used to assess fetal well-being *in utero*. Studies have reported transient reduction of fetal body movements, fetal breathing and fetal heart rate variation after antenatal betamethasone administration [1,2]. Likewise, Doppler velocimetry of the umbilical (UA) and middle cerebral arteries (MCA) has also been found to be affected by corticosteroid administration. Prior studies revealed that the maternal administration of betamethasone was associated with a transient decrease in the pulsatility index (PI) [3-5]. However, the mentioned studies had methodological limitations in some aspects. First, precise timing of the onset of the steroid effect was not determined due to the retrospective review of pregnancies [6,7]. Second, other components of fetomaternal vasculature such as ductus venosus and uterine arteries were not assessed in a majority of the studies [8-11]. The study included 30 women at risk of preterm birth. We anticipated the risk of preterm birth on the basis of; preterm uterine contractions (n=17), placenta previa (n=8) and pre-eclampsia (n=45). In this study, dexamethasone administration was found to have a beneficial effect on fetuses at risk for preterm birth as evident by the decrease in the Doppler indices of umbilical artery, MCA and uterine artery. Umbilical artery Doppler indices showed statistically significant reduction 24 hours after dexamethasone administration. Our results agreed with Senat *et al* [12] study that reported an association between betamethasone treatment and decreased placental vascular resistance as reflected by waveforms obtained from umbilical artery. This is similarly agreed by Nozaki *et al* [13] who found a reduction in the umbilical artery PI within 24 hours following antenatal corticosteroid therapy. MCA Doppler indices decreased after the treatment. These findings are in agreement with the results of Chitrit *et al* [14] who observed a transient and significant decrease in fetal MCA (PI, RI) after maternal dexamethasone administration. However some studies disagree with

our results as Miracle *et al* [15] and Wijnberger *et al* [16] , they were on growth-restricted preterm fetuses; no effect was found from betamethasone on PI in fetal MCA. In the latter study, circulation in fetuses was studied for up to 14 days, indicating that placental insufficiency was probably not severe enough to indicate early delivery[17]. Moreover, Piazze *et al* [18] examined the effect of steroids on blood flow waveforms in IUGR fetuses and found no significant changes of PI, RI values in the different vessels after dexamethasone course. There was statistical significant reduction in the uterine artery Doppler indices before and 24 hours after dexamethasone administration in the present study. These findings are in agreement with data published by Chitrit et al who observed similar transient and significant decrease in uterine artery PI and RI after maternal dexamethasone administration in healthy fetus[19]. However, other studies reported that there was no significant influence of betamethasone therapy on Doppler indices in uterine circulation in pregnancies with imminent preterm delivery[20,21]. A study on human placentas by some authers showed that the mechanism behind dexamethasone-induced vasodilatation might be an endothelium independent mechanism, as they did not find any involvement of endothelium-derived products such as prostaglandin I and nitric oxide[22,23]. In concordance with our findings, a previous retrospective cohort study showed that corticosteroids administration was associated with significant change in umbilical artery PI and a transient return of end-diastolic umbilical artery flow[24]. Another study showed that maternal antenatal corticosteroids resulted in a significant transient change in the velocity waveform and a decrease in the PI in the umbilical artery and ductus venosus[25]. Similarly, Elsnosy and colleagues[26]. concluded that maternal dexamethasone administration to pregnant women at risk of preterm improves the blood flow of umbilical artery and MCA. In addition, a previous report showed that the MCA PI showed a trend to decrease 24–48 h and 4–7 days after steroids were given to the mother when compared to pretreatment values[27]. In contrary, Yvon Chitrit and colleagues17 showed that no significant change was documented on days 2 and 7 in umbilical artery PI after dexamethasone administration. Additionally, Salama *et al* [28] reported no significant variations were observed in the umbilical artery PI throughout dexamethasone therapy. In addition, a previous report showed no significant effects of corticosteroids were observed in the uteroplacental circulation[29]. The exact causes of such discrepancies between our findings and the abovementioned studies is unclear, however, it can be attributed to many factors. Firstly, the dose and type of antenatal corticosteroids were different between our study and those reports; for example, Salama and colleagues administrated 24 mg of dexamethasone intramuscularly in three divided doses 8 h apart), while Müller and colleagues administrated betamethasone. Secondly, the sample size varied greatly among the abovementioned studies which may have attributed for such heterogeneity. The characteristics of the included women were apparently different which can be considered as another factor.

Conclusion

The administration of dexamethasone to pregnant women at risk of preterm birth could improve the blood flow in the uterine arteries, fetal MCA, and umbilical artery 24 hours after its administration.

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Conflict of Interest: None to declare.

Ethical Clearance: "All experimental protocols were approved under the Diyala Health directorate and carried out in accordance with approved guidelines".

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