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# EFFECT OF MAGNESIUM SULFATE ON DOPPLER INDICES OF UTERINE, UMBILICAL AND FETAL MIDDLE CEREBRAL ARTERIES IN WOMEN WITH THREATENED PRETERM LABOUR

By

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## ABSTRACT

**Background:** Preterm labor is one of the commonest clinical events where traditional pregnancy can turn into a high risk situation for the mother as well as the fetus. Magnesium sulfate ($MgSO_4$), which is a calcium antagonist, has been used for over 30 years as short-term treatment (less than 48 h) for acute preterm labor. It acts by inhibiting voltage independent calcium channels in the myometrial cell surface. Extracellular magnesium suppresses calcium influx across cell membranes, whereas intracellular magnesium competes with calcium, there by inhibiting myosin light-chain kinase activity.

**Objective:** To assess the effect of $Mgso_4$ as a tocolytic agent on Doppler parameters of fetal middle cerebral, umbilical and uterine arteries in women with threatened preterm labor.

**Patients and methods:** A prospective observational study was conducted in Al Shohadaa Central Hospital in the period between September 2018 and September 2020. A total of 300 women with threatened preterm labor were included in the study. The study group underwent a Doppler ultrasound study to evaluate the flow velocity parameters resistibility index (RI), pulsatility index (PI) and systolic/ diastolic ratio (S/D) of fetal middle cerebral artery (MCA), umbilical artery (UA) and uterine artery (UtA) using the abdominal probe of the ultrasound device. Then immediately they were given an intravenous infusion of 4- 6 gm of magnesium sulphate as a loading dose then 1 gm / hour as $Mgso_4$ maintenance dose. The same Doppler Ultrasound parameters were recorded again after 24 hours $Mgso_4$ tocolysis to evaluate the effect of magnesium sulphate administration.

**Results:** There was a no statistically significant reduction in RI, PI, SD ratio of the UA before 32 weeks gestation while a statistically significant reduction in these parameters after 32 weeks gestation following magnesium sulphate infusion. Regarding MCA Doppler parameters in our study, there was a statistically significant reduction in RI, PI, SD ratio after magnesium sulphate infusion. Regarding UtA Doppler parameters in our study, there was no statistically significant differences were found in uterine artery RI and S/D ratio following magnesium sulphate infusion, whereas uterine artery PI showed statistically significant reduction after magnesium sulphate infusion.

**Conclusion:** Although the use of $Mgso_4$ as a tocolytic agent is controversial but it is valuable as neuroprotective agent and for treatment of eclamptic seizures. Its effect on the fetal blood flow has a very beneficial role till now. In this study it was found that it has significant effect on fetal MCA, UA and UtA Doppler parameters (RI, PI and S/D ratio). More studies with larger cohorts are needed to support these results.

**Keywords:** Magnesium Sulfate, Doppler Indices of Uterine, Umbilical and Fetal Middle Cerebral Arteries, Threatened Preterm Labour.

## INTRODUCTION

Preterm labor is one of the biggest challenges for obstetricians and so are the preterm babies for the neonatologists. Preterm delivery is defined as labor beginning before completed 37 weeks of gestation. The incidence of preterm labor is reported by the WHO to be 5-11% *(Dodd et al., 2013)*. Preterm delivery is an international health problem and is responsible for approximately two-thirds of early neonatal morbidity and mortality *(Beck et al., 2010)*.

Clinicians use tocolytics for pregnancy prolongation for 48-hours to permit the administration of corticosteroids to enhance fetal lung maturity and reduce neonatal morbidity and mortality. There is considerable variation in the type of tocolytic agent used in different parts of the world. Magnesium sulphate has been widely used as a tocolytic in the United States of America *(Flenady et al., 2014)*.

Magnesium sulphate can be used as atocolytic and also in the management of pre- eclampsia, eclampsia and neuroprotective for neonates. The exact mechanism of magnesium sulphate as a tocolytic agent is partially understood. It acts by decreasing the frequency of depolarisation of smooth muscle, by modulating calcium uptake, binding and distribution in smooth muscle cells to inhibit uterine contractions *(Crowther et al., 2014)*.

The precise mechanism by which magnesium sulfate exerts a neuroprotective benefit is not known, but it is speculated that it possess anti-inflammatory and anti-excitotoxic effects while also improving cerebral blood flow and stabilizing fluctuations in blood pressure in the newborn infant *(Berger et al., 2016)*.

To assess the fetal circulation Doppler sonography is used to provide valuable information regarding neonatal prognosis and fetal well-being in compromised pregnancies. Doppler sonography has also been used for evaluation of effect various drugs on Doppler blood waveforms *(Sayin et al., 2010)*.

In pregnancy, umbilical artery (UA), uterine artery (UtA) and fetal middle cerebral artery (MCA) Doppler parameters can be assessed carefully improving detection of disturbances in fetus wellbeing *(Figueira et al., 2016)*. The ratio of middle cerebral artery to umbilical artery (MCA/U) can be used as a good indicator of fetal prognosis and fetal well-being *(Tarzamni et al., 2012)*. Assessment of the changes in the arteries with Doppler ultrasound can show the adaptation of the fetal haemodynamics *(Mihu et al., 2011)*.

Investigating the mechanism of action of $Mgso_4$ on the fetus is an important issue. Studies are needed to evaluate the effect of $Mgso_4$ on Doppler parameters of uterine, fetal middle cerebral and umbilical arteries in patients with threatened preterm labour *(Ebrashy et al., 2010)*.

**The aim of the study was to** assess the effect of $Mgso_4$ as a tocolytic agent on Doppler parameters of Fetal Middle Cerebral, umbilical and uterine Arteries in Women with threatened preterm labour.

## PATIENTS AND METHODS

A prospective observational study was conducted in Al Shohadaa Central Hospital in the period between September 2018 and September 2020. A total of 300 women with threatened preterm labor were included in the study.

**Inclusion Criteria:** age between 25 to 35 years, gestational age between 28-34 weeks, and threatened preterm labour: Frequent uterine contractions 2 or more/10 minutes, and without cervical changes.

**Exclusion criteria:** Gestational ages < 28 weeks or > 34 weeks, twin or higher order pregnancy, fetal congenital anomalies, intrauterine growth restriction, cervical dilatation of more than 4 cm or effacement more than 80%, maternal complications as preeclampsia, eclampsia, abruptioplacenta, placenta previa, chorioamnionitis, diabetes mellitus, maternal heart disease, women with a previous preterm labor episode in the current pregnancy or delivered before 48 h after initiating therapy, patients sensitive to magnesium sulphate, patients receiving any other tocolytic agent, and patients with medical disorders in which magnesium sulphate is contraindicated.

**Sample Size Justification:**

The required sample size has been calculated using the G*Power Software (Universität Düsseldorf, Germany).

The primary outcome measure is the difference between the MCA, UA and UtA Doppler indices (RI, PI and S/D ratio) before and after treatment with $MgSO_4$.

Currently, there is no adequate information regarding the effect of $MgSO_4$ on the outcome measures; therefore, the present exploratory study would target an effect size that would be clinically relevant.

So, it is estimated that a sample size of 300 patients would achieve a power of 80% (type II error, 0.2) to detect a statistically significant difference between the pre-treatment and post-treatment Doppler indices for an effect size corresponding to a Cohen dz coefficient of 0.2 using a two-sided paired t test with the test confidence set at a level of 95% (type I error, 0.05). The effect size (dz) is calculated as follows *(Chow et al., 2010)*:

$$dz = \frac{\text{mean of the differences between the Doppler index before}}{\text{standard deviation of the differences}}$$

The targeted effect sizes of dz = 0.2 has been selected as it could be regarded as the smallest effect size that may be clinically relevant to seek in this exploratory study.

According to Sayin et al. (2010) Mgso4 decreases MCA PI by 0.14 and this makes the effect size 0.14 with a SD of 0.26 before Mgso4 and using the equation by Chow et al. (2010) sample size to be 302 and will be rounded to 300 female patients.

**All patients were subjected to the following:**

1. **History:**

- **Personal history:** Name, Age, Occupation, Residence, special habits of medical importance.
- **Obstetric history:** Gravidity, Parity, Mode of previous delivery, First day

of last menstrual period and menstrual regularity.

- **Past history:** History of any medical disorder or surgical history.
- **History of the present pregnancy:** Medical or surgical condition to define high risk pregnancy.

**2. Examination:**

- **General examination:** for vital signs (blood pressure, pulse and temperature).
- **Local examination.**
- **Abdominal examination:** for assessment of uterine contractions.
- **Vaginal examination:** for detection of cervical changes.
- **Laboratory testing:** Complete blood picture, liver function tests, renal function tests and urine dipstick test for exclusion of hypertensive disorders with pregnancy.
- **Ultrasonographic scanning:**

Was done trans-abdominally using Philips clearvue 350 machine equipped with a 5 MHZ convex probe to evaluate the following:

- Fetal biometry: Biparietal diameter (BPD), abdominal circumference (AC), Femur length (FL), Gestational age (GA).
- Fetal weight.
- Doppler studies of the following arteries: Umbilical artery (UA) Middle cerebral artery (MCA) Uterine artey. Doppler indices were calculated by the built-in software programs in the machine.
- Systolic/diastolic ratio (S/D) The systolic /diastolic ratio is the simplest of all indices and is expressed by S/D, where S is the peak systolic frequency and D is the end diastolic frequency.
- Resistance index (RI): this index, also known as pourcelot`s ratio examines the difference between the peak systolic and end diastolic velocity and is expressed by:

$$RI = (S\_D)/S$$

**Pulsatility index (PI):** This index was expressed by:

$$PI = (S\_D) / Velocity\ mean$$

**Where:**

S: is the peak systolic velocity.

D: is the minimum or end distolic velocity.

Mean: is not mathematical mean, but the mean velocity throughout the cardiac cycle.

**Magnesium sulphate tocolysis:**

The use of magnesium sulfate usually requires baseline maternal laboratory evaluation, including CBC count and serum creatinine level, normal vital signs, and appropriate maternal mentation. The initial recommended loading dose is 4-6 g IV over 20 minutes, followed by a maintenance dose of 1-2 g/h depending on persistence of uterine contractions for 24 hours. After 24 hours of magnesium sulphate tocolysis, Doppler parameters (RI, PI and S/D ratio) of fetal MCA, UA and UtA were repeated again.

**Protocol approval:**

According to the local regulation followed and before the beginning of the study, the protocol and all the corresponding documents were declared for Ethical and Research approval by the council of Obstetrics and Gynecology Department - Alazhar University.

**Data management and Analysis**

Data were collected, tabulated, then analyzed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY). Normally distributed numerical data were presented as mean and SD, and skewed data as median and interquartile range. Qualitative data were presented as number and percentage. Comparison of normally distributed paired numerical data was done using the paired t test. Paired skewed data were compared using the Wilcoxon signed ranks test. Paired categorical data were compared using the McNemar test. A two-sided p-value <0.05 were considered statistically significant.

## RESULTS

These include age, BMI, parity, gestational age and estimated fetal weight **(Table 1)**.

**Table (1): Descriptive statistics for the study population as regards their basic demographic data**

| | **Value** |
|---|---|
| **Age (Yrs)** | |
| Range | 25.0 – 34.0 |
| Mean±SD | 29.2 ± 3.31 |
| **BMI (Kg/m$^2$)** | |
| Range | 18.9 – 35.27 |
| Mean±SD | 25.76 ± 4.01 |
| **Parity** | |
| Range | 0 – 3 |
| Median (IQR) | 1 (0 – 2) |
| **Gestational Age (wks)** | |
| Range | $28^{+0}$ – $33^{+6}$ |
| Median (IQR) | $31^{+4}$ ($30^{+4}$ – $32^{+5}$) |
| **EFW (gm)** | |
| Range | 1022.0 – 2314.0 |
| Mean±SD | 1683.0 ± 295.6 |

**Effect of magnesium sulphate infusion on umbilical artery Doppler indices:**

Umbilical artery RI was statistically significantly lower after magnesium sulphate infusion with a mean drop of 0.07±0.10 (95% CI: -0.08 – -0.06). The same finding was also noted umbilical artery PI and S/D ratio with a statistically significant reduction in PI averaging 0.16±0.13 (95% CI: -0.17 – -0.14) and a statistically significant reduction in S/D ratio with a mean of 0.34±0.44 (95% CI: -0.40 – -0.29) **(Table 2)**.

Multivariable regression analysis **(Table 3)** revealed a statistically significant contribution for the variation in gestational age and estimated fetal weight on the variation in paired difference of the three Doppler indices before and after magnesium sulphate infusion. This was evident in the scatter plot analysis for the trend of distribution of paired difference

in the three Doppler indices before and after magnesium sulphate infusion against gestational age; where the paired difference in Doppler indices tended to be evident in the larger gestational ages compared to the smaller ones.

There was no statistically significant change in the umbilical artery Doppler indices before 32 weeks of gestational age; whereas a statistically significant change was found following magnesium sulphate infusion after 32 weeks of gestational age. Subgroup analysis of our results before and after 32 weeks gestational age **(Table 4)**.

**Table (2): Comparison between umbilical artery Doppler indices before and after magnesium sulphate infusion**

| | **Before Magnesium Sulphate** | **After Magnesium Sulphate** | **Mean Paired Difference (95% CI)** | **P †** |
|---|---|---|---|---|
| **Umbilical artery RI** | | | | |
| Range | 0.53 – 0.89 | 0.50 – 0.76 | -0.07 ± 0.10 | **<0.001** |
| Mean ± SD | 0.67 ± 0.07 | 0.59 ± 0.06 | (-0.08 – -0.06) | |
| **Umbilical artery PI** | | | | |
| Range | 0.68 – 1.25 | 0.59 – 1.23 | -0.16 ± 0.13 | **<0.001** |
| Mean ± SD | 0.95 ± 0.11 | 0.79 ± 0.15 | (-0.17 – -0.14) | |
| **Umbilical artery S/D ratio** | | | | |
| Range | 2.02 – 5.03 | 1.63 – 3.91 | -0.34 ± 0.44 | **<0.001** |
| Mean±SD | 2.97 ± 0.53 | 2.62 ± 0.59 | (-0.40 – -0.29) | |

† Analysis using paired t-test.

**Table (3): Multivariable regression analysis of the various independent variables affecting UA-RI, UA-PI and UA-S/D**

| | **UA-RI** | | **UA-PI** | | **UA-S/D** | |
|---|---|---|---|---|---|---|
| | **$r_{partial}$** | **p** | **$r_{partial}$** | **P** | **$r_{partial}$** | **P** |
| Age | 0.046 | 0.467 | -0.041 | 0.518 | -0.002 | 0.968 |
| BMI | 0.073 | 0.246 | 0.022 | 0.683 | 0.027 | 0.663 |
| EFW | -0.44 | **<0.0001** | -0.132 | **0.037** | -0.136 | **0.031** |
| Gestational age | -0.079 | **0.021** | -0.369 | **<0.0001** | -0.235 | **0.0002** |

**Table (4): Subgroup analysis of mean paired difference of umbilical artery Doppler indices following magnesium sulphate infusion before and after 32 weeks gestational age**

| | | **Mean Paired Difference** | **P †** |
|---|---|---|---|
| **UA – RI** | < 32 wks | -0.002 ± 0.01 | **< 0.001** |
| | > 32 wks | -0.17 ± 0.08 | |
| **UA – PI** | < 32 wks | -0.05 ± 0.05 | **< 0.001** |
| | > 32 wks | -0.29 ± 0.08 | |
| **UA – S/D** | < 32 wks | -0.05 ± 0.11 | **< 0.001** |
| | > 32 wks | -0.71 ± 0.43 | |

† Analysis using unpaired t-test with Welch's correction.

**Effect of magnesium sulphate infusion on middle cerebral artery Doppler indices:**

Middle cerebral artery Doppler indices (RI, PI and S/D ratio) were all statistically significantly lower after magnesium sulphate infusion with a mean drop of 0.06±0.07 (95% CI: -0.06 – -0.05), 0.21±0.26 (95% CI: -0.24 – -0.17) and 0.56±0.66 (95% CI: -0.65 – -0.48).

Mutivariable regression analysis revealed a negative correlation between gestational age and middle cerebral Doppler indices that remained statistically significant after adjustment for other independent variables, paired difference in Doppler indices after magnesium sulphate infusion tended to increase with advancing gestational age. Mean paired difference in MCA Doppler indices (RI, PI, S/D ratio) after magnesium sulphate infusion was statistically significantly higher after 32 weeks gestational age **(Tables 5, 6, 7)**.

**Table (5): Comparison between middle cerebral artery Doppler indices before and after magnesium sulphate infusion**

| | **Before Magnesium Sulphate** | **After Magnesium Sulphate** | **Mean Paired Difference (95% CI)** | **P †** |
|---|---|---|---|---|
| **Middle cerebral artery RI** | | | | |
| Range | 0.60 – 0.89 | 0.60 – 0.91 | -0.06 ± 0.07 | **<0.001** |
| Mean ± SD | 0.79 ± 0.08 | 0.73 ± 0.08 | (-0.06 – -0.05) | |
| **Middle cerebral artery PI** | | | | |
| Range | 1.40 – 2.72 | 1.14 – 2.48 | -0.21 ± 0.26 | **<0.001** |
| Mean ± SD | 2.04 ± 2.29 | 1.83 ± 0.33 | (-0.24 – -0.17) | |
| **Middle cerebral artery S/D ratio** | | | | |
| Range | 3.00 – 4.90 | 1.52 – 4.90 | -0.56 ± 0.66 | **<0.001** |
| Mean±SD | 4.07 ± 0.63 | 3.50 ± 0.88 | (-0.65 – -0.48) | |

† Analysis using paired t-test.

**Table (6): Multivariable regression analysis of the various independent variables affecting MCA-RI, MCA-PI and MCA-S/D**

| | **MCA-RI** | | **MCA-PI** | | **MCA-S/D** | |
|---|---|---|---|---|---|---|
| | **$r_{partial}$** | **p** | **$r_{partial}$** | **P** | **$r_{partial}$** | **p** |
| Age | 0.036 | 0.566 | 0.129 | 0.042 | -0.009 | 0.877 |
| BMI | -0.012 | 0.840 | 0.064 | 0.311 | 0.006 | 0.923 |
| EFW | -0.262 | **<0.0001** | -0.504 | **<0.001** | -0.298 | **<0.001** |
| Gestational age | -0.253 | **0.0001** | -0.092 | **<0.001** | -0.186 | **0.003** |

**Table (7): Subgroup analysis of mean paired difference of middle cerebral artery Doppler indices following magnesium sulphate infusion before and after 32 weeks gestational age**

| | | **Mean Paired Difference** | **P †** |
|---|---|---|---|
| **MCA – RI** | < 32 wks | -0.002 ± 0.02 | **< 0.001** |
| | > 32 wks | -0.13 ± 0.03 | |
| **MCA – PI** | < 32 wks | -0.01 ± 0.06 | **< 0.001** |
| | > 32 wks | -0.46 ± 0.19 | |
| **MCA – S/D** | < 32 wks | -0.04 ± 0.36 | **< 0.001** |
| | > 32 wks | -1.22 ± 0.22 | |

† Analysis using unpaired t-test with Welch's correction.

**Effect of magnesium sulphate infusion on uterine artery Doppler indices:**

No statistically significant differences were found in uterine artery RI and S/D ratio following magnesium sulphate infusion; whereas uterine artery PI showed statistically significant reduction averaging 0.14±0.17 (95% CI: -0.16 – -0.12) after magnesium sulphate infusion.

Multivariable regression analysis revealed no statistically significant contribution of other independent variables (age, BMI, EFW and gestational age) to the variation in mean paired difference in RI and S/D ratio following magnesium sulphate; whereas the negative correlation between gestational age and estimated fetal weight and uterine artery PI. The effect of advanced gestational age was evident only on uterine artery PI **(Tables 8, 9, 10)**.

**Table (8): Comparison between uterine artery Doppler indices before and after magnesium sulphate infusion**

| | **Before Magnesium Sulphate** | **After Magnesium Sulphate** | **Mean Paired Difference (95% CI)** | **P †** |
|---|---|---|---|---|
| **Uterine artery RI** | | | | |
| Range | 0.50 – 0.74 | 0.49 – 0.76 | -0.0003 ± 0.02 | 0.75 |
| Mean ± SD | 0.63 ± 0.07 | 0.62 ± 0.07 | (-0.002 – 0.002) | |
| **Uterine artery PI** | | | | |
| Range | 0.58 – 1.39 | 0.45 – 1.13 | -0.14 ± 0.17 | **<0.001** |
| Mean ± SD | 0.89 ± 0.17 | 0.74 ± 0.15 | (-0.16 – -0.12) | |
| **Uterine artery S/D ratio** | | | | |
| Range | 2.00 – 3.73 | 1.99 – 3.94 | 0.002 ± 0.03 | 0.31 |
| Mean±SD | 2.76 ± 0.44 | 2.76 ± 0.45 | (-0.002 – 0.006) | |

† Analysis using paired t-test.

**Table (9): Multivariable regression analysis of the various independent variables affecting Ut A-RI, Ut A-PI and Ut A-S/D**

| | **Ut A-RI** | | **Ut A-PI** | | **Ut A-S/D** | |
|---|---|---|---|---|---|---|
| | **$r_{partial}$** | **P** | **$r_{partial}$** | **P** | **$r_{partial}$** | **p** |
| Age | 0.027 | 0.668 | -0.041 | 0.518 | 0.081 | 0.199 |
| BMI | 0.070 | 0.270 | 0.022 | 0.683 | -0.048 | 0.449 |
| EFW | 0.030 | 0.633 | -0.132 | **0.037** | 0.125 | 0.066 |
| Gestational age | 0.013 | 0.827 | -0.369 | **<0.0001** | 0.037 | 0.553 |

**Table (10): Subgroup analysis of mean paired difference of uterine artery Doppler indices following magnesium sulphate infusion before and after 32 weeks gestational age**

| | | **Mean Paired Difference** | **P †** |
|---|---|---|---|
| **Ut A – RI** | < 32 wks | -0.001 ± 0.01 | 0.21 |
| | > 32 wks | 0.001 ± 0.02 | |
| **Ut A – PI** | < 32 wks | -0.09 ± 0.10 | **< 0.001** |
| | > 32 wks | -0.22 ± 0.21 | |
| **Ut A – S/D** | < 32 wks | -0.002 ± 0.01 | 0.06 |
| | > 32 wks | 0.008 ± 0.05 | |

† Analysis using unpaired t-test with Welch's correction.

## DISCUSSION

The current study was conducted in alshohadaa central hospital in the period from September 2018 till September 2020. A total of 300 women with threatened preterm labor were included in a prospective observational study to detect the effect of magnesium sulfate on Doppler parameters of fetal middle cerebral, umbilical and uterine arteries in women with threatened preterm labour and also observed its effect on neonatal outcome by the assessment of APGAR score for neonate in 1, and 5 minute after labor.

Concerning the process of recruitment and handling of the study population during the course of the study a total number of women with threatened preterm labour (n 300) were collected.

Doppler ultrasound was performed on fetal middle cerebral, umbilical and uterine arteries for these patients before and after receiving $Mgso_4$ as tocolysis for 24 hours.

A number of patients (n 46) was excluded from the study due to Undiagnosed oligohydraminos, Undiagnosed fetal growth restriction, Established preterm labor, Placental abruption, Chorioamnionitis, Non-reassuring fetal status, and for the Need of other tocolytic agent.

Concerning Doppler analysis in the current study, there is a non-statistically significant reduction in RI, PI, SD Ratio of the UA before 32 weeks gestation while a statistically significant reduction in these parameters after 32 weeks gestation following magnesium sulphate infusion.

Regarding MCA Doppler parameters in this study, there is a statistically significant reduction in RI, PI, SD ratio after magnesium sulphate infusion.

Regarding UtA Doppler parameters in this study, There are No statistically significant differences were found in uterine artery RI and S/D ratio following magnesium sulphate infusion; whereas uterine artery PI showed statistically significant reduction after magnesium sulphate infusion.

*Keeley et al. (2010)* performed a study to detect the effect of $mgso_4$ on fetal hemodynamics through a twenty women presented with preterm labour between 24-35 weeks gestation. In contradiction to this study, *Keeley et al. (2010)*, demonstrated that there is an increase in the MCA PI indictes decreasing intracranial blood flow velocity after adminstration of $Mgso_4$ as a tocolytic agent.

In agreement with this study, *Keeley et al. (2010)*, although demonstrated that there is a decrease in PI of the UtA after adminstration of Mgso4 indicating an increase in the blood flow velocity caused by Mgso4 (vasodilatation effect).

In contradiction to this study, *Keeley et al. (2010)*, failed to show significant changes in the UA PIs after Mgso4 infusion.

Several studies used other tocolytic agents to detect their effect on Doppler parameters, one of them *Guclu et al. (2012)*. They used nifedipine on 28 pregnant females with preterm labour. Doppler ultrasound was performed before, 24 and 48 hours after tocolysis with nifedipine In agreement with our study,

*Guclu et al. (2012),* stated that there is a decrease in the PI of the UtA and MCA at 24 and 48 h after using Nifedipine as a single tocolytic agent while their results regarding UA PI go against this study (no significant change) after nifedipine tocolysis.

According to *Sayin et al. (2010),* 85 pregnant women with preterm labour were recruited. The study group devided into 2 groups. The first group (n 46) received ritodrine as tocolytic agent and the second group (n 39) received Mgso4 as tocolytic agent. Healthy pregnant women served as the controls (n 83). All three groups subdevided into 2 groups (before and after 32 weeks) since the incidence of neonatal respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage and sepsis markedly decreases after 32 weeks of gestation. Doppler blood flow examinations were performed, before and 48 h after initiating therapy, from the umbilical artery (UA), middle cerebral arteries (MCA), uterine arteries (Ut.A).

Accordingly, although the difference was significant compared to controls, ritodrine therapy did not cause a decrease in UA PI values, but a non-significant increase in uterine arteries, particularly compared to controls. In women between 26 and 32 weeks, Ut. A PI values also significantly decreased in women receiving ritodrine whereas they increased in those receiving $MgSO_4$ (against this study results). However, UA PI values showed a lesser decrease in women receiving both tocolytic drugs than in controls.

In patients between 32 and 36 weeks, UA and MCA PI values did not significantly decrease in women receiving both tocolytics compared to controls.

In agreement with this study, *Sayin et al. (2010)* found that a non-statistically significant change in the umbilical artery Doppler indices before 32 weeks of gestational age; whereas a statistically significant change was found following magnesium sulphate infusion after 32 weeks of gestational age.

According to *Guden et al. (2016),* the purpose of their study was to detect the effect of both nifedipine and $MgSO_4$ as atocolytic agents on Doppler parameters of UA, MCA, UtA in women with preterm labour.

In $MgSO_4$ group, the PI of the right uterine and the Ris were significantly higher following the treatment However, no changes were observed in the left artery PI and RI (against this study results). No statistically significant difference was observed in umbilical artery PI, RI and systole to diastole (S/D) rates (against this study results). In addition, an increase in the PI of the MCA was observed (against this study results), whereas a decrease in the RI was seen.

In nifedipine group, a decrease in PI in right uterine artery was observed, and no change was determined in the RI. However, a significant decrease was determined in the left uterine artery PI. Although a significant decrease was detected in the umbilical artery RI and S/D rates, an increase was observed in the PI. However, while the PI was decreasing, no change was detected in RI of MCA.

Several studies were performed before to detect the effect of $MgSO_4$ on doppler parameters not only in women with

preterm labour but also in women with severe preeclampsia such as *Maged et al. (2016)*. A case control study included 100 pregnant women with severe preeclampsia. Umbilical artery, uterine artery, and fetal middle cerebral artery Doppler were measured before and 20 minutes after intravenous administration of 6 g of magnesium sulfate. There was a significant difference between umbilical artery, middle cerebral artery, and uterine artery Doppler parameters before and after administration of $MgSO_4$ in the studied women. There was significant difference with regard to the S/D ratio. The decrease in the values of Doppler parameters before and after administration of $MgSO_4$ was more in the middle cerebral artery than in the umbilical artery.

## CONCLUSION

Although the use of Mgso4 as a tocolytic agent is controversial but it is valuable as neuroprotective agent and for treatment of eclamptic seizures. Its effect on the fetal blood flow has a very beneficial role till now. In this study it was found that it has significant effect on fetal MCA, UA and UtA Doppler parameters (RI, PI and S/D ratio). More studies with larger cohorts are needed to support these results.

It's recommended to use magnesium sulphate in women with threatened preterm labour as it improves fetal blood flow.

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# تأثير سلفات الماغنسيوم على تدفق الدم داخل الشريان المخى الاوسط والشريان السرى والشريان الرحمى لدى النساء المصابات بالولادة المبكرة

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**خلفية البحث:** الولادة المبكرة هي واحدة من أكثر الأحداث السريرية شيوعًا حيث يمكن أن يتحول الحمل التقليدي إلى حالة عالية الخطورة للأم والجنين. سلفات الماغنسيوم تم استخدامه من قبل وعلى مدار 30 عام كعامل مثبط لاعراض الولاده المبكره وذلك لانه يعاكس ايونات الكالسيوم والتى تساعد على انقباض الرحم وهو يعمل عن طريق تثبيط قنوات الكالسيوم مستقلة الجهد في سطح جدار الرحم حيث يقوم الماغنيسيوم خارج الخلية بقمع تدفق الكالسيوم عبر أغشية الخلايا، في حين يتنافس الماغنيسيوم داخل الخلايا مع الكالسيوم، وذلك عن طريق تثبيط نشاط كيناز السلسلة الخفيفة من الميوسين.

**الهدف من البحث:** تقييم تأثير سلفات الماغنيسيوم قبل وبعد إعطاؤه كعامل مثبط للولادة على مقاييس الموجات فوق الصوتية (دوبلر) بالنسبة للوريد الرحمي والوريد السري والأوردة الدماغية المتوسطة للجنين عند المرأة الحامل التي تعاني من خطر الولادة المبكرة.

**المريضات وطرق البحث:** تم إجراء دراسة وصفية مستقبلية في مستشفى الشهداء المركزي في الفترة ما بين سبتمبر 2018 حتى سبتمبر 2020. تم تضمين ما مجموعه 300 امرأة مهددة بالولادة المبكرة. خضعت مجموعة الدراسة لدراسة دوبلر بالموجات فوق الصوتية لتقييم مؤشر مقاومة معاملات سرعة التدفق، ومؤشر النبض، ونسبة الانقباض/ الانبساطي، للشريان الدماغي الأوسط للجنين، والشريان السري، و الشريان الرحمي، بإستخدام مسبار البطن لجهاز الموجات فوق الصوتية. ثم على الفور تم إعطاؤهم تسريبًا في الوريد من 4 إلى 6 جم من كبريتات المغنيسيوم كجرعة تحميل ثم 1 جم / ساعة كجرعة صيانة مجمعة.

**نتـــائج البحـــث:** تـــم تســـجيل النتـــائج ووجـــد ان هنـــاك انخفـــاض غيـــر ذي دلالـــة إحصـــائية فـــي مقاومـــة مؤشـــر ســـرعة التـــدفق (RI)، مؤشـــر النـــبض (PI) ونســـبة الانقباضـــي/ الانبســـاطي (S/D) فـــى الشـــريان الســـرى قبـــل الأســـبوع 32 مـــن الحمـــل فـــي حـــين أن انخفـــاض كبيـــر إحصـــائيا فـــي هـــذه المعـــاملات بعـــد 32 أســـبوعا مـــن الحمـــل بعـــد اســـتخدام ســـلفات الماغنيســـيوم. فيمـــا يتعلـــق بمعـــاملات دوبلـــر الشـــريان المخـــى الوســـطى فـــي دراســـتنا، هنـــاك انخفـــاض ذو دلالـــة إحصـــائية فـــي نســـبة RI، PI، SD بعـــد اســـتخدام ســـلفات الماغنيســـيوم. فيمـــا يتعلـــق بمعـــاملات الشـــريان الرحمـــى دوبلـــر فـــي دراســـتنا، لا توجـــد فـــروق ذات دلالـــة إحصـــائية فـــي شـــريان الـــرحم RI و S/D نســـبة بعـــد اســـتخدام ســـلفات الماغنيســـيوم. بينمـــا أظهـــر شـــريان الـــرحم PI انخفاضًـــا كبيـــرًا إحصـــائيًا بعـــد استخدام سلفات الماغنيسيوم.

**الاســـتنتاج:** إنـــه علـــى الـــرغم مـــن أن إســـتخدام ســـلفات الماغنيســـيوم كمثـــبط لأعـــراض الـــولادة المبكـــرة مثيـــر للجـــدل، إلا أنـــه ذو قيمـــة كعامـــل وقـــائي للخلايـــا العصـــبية ولعـــلاج نوبـــات التشـــنج الخاصـــة بتســـمم الحمـــل. فـــي هـــذه الدراســـة ووجـــد ان لـــه تـــأثير مفيـــد للغاية على تدفق الدم للجنين.

**الكلمـــات الدالـــة:** كبريتـــات المغنيســـيوم، مؤشـــرات دوبلـــر للـــرحم، الشـــرايين الدماغيـــة الوسطى والجنينية، الولادة المبكرة المهدد.

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