Effects of antenatal dexamethasone administration on Doppler of Umbilicalartery, Middle cerebral artery and uterine artery in women at risk for spontaneous preterm birth

Aziza H. Nassef[1], Sonia M. Fouad [2], Safaa M. Ibrahem[3]

[1]MD,Lecturer of Obstetrics and Gynecology, Faculty of Medicine for girls, Al-Azhar University, Cairo, Egypt
[2] MD, Professor of Obstetrics and Gynecology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt
[3] Resident of Obstetrics and Gynecology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.
Sfamhmd799@gmail.com; alaa.abosleim@gmail.com

Abstract Objective: The current study aimed to evaluate the effect of administration of maternal administration of dexamethasone on the fetal and uteroplacental circulation as measured by Doppler ultrasound in pregnant women at risk for preterm birth before and after 24 hours of its administration. **Materials and methods**: A prospectively study that was carried out60 women with gestational age from 28 to 34 weeks and singleton pregnancies at risk for preterm labor. All cases were received two dosesof intramuscular injection of 12mg Dexamethasone 12hour apart. Doppler ultrasound was performed on the umbilical artery, fetal middle cerebral artery (MCA) (just before dexamethasone administration and repeated 24 hours after completion of the dexamethasone course). Then, follow up till delivery was done to assess neonatal outcome. **Results:** In the current study, the mean age of the group was 28.28 ± 4.5 years. The mean gestational age was 32.06weeks, Doppler indices in umbilical artery, fetal MCA and uterine artery were significantly decreased24 hours after maternal administration of dexamethasone. **Conclusion:** Administration of dexamethasone to pregnant women at risk of preterm labor can improve the blood flow of the maternal uterine artery, fetal MCA, and umbilical artery after 24 hours of its administration.

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1. Introduction:

Premature labor is a serious problem because premature infants may have underdeveloped lungs due to deficient production of thesurfactant. This can cause neonatal respiratory distress syndrome (RDS). Glucocorticoids is used to reduce the risk of the complications of prematurity. Glucocorticoids are steroid that crosses the placental barrier and stimulates the synthesis of surfactant in the fetal lungs (1). In imminent premature labor, a second "rescue" course of steroids may be given 12 to 24 hours before the anticipated labor. The efficacy and side effects of a second course of steroids are still with some concerns. At 2015 Cochrane review supports the administration of repeat dose(s) of prenatal corticosteroids in pregnant women at risk of preterm labor seven days after the first course (2).

2. Patients and Methods:

His is a prospective study that was carried out in the period between December 2017 and April 2018, at the department of obstetrics and gynecologyat Al Zahraa university hospital,Al Azhar faculty of medicine for girls after approval by themedical ethics of the committee of the faculty of medicine for girls, Al Azhar university,Cairo, Egypt. Informed consent was obtained from all cases.60 pregnant women werereceived dexamethasone injection (Two doses of 12 mg dexamethasone intramuscularly 12hourrs apart) after fulfillment of the inclusion criteria including: gestational age from 28 to 34 weeks, Singleton pregnancy, at risk for preterm delivery, which includes one of the following: 1- history of preterm birth, 2- maternal hypertension or preeclampsia, 3-antepartum bleeding secondary to placental separation or placenta previa. Exclusion criteria include: 1- gestational age less than 28 weeks or more than 34 weeks, 2-patients in labor, 3-multiple pregnancy, 4-women had contraindications to corticosteroids, 5- intrauterine growth restriction (IUGR), 6- patients presented with premature rupture of membranes,and 7-those who had received corticosteroids in their pregnancies.All cases were subjected to history taking, general examination, and speculum examination to exclude cervical dilation and rupture of membranes. Doppler ultrasound examinationsof umbilical artery, fetal middle cerebral artery and uterine artery were done before dexamethasone administration and 24 hours after the administration of the last dose.The Doppler examination were donetransabdominallyusing MedisonSonoAce R5 with a convex linear transducer 2-MHz. The umbilical artery was assessedin the freemiddle partof the umbilical cord.A transverse view of the fetal brain was obtained at the level of biparietal diameter,color flowimaging was done to help to detect the middle cerebral artery as a major lateral branch of the circle of Willisrunning

anterolaterally between the middle and the anterior cerebral fossae. Color flow imaging was used to visualize the flow through the main uterine artery at the level of internal os of the cervix and the Doppler sample gate was placed at the point of maximal color brightness.Doppler examinations was done with the lowest angle of insonation (less than 45°)as much as possible. Pulsatility index (PI), and resistance (RI) were assessed for the umbilical artery, fetal middle cerebral artery, and maternal uterine arteries.Then follow up for all casesto evaluate the neonatal outcome.

3. Results

In table (1): the mean maternal age was 28.28 ±5.18years. The risk factors for preterm labor include previous preterm labor (occurred in 38.3%). And 60% of cases had current preterm labor pains.

Table (1): Characteristic demographic data of studied group:

		No. = 60
Age (years)	Mean±SD Range	28.28 ± 5.18 19 – 38
Parity	0 {Nullipara} 1 2 3 4	13 (21.7%) 12 (20.0%) 15 (25.0%) 19 (31.7%) 1 (1.7%)
Gastational Age(weeks)	Mean±SD Range	32.06 ± 1.51 29 – 34
Number of Previous preterm deliveries	None One Two	37 (61.7%) 17 (28.3%) 6 (10.0%)
Number of Previous Abortion	None 1-2 abortions > 2 abortions	42 (70.0%) 14 (23.3%) 4 (6.7%)
Placental Location:	1)normal location 2)previa _PP centralis _LL placenta	48 (80.1%) 12 (20%) 7 (11.67%) 5 (8.33%)
Number of cases with Current preeclampsia	16 cases	(26.7%)
Number of cases with Current PTL*	36 cases	(60.0%)

*PTL: preterm labor

Figure 1illustrate that 38.3% of cases had previous preterm labor.

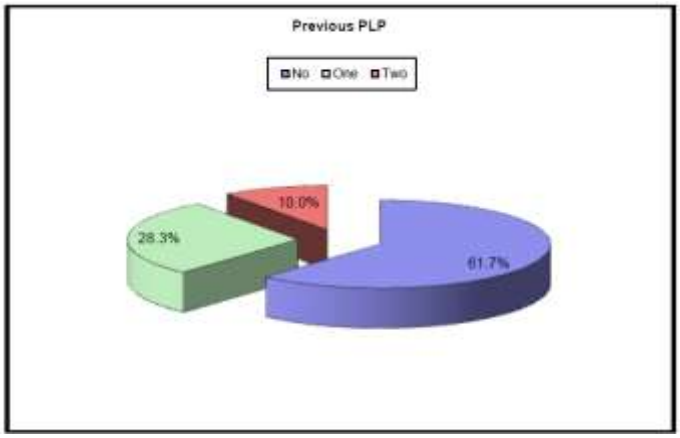

Figure (1): Distribution of cases according to history of PTL in previous pregnancies as the main risk factors:

Table (2): Comparison between Doppler indices (PI) before and after administration of dexamethasone:

		Before	After	Test value•	P-value	Sig.
		No. = 60	No. = 60			
UA PI*	Mean±SD Range	1.24 ± 0.26 0.87 – 1.95	1.14 ± 0.19 0.83 – 1.53	5.231	0.000	Highly
Ut A PI **	Mean±SD Range	1.10 ± 0.20 0.81 – 1.5	1.04 ± 0.18 0.77 – 1.45	6.702	0.000	HS
MCA PI***	Mean±SD Range	2.39 ± 0.28 1.85 – 3	2.28 ± 0.22 1.83 – 2.65	6.029	0.000	HS

HS: Highly significant. * UA PI: Umbilical Artery pulsatility index. **Ut A PI: Uterine Artery pulsatility index. ***MCA PI: Middle Cerebral Artery pulsatility index. •: Paired t- test

Table (3): Comparison between Doppler indices (RI) before and after administration of dexamethasone:

		Before	After	Test value•	P-value	Sig.
		No. = 60	No. = 60			
UA RI*	Mean±SD Range	0.61 ± 0.09 0.44 – 0.78	0.59 ± 0.08 0.46 – 0.75	3.514	0.001	HS****
UtA RI**	Mean±SD Range	0.60 ± 0.06 0.48 – 0.72	0.58 ± 0.06 0.42 – 0.71	5.853	0.000	HS****
MCA RI***	Mean±SD Range	0.93 ± 0.10 0.7 – 1.3	0.90 ± 0.08 0.72 – 1.15	6.172	0.000	HS****

UA RI*: Umblical Artery Resistant index. Ut A RI**: Uterine Artery Resistant index. MCA RI***: Middle Cerebral Artery Resistant index.HS****: Highly significant•: Paired t- test

Table (4): Relation between the changes in Doppler indices and need of NICU admission.

Changes of Doppler indices between Values before and after dexamethasone		No NICU admission	NICU admission	Test value•	P-value	Sig.
UAPI	Mean±SD Range	-0.07 ± 0.15 -0.57 – 0.19	-0.13 ± 0.15 -0.56 – -0.01	1.398	0.167	*NS
UARI	Mean±SD Range	-0.01 ± 0.05 -0.08 – 0.12	-0.02 ± 0.02 -0.05 – 0.03	1.761	0.084	*NS
UtAPI	Mean±SD Range	-0.06 ± 0.06 -0.22 – 0.03	-0.05 ± 0.07 -0.20 – 0.06	-0.281	0.780	*NS
UtARI	Mean±SD Range	-0.02 ± 0.03 -0.07 – 0.05	-0.02 ± 0.02 -0.05 – 0.06	-0.442	0.660	*NS
MCAPI	Mean±SD Range	-0.09 ± 0.12 -0.41 – 0.04	-0.12 ± 0.16 -0.51 – 0.15	0.814	0.419	*NS
MCARI	Mean±SD Range	-0.03 ± 0.04 -0.15 – 0.03	-0.03 ± 0.04 -0.10 – 0.03	0.194	0.847	*NS

*NS: Non-significant. •: Independent t-test

Table (5): Relation between the changes in Doppler indices and development of RDS.

Changes of dopplar indices between Values befor and after dexamethasone		Negative RDS	RDS	Test value•	P-value	Sig.
UAPI	Mean±SD Range	-0.10 ± 0.17 -0.57 – 0.19	-0.10 ± 0.11 -0.54 – -0.01	-0.087	0.931	*NS
UARI	Mean±SD Range	-0.01 ± 0.04 -0.08 – 0.12	-0.02 ± 0.02 -0.05 – 0.03	1.190	0.239	*NS
UtAPI	Mean±SD Range	-0.06 ± 0.06 -0.22 – 0.03	-0.05 ± 0.07 -0.20 – 0.06	-0.166	0.868	*NS
UtARI	Mean±SD Range	-0.02 ± 0.02 -0.07 – 0.05	-0.02 ± 0.03 -0.05 – 0.06	-0.746	0.458	*NS
MCAPI	Mean±SD Range	-0.07 ± 0.12 -0.41 – 0.15	-0.17 ± 0.16 -0.51 – -0.02	2.679	0.010	**S
MCARI	Mean±SD Range	-0.03 ± 0.04 -0.15 – 0.03	-0.04 ± 0.04 -0.10 – 0.03	1.508	0.137	*NS

*NS: Non-significant. ** S: Significant.•: Independent t-test

Table (6): Relation betweenthe changes in Doppler indices and neonatal death.

Changes of dopplar indices between Values befor and after dexamethasone		Negative Survival	Survival	Test value•	P-value	Sig.
UAPI	Mean±SD Range	-0.15 ± 0.10 -0.21 – -0.04	-0.10 ± 0.15 -0.57 – 0.19	-0.598	0.552	*NS
UARI	Mean±SD Range	-0.03 ± 0.01 -0.03 – -0.02	-0.02 ± 0.04 -0.08 – 0.12	-0.548	0.586	*NS
UtA PI	Mean±SD Range	0.04 ± 0.03 0.01 – 0.06	-0.06 ± 0.06 -0.22 – 0.03	2.937	0.005	**HS
UtARI	Mean±SD Range	-0.01 ± 0.01 -0.02 – -0.01	-0.02 ± 0.02 -0.07 – 0.06	0.355	0.724	*NS
MCAPI	Mean±SD Range	-0.10 ± 0.09 -0.21 – -0.05	-0.11 ± 0.14 -0.51 – 0.15	0.091	0.928	*NS
MCARI	Mean±SD Range	-0.05 ± 0.05 -0.08 – 0.01	-0.03 ± 0.04 -0.15 – 0.03	-0.783	0.437	*NS

*NS: Non-significant. ** HS: Highly significant •: Independent t-test

4. Discussion:

About 75% of about a million deaths because of pretermbirth would survive if had adequate warmth, breastfeeding, treatments of infection, and breathing support (3). If the infant delivered with cardiac arrest at birth and is below 400 g or before 23 weeks, attempts at resuscitation are not indicated (4). Preterm delivery affects 5% to 18% of births worldwide (Roberts 2015). In Europe and many developed countries the preterm birth rate is generally 5–9%, and in the USA it has even risen to 12–13% in the last decades (5).

The current study showed statistically significant reduction in the Doppler indices of umbilical, MCA and uterine arteries (before and 24 hours after administration of dexamethasone) (table2&3).These results agreed with Wallace and Baker study who proveda relation between betamethasone therapy and reduction of the resistanceindex RI of umbilical artery (6), Also, these were similar to results of the study published by Nozaki et al. who stated a reduction in PI of umbilical artery within 24 h after prenatal administration of corticosteroid (7).Also, these results are in agreement with the results of Chitrit et al. who found a transient decrease in fetal MCA (PI, RI) after maternal administration of dexamethasone (8). Disagree with(Wijnberger et al., 2004)who stated that prenatal glucocorticoids do not affect fetal Doppler waveform patterns of the UA, and MCA in severely IUGR fetuses (9).

In this study, after maternal administration of dexamethasone the changes in MCA PI was significant in cases of neonatal RDS (P value 0.01), other indices showed no significant correlation with neonatal RDS (table 5). Also, the changes in uterine artery PI after maternal administration of dexamethasone is highly significant in cases of neonatal deaths (P value 0.005), other indices showedno significant correlation with neonatal deaths(table6). Disagree with Marie. 2000, who found that No significant changes were found in the pulsatility indices (PI) in maternal uterine artery, umbilical artery, and fetal MCA during the course and after maternal administration of steroids when compared to pretreatment results (10).

The study on human placentas by Clifton et al. 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 I2 and nitric oxide (11). Wijnberger et al. concluded that the underlying mechanisms responsible for the alterations in fetoplacental circulation after antenatal betamethasone administration are not clear (9).

Disagree with McLaughlin et al ., (2003) who found that infants exposed to corticosteroids more than 7 days before birth had no reduction in risk of respiratory distress syndrome but increased perinatal mortality(12).Use of dexamethasone in anticipated preterm labor in a low-resource setting has been discussed by Althabe and colleagues', and they report of an excess of 3.5 neonatal deaths per 1000 women exposed to prenatal corticosteroids (13).

In this study, after maternal administration of dexamethasone, there were no statistically significance relation with Doppler indices and NIC admission (table 4).

Conclusion:

Maternal administration of dexamethasone to pregnant women at risk of preterm birth can enhance the blood flow of the maternal uterine artery, fetal MCA, and umbilical artery. Also, changes in uterine artery PI is significant in neonatal deaths , and changes in MCA PI is significant in neonatal RDS.

Recommendation:

Women at risk of preterm labor should receive dexamethasone to improve the blood flow of uteroplacental circulation so reducing complication of prematurity. It is recommended to perform further large studies with a control group which may give more reliable statistical resultsto assess long term effects ofmaternal administration of dexamethasone at high risk pregnancy.

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