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THE SHORT-TERM EFFECT OF NIFEDIPINETOCOLYSIS ON PLACENTAL, FETAL CEREBRAL AND ATRIOVENTRICULAR DOPPLER WAVEFORMS

By

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ABSTRACT

Background: Preterm delivery is the leading cause of neonatal morbidity and is the most common reason for hospitalization during pregnancy. Nifedipine is characterized by lack of tachyphylaxis and by a reversible effect after discontinuation of the treatment. The vascular relaxation obtained with nifedipine in hypertensive women does not occur significantly in normotensive patients. This explains the absence of severe hypotension induced by high doses of calcium antagonists for tocolysis in normotensive patients.

Objective: To assess the acute effects of maternal nifedipine administration on placental and fetal cerebral blood flow resistance as well as on diastolic fetal cardiac function.

Patients and methods: This study was an observational prospective study, on 30 healthy pregnant women with singleton fetuses who admitted to labor ward with the diagnosis of preterm labor, gestational ages of 28-34 weeks, intact membranes and received nifedipine maintenance tocolysis for persistent uterine contractions under surveillance of maternal vital signs and Doppler examinations performed prior to nifedipine administration, 3 hours after the first dose and after 48 hours on umbilical artery, middle cerebral artery, mitral valve and tricuspid valve. The study was done at Bab El-Shaaria University Hospital during the time of the study between August 2019 and September 2020.

Results: In this study we found that, the P value for both systolic and diastolic blood pressure after 3 hours and after 48 hours was <0.001 which is statistically significant. Also the study found that, as regards the maternal heart rate, the P value was 0.065 which is statistically insignificant. As regards the fetal heart rate, P-value was 0.062 which is statistically insignificant. As regards Umbilical artery PI, P-value was 0.149 which is statistically insignificant. Regarding umbilical artery S/D, P-value was 0.284 which is statistically insignificant. As regards MCA PI, P-value was <0.001 which is statistically significant. Regarding MCA S/D, P-value was 0.562 which is statistically insignificant. Also results found that, the P-value for cerebroplacental ratio was <0.001 which is statistically significant. The mean E/A values, TVIs and TVI x FHR values after 3 hrs and after 48 hrs were unchanged from the baseline values.

Conclusion: Nifedipine maintenance tocolysis is associated with significant changes in maternal vital parameters, utero-placental blood-flow resistance and results in fetal redistribution. Fetal cardiac diastolic function is unaffected and the significant redistribution is likely to be attributable to altered cerebral blood flow.

Keywords: Nifedipinetocolysis, preterm labor, umbilical artery, middle cerebral artery, Atrioventricular Doppler waveforms.

INTRODUCTION

Preterm delivery remains one of the top three causes of perinatal morbidity worldwide. Various pharmacological agents have been used to stop preterm uterine contractions in an attempt to prevent preterm delivery *(AbdelRazeqet al., 2017)*. When using tocolytic agents the maternal and fetal side-effect profiles are important considerations. Following the most recent Cochrane database review the preferential use of calcium channel blockers over other tocolytic agents is likely to increase *(Baykal and Avcıoğlu, 2015)*.

Nifedipine, a dihydropyridine calcium entry blocker, is an effective tocolytic agent with low toxicity and teratogenicity, but has potential cardiovascular side effects that may affect the mother as well as the fetus *(Samy and Elshourbagy, 2017)*. Animal studies suggest that administration of calcium channel blockers may result in impaired uterine blood flow, potentially resulting in fetal hypoxemia and academia *(Ulubaşoğlu et al., 2015)*. However, studies in human pregnancies did not confirm significant alterations in uterine blood flow *(Blencowe., 2013)*. Fetal cardiovascular responses to nifedipine have not been reported in details. The cerebral circulation in the human fetus is capable of active auto regulation, and a decrease in blood flow resistance with perceived hypoxemia *(Mahaseth et al., 2017)*.

In addition, differential changes in the placental and cerebral blood flow resistances may affect the cerebroplacental Doppler ratio, and the overall distribution of cardiac output. In addition, cardiac effects of nifedipine may affect the contractility and diastolic cardiac function *(Namazov et al., 2018)*.

The data about preterm birth is becoming increasingly worrisome. This complication is responsible for approximately 75% of all neonatal deaths and 50% of childhood neurological morbidities. Apart from great progress in medical care, the rate of preterm labor seems to increase in most of Western countries *(Indarti et al., 2020)*.

Present treatment policy in spontanous preterm labor is concentrated on postponing delivery for at least 48 hours. Benefits are associated with completing a course of steroids in order to induce fetal lung maturation and/or ‘in utero‘ transfer to the referalcentre *(Purisch and Gyamfi-Bannerman, 2017)*.

The aim of this study was to assess the acute effects of maternal nifedipine administration on placental and fetal cerebral blood flow resistance as well as on diastolic fetal cardiac function.

PATIENTS AND METHODS

In this observational prospective study, we enrolled a total of thirty healthy pregnant women with singleton fetuses admitted to labor ward with the diagnosis of preterm labor, gestational ages of 28-34 weeks and intact membranes. The study was done at Bab El-Shaaria University Hospital during the time of the study between August 2019 and September 2020. The primary outcome was to assess the acute effects of maternal nifedipine administration on placental and fetal cerebral blood flow resistance as well as on diastolic fetal cardiac function.

Inclusion criteria:

- Patients admitted to labor ward with the diagnosis of preterm labor (latent phase).
- Gestational ages ranging from 28-34 weeks.
- Intact membranes.
- Patients who agreed to participate in the study with written consent.

Exclusion criteria:

- Patients in active labor.
- Multiple pregnancies.
- Chorioamnionitis.
- Congenital anomalies of the fetus.
- A clinical diagnosis of partial placental abruption.
- Severe fetal growth restriction.
- Vaginal bleeding.
- Acute fetal distress.
- Patients with circulatory system diseases (e.g. heart defects, hypertension).
- Patients with diabetes mellitus (pre- and gestational).
- Use of any tocolytic agents during pregnancy before admission.
- Any maternal contraindication for the use of nifedipine.

Thirty healthy pregnant women with singleton fetuses participated in the study. Preterm labor diagnosed when regular uterine contractions associated with cervical changes. Management protocol was under ongoing surveillance of maternal vital signs. After intravenous hydration therapy, nifedipine therapy administered in patients with persistent uterine contractions. An initial sublingual dose of 10 mg nifedipine capsule (Epilat), E.I.P.I.CO., 10th of RAMDAN City, repeated at 15-min intervals. The capsule was punctured and the liquid squeezed. If contractions persisted, up to a total maximum dose of 40 mg (loading therapy) given. The maintenance therapy consisted of 20 mg (Epilat Retard), E.I.P.I.CO., 10th of RAMDAN City, taken orally every 6 hours for a further 48 hours.

To study the effects of nifedipine administration, Doppler examinations performed prior to nifedipine administration, 3 hours after the first dose and after 48 hours. This time frame was chosen since the onset of action following an oral nifedipine dose is less than 20 minutes and peak plasma concentrations reached in 1 hour, with a half-life of 3 hours. A Voluson P8 ultrasound machine (GE, Medical Systems, Austria) with 3.5-MHzand 5-MHz convex probes was used. The same investigator performed all scans. The investigator performed all measurements during periods without uterine contractions with the mother lying in a left recumbent position. Doppler measurements obtained from the umbilical artery (UA) at the midsection of the umbilical cord *(Haas et al., 2012)*.

The distal middle cerebral artery (MCA) insonated through the temporal or occipital bone after its origin from the circle of Willis and identified on an axial section of the fetal brain. Color Doppler imaging used to optimize placement of the pulsed wave Doppler gate by adjusting the velocity scale to identify area, and direction of maximum blood flow. The

insonation angle was kept as close to 0◦ as possible, and the sample volume adjusted to cover the entire vessel. The pulsatile index (PI) and systolic diastolic (S/D) ratio were calculated as the mean value from five consecutive Doppler waveforms of the UA and MCA, obtained in the absence of fetal breathing and movement. The S/D ratio and PI were selected because they have different variance and measurement distributions, and may, therefore, affect differently by changes in the input pressure waveform *(Baykal and Avcıoğlu, 2015)*.

The resistance index was not used in the analysis because it only has a small measurement range (0–1) and may not show significant differences in Doppler measured blood flow resistance. In addition, the cerebro-placental Doppler ratio (MCA-PI/UA-PI) was calculated. The atrio-ventricular valves were examined from an apical, or basal four-chamber view of the heart. After placement of the sampling gate just distal to the mitral (MV) and (TV) valves, the time velocity integrals (TVI) for the respective valves was also measured. The fetal heart rate (FHR) was measured and multiplied with the TVI to provide an index of cardiac output. The flow velocity waveforms at the level of the mitral valve (MV) and tricuspid valve (TV) characterized by two diastolic peaks, corresponding to early ventricular filling (E-wave) and to active ventricular filling during atrial contraction (A-wave). E and A peak velocities were measured and the E/A ratio was calculated *(Granese et al., 2017)*.

Statistical Methods:

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for the Social Sciences) software version 18.0, IBM Corp., Chicago, USA, 2009. Descriptive statistics were done for quantitative data as mean±SD (standard deviation) for quantitative normally distributed data, median and 1st& 3rd inter-quartile range for quantitative non-normally distributed data, while it was done for qualitative data as number and percentage. The ANOVA test was used to compare differences in the measurements before and after nifedipine therapy according to their distribution. Post hoc analysis was done. Inferential analyses were done for quantitative variables using Shapiro-Wilk test for normality testing. The level of significance was taken at P value < 0.05.

RESULTS

The mean age of the whole study population was 28 years with a standard deviation of 4 years. Regarding gestational age and gestational age at delivery, the means were 31 and 34 weeks, respectively. The most frequent gravidity and Parity were three (50.0%) and two (43.3%), respectively. Most females underwent normal delivery (53.3%). Maternal side effects related to nifedipine therapy were as follows: flushing in 12 patients, headache in 5patients and nausea in 2 patients. None of the patients had tachycardia. None of the patients delivered within 72 hours, only 3 patients delivered within 2 weeks. (Commonly reported maternal side effects of nifedipine are tachycardia, palpitations, flushing, headaches, dizziness and nausea).

The mean birth weight was 2573 grams. Regarding APGAR scores at one and five minutes, they were 6 & 9, respectively. 20.0% of neonates needed NICU admission **(Table 1)**.

Table (1): Maternal and fetal characteristics in the study population

Maternal characteristics		**Mean ±SD**
Age (years)		28 ±4
Gestational age (weeks)		31 ±2
Gestational age at delivery (weeks)		34 ±2
		n (%)
Parity	P0	3 (10.0)
	P1	10 (33.3)
	P2	13 (43.3)
	P3	4 (13.3)
Mode of delivery	Cesarean	14 (46.7)
	Normal	16 (53.3)
Fetal characteristics		
Birth weight (g)	Mean ±SD	2573 ±542
APGAR 1m	Median (range)	6 (8 - 4)
APGAR 5m	Median (range)	9 (10 - 6)
NICU admission	n (%)	6 (20.0)

Systolic blood pressure showed an overall significant difference between follow-up points, the P-value was <0.001. Post hoc analysis showed that it was significantly higher pre (123 mmHg) than after 3 hours (117 mmHg) and 48 hours (92mmHg). Also, it was significantly higher after 3 hours than after 48 hours. Diastolic blood pressure showed an overall significant difference between follow-up points, the P-value was <0.001. Post hoc analysis showed that it was significantly higher pre (81 mmHg) than after 3 hours (76 mmHg) and 48 hours (59 mmHg). Also, it was significantly higher after 3 hours than after 48 hours. There was no significant difference was reported regarding maternal heart rate pre, after 3 hours, and after 48 hours. P-value was 0.065. Fetal heart rate showed insignificant difference between follow up points, P-value was 0.062. Umbilical artery PI showed insignificant difference between follow-up points; the P-value was 0.149. There was no significant difference detected regarding umbilical artery S/D pre, after 3 hours and after 48 hours. P-value was 0.284. MCA PI showed an

overall significant difference between follow-up points, the P-value was <0.001. Post hoc analysis showed that it was significantly higher pre (1.92) than after 3 hours (1.9) and 48 hours (1.77). Also, it was significantly higher after 3 hours than after 48 hours. There was no significant difference found regarding MCA S/D pre, after 3 hours, and after 48 hours. P-value was 0.562 **(Table 2)**.

Table (2): Systolic blood pressure, diastolic blood pressure, maternal heart rate, fetal heart rate, umbilical artery PI, umbilical artery S/D, MCA PI, MCA S/D, cerebroplacental ratio, at baseline, 3 hours and 48 hours

		Mean ±SD	P-value
Systolic blood pressure	**Pre**	123 ±7	<0.001
	After 3 hours	117 ±6	
	After 48 hours	92 ±7	
Diastolic blood pressure	**Pre**	81 ±4	<0.001
	After 3 hours	76 ±6	
	After 48hour	59 ±6	
Maternal heart Rate	**Pre**	88.1±5.2	0.065
	After 3 hours	90.5 ±3.4	
	After 48hour	89.6 ±2.7	
Fetal heart rate	**Pre**	147.5±6.1	0.062
	After 3 hours	142.3±9.4	
	After 48hour	139.9 ±9.1	
Umbilical artery PI	**Pre**	0.98 ±0.14	0.149
	After 3 hours	0.90 ±0.19	
	After 48hour	0.95 ±0.17	
Umbilical artery S/D	**Pre**	2.19 ±0.35	0.284
	After 3 hours	2.21 ±0.34	
	After 48hour	2.2 ±0.33	
MCA PI	**Pre**	1.92 ±0.25	<0.001
	After 3 hours	1.9 ±0.25	
	After 48hour	1.77 ±0.24	
MCA S/D	**Pre**	4.01 ±0.14	0.562
	After 3 hours	4.01 ±0.14	
	After 48hour	4 ±0.14	
Cerebroplacental ratio	**Pre**	1.86 ±0.37	<0.001
	After 3 hours	1.84 ±0.37	
	After 48 hours	1.68 ±0.34	

Repeated measures ANOVA were used. Post hoc analysis was done.

The cerebroplacental ratio showed an overall significant difference between follow-up points, the P-value was <0.001. Post hoc analysis showed that it was significantly higher pre (1.86) than after 3 hours (1.84) and 48 hours (1.68). Also, it was significantly higher after 3 hours than after 48 hours. MV TVI showed insignificant difference between follow-up points; the P-value was 0.521. MV TVI x FHR showed insignificant difference between follow-up points; the P-value was 0.231. There was no significant difference reported regarding E/A TVI of MV pre, after 3 hours, and after 48 hours. P-value was 0.479. TV TVI showed insignificant difference between follow-up points; the P-value was 0.532. TV TVI x FHR

showed insignificant difference between follow-up points; the P-value was 0.245. There was no significant difference reported regarding E/A TVI of TV pre, after 3 hours, and after 48 hours. P-value was 0.271 **(Table 3)**.

Table (3): MV TVI,MV TVI x FHR,E/A TVI of MV, TV TVI, TV TVI x FHR and E/A TVI of TV, at baseline, 3 hours and 48 hours

		Mean ±SD	P-value
MV TVI	**Pre**	0.11 ±0.01	0.521
	After 3 hours	0.1 ±0.01	
	After 48 hours	0.09 ±0.02	
MV TVI x FHR	**Pre**	14.3 ±1.3	0.231
	After 3 hours	15.6 ±1.6	
	After 48 hour	14.9 ±1.5	
E/A TVI of MV	**Pre**	0.84 ±0.14	0.479
	After 3 hours	0.84 ±0.12	
	After 48 hours	0.82±0.13	
TV TVI	**Pre**	0.11 ±0.01	0.532
	After 3 hours	0.1 ±0.01	
	After 48 hours	0.09 ±0.02	
TV TVI x FHR	**Pre**	14.4 ±1.5	0.245
	After 3 hours	13.5 ±1.5	
	After 48 hours	14.7 ±1.2	
E/A TVI of TV	**Pre**	0.85 ±0.06	0.271
	After 3 hours	0.85 ±0.08	
	After 48 hours	0.84 ±0.07	

DISCUSSION

Our study has shown that nifedipine maintenance tocolysis was associated with a significant decline in middle cerebral artery Doppler indices. Fetal diastolic function was unaffected and the significant redistribution observed was attributable primarily to altered cerebral blood flow. Doppler parameters in the placental, fetal middle cerebral arteries and across the fetal atrio-ventricular valves were equally unaffected by nifedipine loading. These findings suggested that nifedipine loading did not trigger fetal brain sparing, and did not affect fetal cardiac function or downstream distribution of cardiac output. In clinical practice, nifedipine loading was typically followed by maintenance tocolysis for at least 48 hours. However, there was scant information regarding the effects of nifedipine therapy in the first 48 hours on umbilical, fetal middle cerebral, and fetal cardiac blood-flow indices *(Grin et al., 2018)*.

In this observational prospective study, we enrolled a total of thirty healthy pregnant women with singleton fetuses admitted to labor ward with the diagnosis of preterm labor, gestational ages of 28-34 weeks and intact membranes. After intravenous hydration therapy, nifedipine therapy administered in patients with persistent uterine contractions with initial sublingual dose of 10 mg nifedipine, repeated at 15-min intervals under ongoing surveillance of maternal vital signs. If contractions persist, up to a total

maximum dose of 40 mg (loading therapy). The maintenance therapy of 20 mg taken orally every 6 h for further 48 h. Doppler examinations performed prior to nifedipine administration, 3 hours after the first dose and after 48 hours on umbilical artery, middle cerebral artery, mitral valve and tricuspid valve *(Nicolaides et al., 2018).*

In this study, analysis of data revealed that nifedipine maintenance and tocolysis was associated with a significant decline in maternal systolic and diastolic blood pressure. However, it had insignificant change on both MHR and FHR either after 3 hours or after 48 hours compared with before nifedipine. Also, UA PI did not change significantly. MCA PI decreased significantly after 3 hours and again after 48 hours. A significant fall in the cerebroplacental Doppler ratio was noticed after 3 hours and again after 48 hours. The mean E/A values, TVIs, and TVI x FHR values for both MV and TV remained unaltered during nifedipine therapy. In this study, results found that both systolic and diastolic blood pressure after 3 hours and after 48 hours was statistically significant (it was significantly higher pre than after 3 hours and after 48 hours). Also, it was significantly higher after 3 hours than after 48 hours for both systole and diastole. Also, the study found that, maternal heart rate was statistically insignificant (no significant difference was detected between MHR before nifedipine, after 3 hours and after 48 hours).

The fetal heart rate was statistically insignificant (no significant difference was detected between FHR before nifedipine, after 3 hours and after 48 hours). Umbilical artery PI was statistically insignificant (no significant difference was detected between UA PI pre, after 3 hours and after 48 hours). Umbilical artery S/D was statistically insignificant. MCA PI was statistically significant (it was significantly higher pre than after 3 hours and after 48 hours). Also, it was significantly higher after 3 hours than after 48 hours. MCA S/D was statistically insignificant. Also, results found that cerebroplacental ratio was statistically significant (it was significantly higher pre than after 3 hours and after 48 hours. Also, it was significantly higher after 3 hours than after 48 hours). TVI for both MV and TV were statistically insignificant. Also, results found that TVI x FHR for MV and TV were statistically insignificant. E/A TVI of MV and TV were statistically insignificant *(Baykal and Avcıoğlu, 2015)*.

The effect of nifedipine therapy on various placental and fetal Doppler waveforms has been previously analyzed. Comparative Doppler studies of patients receiving nifedipine and sympathomimetics indicate that fetal cardio-vascular changes are more apparent in the latter. These studies found no differences in UA waveforms between patients receiving ritodrine and nifedipine *(Grin et al., 2018).* However, other investigators have shown that ritodrine augments fetal aortic blood flow and left-sided cardiac output. Increase in blood pressure, associated redistribution and augmentation of cerebral blood flow have been put forward as possible explanations for the higher rate of intracranial hemorrhage observed in preterm neonates receiving ritodrine *(Suhag et al., 2015).*

Several investigators found a transient significant decline in the umbilical artery PI after 15 min with a return to baseline levels at 90 min *(Luewan et al., 2011)*. Another study reported the effect of nifedipine on the fetal aorta, internal carotid artery, umbilical artery, and uteroplacental blood flow in patients with pre-eclampsia, and did not find any difference in the indices assessed. Other studies that used Doppler at a later point (2.5–5 hours after nifedipine administration) failed to show any significant change in the umbilical artery Doppler waveform *(Wagner et al., 2017)*.

In contrast to the study, *Wagner et al. (2017)* evaluated the cerebral, renal and central arterial circulations. Our results indicate that cerebral blood-flow dynamics were altered by nifedipine. This difference could be due to different measurement times in their study, because those authors examined fetal Doppler indices in the first 8 h following commencement of nifedipine therapy. With respect to maternal heart rates, *Luewan et al. (2011)* reported a transient increase in maternal heart rate that had normalized by 45 min.

Cornette et al. (2011) administered a maximum loading dose of 40 mg nifedipine in the first hour. The required maintenance dose was depended on the loading dose and did not exceed the level of 120 mg daily. The total daily dose was 100 mg (apart of 2 patients with 120 mg). As there is no clear nifedipine medication protocol in tocolytic treatment, maximum daily dose of 100 mg is recommended *(RCOG, 2011)*. However, there is evidence that total dose above 60 mg is probably responsible for three- to four-fold increase in adverse events such as hypotension *(ISUOG, 2013)*. The fetal Doppler examination performed by *Nicolaides et al. (2018)* showed the alteration of MCA blood flow between 5 and 24 hours from the time of administered medication. Authors suggested that decreased resistance ratio could be related to decrease peak systolic velocity in MCA. *Hammami et al. (2018)* reported the significant decrease in MCA PI after 24 hours of tocolysis. Furthermore, a significant drop was observed after 48 hours of treatment. *Nicolaides et al. (2018)* presented similar medication protocol. They started with a maximum first hour dose of 60 mg nifedipine. This finding may directly influence the circulatory system and result in blood flow changes in different compartments. As potential impact of nifedipine on cardiac function was an important issue, several hemodynamic parameters were evaluated *(Tay et al., 2019)*.

CONCLUSION

Nifedipine maintenance tocolysis was associated with significant changes in maternal vital parameters (significant decline in both systolic and diastolic blood pressure after 3 hours and again after 48 hours), utero-placental blood-flow resistance and results in fetal redistribution (significant decline in both MCA PI and CPR after 3 hours and again after 48 hours). The maternal blood pressure decreased, while the maternal heart rate remained unaltered. A trend towards increasing umbilical artery blood-flow resistance coupled with a significant decline in fetal middle cerebral artery pulsatility results in redistribution in the

fetus that is not associated with any change in cardiac diastolic function of the fetal heart.

Fetal cardiac diastolic function was unaffected, and the significant redistribution observed was likely to be attributable to altered cerebral blood flow.

REFERENCES

1. **Abdel Razeq N, Khader Y and Batieha A. (2017):** The incidence, risk factors, and mortality of preterm neonates: A prospective study from Jordan (2012-2013). Turk J Obs Gynecol., 14(1):28–36.
2. **Baykal BÖ and Avcıoğlu SN. (2015):** Comparison of effects of nifedipine and ritodrine on maternal and fetal blood flow patterns in preterm labor. J Turkish GerGynecol Assoc., 16(2):80–5.
3. **Blencowe H, Cousens S, Chou D, Oestergaard M, Say L and Moller AB. (2013):** Born Too Soon: The global epidemiology of 15 million preterm births. Reprod Health, 10(1):2-8.
4. **Cornette J, Duvekot JJ, Roos-Hesselink JW, Hop WC and Steegers EA. (2011):** Maternal and fetal haemodynamic effects of nifedipine in normotensive pregnant women. BJOG, 118(4):510–540.
5. **Granese R, Mantegna S and Mondello S. (2017):** Preterm birth: incidence, risk factors and second trimester cervical length in a single center population. A two-year retrospective study.Eur Rev Med Pharmacol Sci., 21:4270–7.
6. **Grin L, Laish-Farkash A, Shenhav S, Piltz X, Ganelin L and Rabinovich M. (2018):** Safety of nifedipine in threatened preterm labor: Investigation by three-dimensional echocardiography. Echocardiography, 35 (8): 1164-70.
7. **Haas DM, Caldwell DM and Kirkpatrick P. (2012):** Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. BMJ (Clinical Research Ed), 345:6226-33.
8. **Hammami A, Mazer Zumaeta A, Syngelaki A, Akolekar R and Nicolaides KH. (2018):** Ultrasonographic estimation of fetal weight: development of new model and assessment of performance of previous models. Ultrasound Obstet Gynecol., 52:35–43.
9. **Indarti J, Nanda A, Fattah A, Dewi Z and Dediat R. (2020):** Teenage Pregnancy: Obstetric and Perinatal Outcome in a Tertiary Centre in Indonesia. Obstet Gynecol Int., 20: 15-21.
10. **International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) Practice Guidelines (2013):** Use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol., 41:233–9.
11. **Luewan S, Mahathep R and Tongsong T. (2011):** Hypotension in normotensive pregnant women treated with nifedipine as a tocolytic drug. Arch Gynecol Obstet., 284(3):527–530.
12. **Mahaseth B, Srivastav M, Das C and Malla T. (2017):** Preterm Delivery Associated Risk Factor and Its Incidence. IOSR J Dent Med Sci., 17(01):51–5.
13. **Namazov A, Grin L and Karakus R. (2018):** An effect of maternal nifedipine therapy on fetoplacental blood flow: a prospective study. Arch Gynecol Obstet., 298 (4): 685-688.
14. **Nicolaides KH, Wright D, Syngelaki A, Wright A and Akolekar R. (2018):** Fetal Medicine Foundation fetal and neonatal population weight charts.Ultrasound Obstet Gynecol., 52: 44–51.
15. **Purisch SE and Gyamfi-Bannerman C. (2017):** Epidemiology ofpreterm birth. Vol. 41, Seminars in Perinatology. Pbl. W.B. Saunders, Pp. 387–91.
16. **Royal College of Obstetricians and Gynecologists (RCOG) (2011):**Tocolysis for Women in Preterm Labor. Green Top Guideline, 1:1–13.
17. **Samy S and Elshourbagy S. (2017):** Assessment of Maternal Nifedipine as a Tocolytic Agent on the Doppler Indices of Uterine and Fetal Umbilical and Middle

Cerebral Arteries. GynecolObs Res Open J., 4(2):44–9.

18. **Suhag A, Saccone G and Berghella V. (2015):** Vaginal progesterone for maintenance tocolysis: a systematic review and metaanalysis of randomized trials. Am J Obstet Gynecol., 213:479–487.
19. **Tay J, Masini G andMcEniery CM. (2019):** Uterine and fetal placental Doppler indices are associated with maternal cardiovascular function. Am J Obstet Gynecol., 220: 1–8.
20. **Ulubaşoğlu H, Özmen Bayar Ü, Kaya C andUngan B. (2015):** The effect of nifedipinetocolysis on Doppler indices of the uterine and umbilical Arteries. J Clin Ultrasound, 43(5):322–6.
21. **Wagner P, Sonek J, Abele H, Sarah L, Hoopmann M and Brucker S. (2017):** Effectiveness of the contemporary treatment of preterm labor: a comparison with a historical cohort. Arch Gynecol Obstet., 296(1):27–34.

التأثير قصير المدي لعقار النيفيديبين علي الدوبلر في الشريان السري والمخ الأوسط والأذينية البطينية

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خلفية البحث: الولادة المبكرة تظل واحدة من أهم ثلاثة مشكلات مرضية في الفترة المحيطة بالولادة في جميع أنحاء العالم. تم استخدام بعض الأدوية لوقف انقباضات الرحم المبكرة في محاولة لمنع الولادة المبكرة. نيفيديبين، وهو دواء مانع دخول الكالسيوم إلي مستقبلاته ويتكون من داي هيدروبيريدين، ويعتبر عامل فعال لتهدئة الطلق ويتميز بانخفاض معدل التسمم والتشوهات الجنينية، ولكنه له آثاراً جانبية علي القلب والأوعية الدموية والتي قد تؤثر على الأم وكذلك الجنين.

الهدف من البحث: تقييم الآثار الحادة الناتجة من إستخدام الأم لدواء النيفيديبين على مقاومة سريان الدم بالمشيمة ومخ الجنين وكذلك على وظيفة القلب الإنبساطية للجنين.

المريضات وطرق البحث: كانت هذه الدراسة عبارة عن دراسة استطلاعية على 30 امرأة حامل بجنين واحد فقط، وتم تشخيص الولادة المبكرة عندما إرتبطت إنقباضات الرحم المنتظمة مع حدوث تغيرات في عنق الرحم. وتعتمد خطة العلاج علي العلامات الحيوية للأم في مثل هذه الحالات والتي كانت كالآتي: نيفيديبين كبسولة 10 ملغ تحت اللسان في حالة إستمرار إنقباضات الرحم حتي بعد إعطاء محاليل. وإذا إستمرت انقباضات الرحم بعد 15 دقيقة، تم إعطاء جرعة ثانية من نيفيديبين 10 ملغ. وكررت هذه الجرعة مرتين أخرتين إذا لزم الأمر، مع الاعتبار أن أقصي جرعة من النيفيديبين يمكن أن تعطي للمريضة في الساعة الأولى هي 40 ملغ. وتتراوح الجرعات التكميلية للنيفيديبين بطئ المفعول مابين 60-160 ملغ يومياً، وكان يعطى قرص 20 مجم كل 6 ساعات لمدة 48 ساعة. وقد تم خفض جرعات النيفيديبين تدريجيا علي مدار 3 أيام عند تحسن الحالة. قد أجريت

الدراسة بمستشفى باب الشعرية الجامعي خلال الفترة من أغسطس 2019 إلى سبتمبر 2020.

نتائج البحث: وجدنا في هذه الدراسة أن القيمة الاحصائية لكل من ضغط الدم الانقباضي والانبساطي بعد 3 ساعات وبعد 48 ساعة كانت <0.001. كما وجدت الدراسة أنه فيما يتعلق بمعدل ضربات قلب الأم فقد كانت القيمة 0.065. وفيما يتعلق بمعدل ضربات قلب الجنين، فان القيمة كانت 0.062، وفيما يتعلق بمعامل النبض PI الخاص بالشريان السري، كانت 0.149. أما مع معدل الانقباضي والانبساطي (S/D) الخاص بالشريان السري، فان القيمة كانت 0.284.

وقد كانت القيمة الخاصة بمعامل النبض PI الخاص بالشريان المخي الأوسط للجنين <0.001. وفيما يتعلق بمعدل الانقباضي والانبساطي (S/D) الخاص بالشريان المخي الأوسط للجنين، فان قيمة P كانت 0.562. كما وجدت النتائج أن الشريان المخي الأوسط للجنين/ الشريان السري كانت <0.001.

الاستنتاج: دواء النيفيديبين المستخدم في تهدئة الطلق مرتبط بفروق ذات دلالة احصائية في العلامات الحيوية للأم (انخفاض كبير ذو دلالة احصائية في ضغط الدم الانقباضي والانبساطي)، ومقاومة تدفق الدم من الرحم إلى المشيمة ويؤدي إلى إعادة توزيع الدم بالجنين (انخفاض كبير ذو دلالة احصائية في كلا من PI&CPR). MCA ينخفض ضغط دم الأم بينما يظل معدل ضربات قلب الأم دون تغيير.

الكلمات الدالة: نيفيديبين للمخاض على المشيمة، دماغ الجنين، الدوبلر في الشريان السري والمخ الأوسط والأذينية البطينية.