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Original Research Article.

Effect of Antenatal Dexamethasone Administration on Foetal and Uteroplacental Doppler Waveforms in Women at Risk of Spontaneous Preterm Birth: A Prospective Study

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ABSTRACT

Introduction: The effects of antenatal dexamethasone on foetal and uteroplacental circulation as measured by Doppler waveform has gained more attention recently. In the present study, we aimed to assess the change in foetal and uteroplacental circulation following antenatal dexamethasone administration to high-risk pregnant women.

Methods: We conducted a prospective cohort study on 50 pregnant women with high risk of preterm birth within the gestational age from 24 to 34 weeks. Two doses of dexamethasone was administrated and. Doppler velocity waveforms were obtained from the umbilical artery, fetal middle cerebral artery (MCA), fetal descending aorta and maternal uterine arteries Data analysis was carried out using SPSS version 22 for Microsoft Windows.

Results: The mean age of the included women were 27.9 ±4.8 years while the mean parity was 2.14 ±1.4. Eighty percent of the children were alive at delivery. In terms of Doppler Indices, the umbilical artery pulsatility index (PI) and resistive index showed a statistically significant reduction after Dexamethasone administration (p <0.001). Similarly, the uterine and MCA arteries PI and RI showed a statistically significant reduction after Dexamethasone administration (p <0.001). In terms of Cerebro-umbilical ratio (CUR), the ratio showed a statistically significant increase after Dexamethasone administration (p =0.015). The CUR increased significantly after dexamethasone administration to reach 2.1 ±0.33. Only one patient had abnormal velicometry before and after dexamethasone.

Conclusion: In conclusion, the present study shows that antenatal dexamethasone administration significantly improve the fetal and uteroplacental hemodynamics, assessed by Doppler, among women with risk of preterm labor.

Keywords: Preterm Labour; Dexamethasone; Doppler Waveforms.

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INTRODUCTION

Prematurity is a major public health concerns. According to recent global figures from the world health organization (WHO), more than 1 in 10 infants is expected to be born as preterm.[1] While the recent advances in healthcare services have led marked reduction in mortality rate among preterm infants, surviving preterm infants are at risk of devastating complications such as lung immaturity, pathological jaundice and kernicterus, necrotizing enterocolitis sepsis, and retinopathy.[2] Moreover, preterm birth can have a great impact on child development, previous reports showed that preterm infants are more liable to developmental and cognitive disorders than children born full-term, with poorer social involvement.[3,4] Throughout the past four decades, antenatal synthetic corticosteroids (betamethasone or dexamethasone) have been used to enhance foetal lung surfactant production and lung maturity in pregnancies at risk for preterm delivery; and therefore, reducing the incidence of neonatal respiratory distress syndrome (RDS).[5] Moreover, corticosteroids were reported to reduce the incidence of intraventricular hemorrhage, necrotizing enterocolitis and overall neonatal mortality in preterm infants.[6]

Moreover, the current body of evidence suggested that synthetic corticosteroids are largely safe with no major adverse events after treatment during the second half of pregnancy. However, previous reports have reported a significant reduction in foetal body movements, foetal breathing movements, and heart rate variation after betamethasone administration, though the reduction was transient.[7]

In addition, there was a trivial decrease in vascular resistance of placenta after betamethasone administration in pregnancies with absent end-diastolic flow in the umbilical artery.[8] Similar effects were not reported to date with dexamethasone administration.

Doppler ultrasound has proven value in assessing foetal and maternal cardiovascular parameters, Doppler examination of blood flow velocity waveforms was reported to be a reliable tool for the evaluation of high-risk pregnancies.[9] Recently, a growing body of evidence has investigated the effects of neonatal dexamethasone on foetal and uteroplacental circulation as measured by Doppler waveforms. Elsnosy and colleagues reported that maternal dexamethasone administration, to pregnant women at risk of preterm labor, improves the blood flow of the maternal uterine artery, foetal middle cerebral artery, descending aorta and umbilical artery 24 h after its administration.[10]

Therefore, we conducted the present study to assess the change in foetal and uteroplacental circulation following antenatal dexamethasone administration to high-risk pregnant women.

MATERIALS AND METHODS:

We followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement recommendations during the preparation of this report.[11] The study's protocol gained the approval of the local ethics and research committee of Banha university hospital. The present study runs in concordance with the Declaration of Helsinki principles and the guidelines of the International Committee of Medical Journal. A written informed consent was obtained from every eligible woman prior to study enrollment.

Study Design, Setting and Participants

The present study was a prospective cohort study that was conducted at Obstetric and Gynecological outpatient clinics of Banha university hospital through the period from March 2018 to August 2018. We included pregnant women with gestational age from 24 to 34 weeks who fulfilled the following criteria: 1) Women with singleton uncomplicated pregnancy; 2) 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 3) Women with risk of preterm labor. The risk of preterm labor was suspected by past or current history of preterm delivery, past history of second trimester fetal loss suggestive of cervical insufficiency, uterine malformation e.g. Mullerian duct anomalies detected before the pregnancy, preterm uterine contractions, heavy stressful work, prior cervical surgery e.g. cone biopsy, cervical cerclage during the current pregnancy, or Placenta previa.

Women who were unfit for conservative management (e.g. patient actually in labor, fetal demise, 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), suspected chorioamnionitis (palpable uterine contractions, abdominal pain, temperature >38.5 °C, white blood cell count > 16 x 1012/L, and/or serum level of C-reactive protein > 10 mg/L), maternal medical conditions e.g. pre-eclampsia, autoimmune diseases, diabetes., maternal obstetrical conditions e.g. Polyhydramnios and oligohydramnios, or non-reassuring fetal wellbeing e.g. presence of fetal bradycardia (FHR<120bp) or tachycardia (FHR>160bp) detected by sonicaide were excluded.

Data Collection and Study's Visits:

At the initial study's visit, the following items were collected from every eligible women: demographic characteristics, full medical and obstetric history, full clinical examination, evaluation of placental site, amniotic fluid amount and turbidity as well as exclusion of fetal congenital anomalies, and ultrasound examination. Then, each woman received the recommended course of corticosteroids to induce fetal lung maturity consists of two doses of 12 mg dexamethasone (Dexamethasone 8 ml, Sigma) intramuscularly 12 hours apart.

Doppler Study

Doppler studies were performed just before dexamethasone administration and will be repeated 24 h after completion of the dexamethasone course using a SonoAce X8 machine (Medison, Korea) with 3.75 MHz curvilinear transabdominal probe. Doppler examination were done with the fetus in a quiet state, in the absence of fetal movements and fetal breathing movements. The angle of insonation were 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 to 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 were done after that; RI and PI 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 waveforms of the spectrum were recorded and analysed.

Statistical Analysis

Data entry, processing, and statistical analysis were carried out using Microsoft Excel 2007 (Microsoft Corporation, NY, and the USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22 for Microsoft Windows. Quantitative data were described in terms of mean ±standard deviation (±SD), while qualitative data were expressed as frequencies (number of cases) and relative frequencies (percentages). Comparisons between quantitative variables were done using paired Student's t-test for parametric data or Mann-Whitney Rank Sum test for non-parametric data. Chi-square test was performed for categorical variables. A probability value (p-value) less than 0.05 was considered statistically significant.

RESULTS

In the present prospective study, we included 50 pregnant women who were pregnant with high risk of preterm birth. The mean age of the included women were 27.9 ±4.8 years while the mean parity was 2.14 ±1.4. The majority of the included women (62%) were delivered by cesarean section. With regard to fetus, the mean gestational age was 29.24 ±2.9 weeks; while the mean age of delivery was 34.54 ±3.4 weeks. Eighty percent of the children were alive at delivery (Table 1).

In terms of Doppler Indices, the umbilical artery PI showed a statistically significant reduction from 1.15 ±0.19 to 1 ±0.16 after Dexamethasone administration ($p < 0.001$). Similarly, the umbilical artery RI showed a significant reduction after Dexamethasone administration to reach 0.63 ±0.06 ($p < 0.001$). With regard to Uterine artery, the PI showed a statistically significant reduction after Dexamethasone administration ($p < 0.001$); while RI showed similar results ($p = 0.027$). The middle cerebral artery PI and RI showed statistically significant reductions after Dexamethasone administration to reach 1.98 ±0.31 and 0.79

±0.07, respectively (p <0.001; Table 2). In terms of CUR, the ratio showed a statistically significant increase after Dexamethasone administration (p = 0.015). The CUR increased significantly after dexamethasone administration to reach 2.1 ±0.33 (Figure 1). Only one patient had abnormal velicometry before and after dexamethasone.

Table 1: Shows the baseline demographic characteristics of the mothers

Variables	Patients (N =50)	
	No	%
Age of the mother (years), Mean (SD)	27.9 (4.8)	
Party, Mean (SD)	2.14 (1.4)	
Mode of Delivery		
CS	31	62.0
VD	19	38.0
Gestational Age (Weeks), Mean (SD)	29.24 (2.9)	
Age at Delivery (Weeks), Mean (SD)	34.54 (3.4)	
Status		
Alive	40	80.0
Dead	10	20.0

Table 2: Shows the change in Doppler Indices after Dexa adminstration

Variable, Mean (SD)	Pre	Post	Paired t-test	P-value
Umbilical Artery PI	1.15 (0.19)	1 (0.16)	9.915	<0.001
Umbilical Artery RI	0.73 (0.08)	0.63 (0.06)	11.836	<0.001
Uterine Artery PI	0.97 (0.15)	0.85 (0.14)	10.424	<0.001
Uterine Artery RI	0.59 (0.08)	0.56 (0.09)	2.284	0.027
MCA Artery PI	2.21 (0.41)	1.98 (0.31)	9.915	<0.001
MCA Artery RI	0.88 (0.08)	0.79 (0.07)	11.836	<0.001

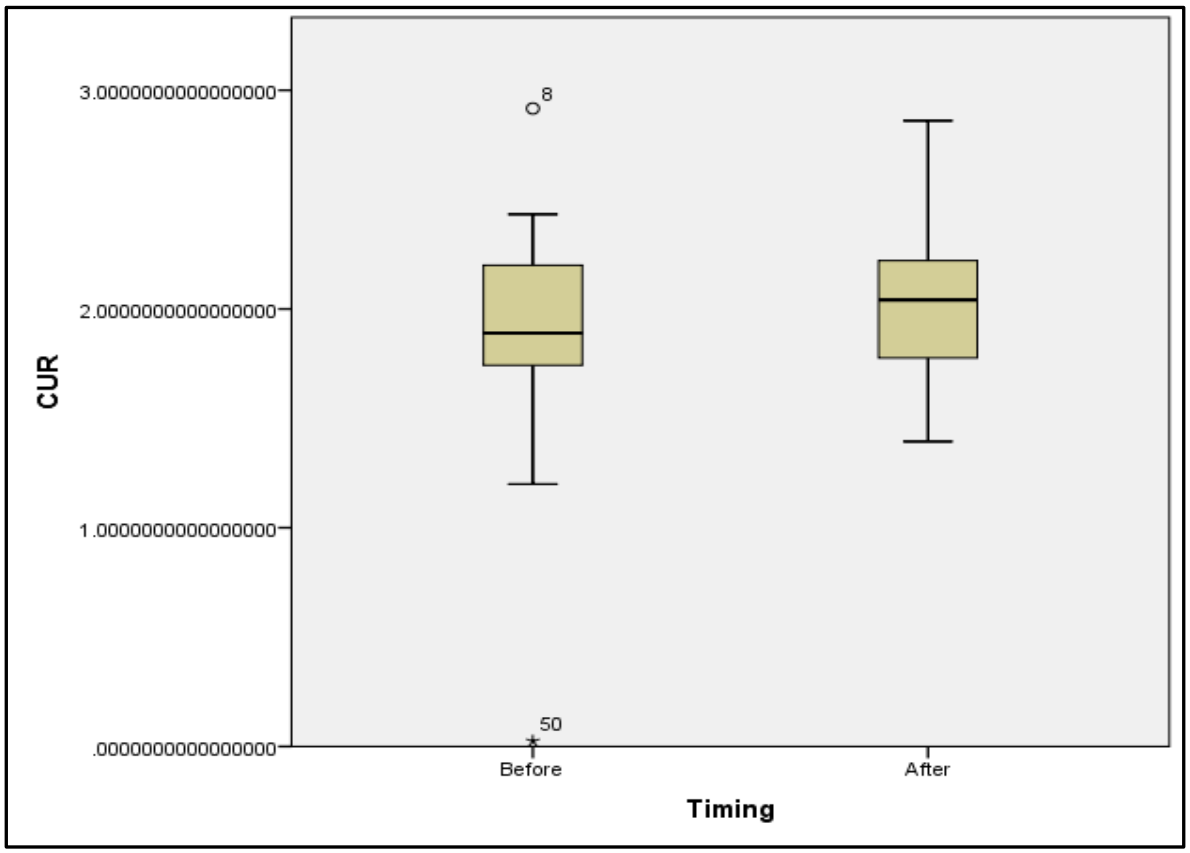

Figure 1: The change in CUR after Dexamethasone

DISCUSSION

While antenatal corticosteroid therapy plays an effective role in the improvement of morbidity and mortality from of preterm neonates, it has been recently suggested that the corticosteroid therapy may lead to a significant reduction in fetal well-being and may lead to fetal growth restriction, especially with betamethasone.[12] In the present study, antenatal dexamethasone lead to significant improvement in the umbilical artery, uterine artery, and MCA PI and the RI; a similar improvement was noted regarding the CUR as well. Arterial RI is a proxy of vascular resistance and compliance; while PI measures the variability of blood velocity between systole and diastole.[13] 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.[14] 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.[15] Similarly, Elsnosy and colleagues[10] 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.[16]

In contrary, Yvon Chitrit and colleagues[17] showed that no significant change was documented on days 2 and 7 in umbilical artery PI after dexamethasone administration. Additionally, Salama and colleagues[18] 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.[15]

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.

We acknowledge that the present study has a number of limitations. The sample size of the included patients were relatively small, which may affect the generalizability of our findings. Moreover, there were no long-term monitoring of the changes in Doppler indices after dexamethasone administration. We did not assess the clinical outcomes of antenatal dexamethasone administration as well.

CONCLUSION

In conclusion, the present study shows that antenatal dexamethasone administration significantly improve the fetal and uteroplacental hemodynamics, assessed by Doppler, among women with risk of PTB. Further large-scale studies are still needed to confirm our findings and to compare the effects of different regimens of antenatal dexamethasone.

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