

CHANGES IN UMBILICAL ARTERY DOPPLER INDICES AFTER LOADING DOSE OF MAGNESIUM SULPHATE IN PATIENTS WITH SEVERE PREECLAMPSIA

By

Karim Hossam El-Din Ahmed Shalaby, Mohamed Mohamed Ibrahim Gebril, Mohamed Mohamed Ibrahim Farahat and Ali Abd El-Moezz Dahi Ali

Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University

Corresponding author: Karim Hossam El-Din Ahmed Shalaby;

E-mail: k.shalaby@gmail.com

ABSTRACT

Background: Preeclampsia is a disease that commonly develops during the 2nd half of pregnancy. There were many attempts to test a variety of biological, biochemical and biophysical markers to predict the occurrence of the disease, but so far there is no reliable screening tests for that as well as no prevention measures could be efficacious for the disease. Doppler ultrasound is considered one of the most important tools for assessment of fetal wellbeing through applying Doppler velocimetry studies on the umbilical artery.

Objective: To compare between umbilical artery Doppler indices (resistance index, pulsatility index and the systolic/diastolic ratio) before and after use of loading dose of magnesium sulfate over 20 minutes in pregnant women with severe preeclampsia, and the possible effects of such changes on the mode of delivery and neonatal outcome.

Patients and Methods: A prospective observational cohort study in 100 pregnant women was conducted at the Obstetrics and Gynecology Department, Al-Galaa Teaching Hospital. Cases were recruited from the emergency unit during the period from November 2019 to July 2020. Doppler ultrasonography of the umbilical artery underwent before and after intravenous administration of 6 g of magnesium sulfate (loading dose) over 20 minutes. The variables studied were the Doppler velocimetry parameters of the umbilical artery. The comparison of means between the measurements (before and after) of each individual was performed.

Results: There was a significant difference between umbilical artery resistance index (RI) before, and 20 minutes after administration of the loading dose of MgSO₄. It was found that the loading dose of MgSO₄ elicited a slight reduction in umbilical artery resistive index (RI) from before taking it and 20 minutes after (0.69 ± 0.05 vs 0.65 ± 0.05). There was a significant difference between umbilical artery pulsatility index (PI) before, and 20 minutes after administration of the loading dose of MgSO₄. There was a statistically highly significant difference of means of umbilical artery Doppler indices after magnesium sulfate. Magnesium sulphate did not affect the neonatal Apgar score, and the need for resuscitation and intensive care unit (ICU) admission.

Conclusion: Intravenous administration of magnesium sulfate in pregnant women with severe preeclampsia resulted in a reduction in umbilical artery Doppler indices with reduced resistance to blood flow in these vessels.

Keywords: Hypertension, Umbilical artery, Doppler ultrasound, Preeclampsia, Magnesium sulphate.

INTRODUCTION

Hypertensive disorders complicate 5 to 10 percent of all pregnancies and together with bleeding and infection form a deadly triad. Despite recent advances in antenatal care, hypertensive disorders of pregnancy remain a major cause of maternal and fetal morbidity and mortality (*Martin et al., 2011*).

Preeclampsia is diagnosed by the rise of blood pressure more than or equal to 140/90 mmHg, recorded on two separate occasions, 6 hours apart. In addition to proteinuria (0.3 gm or more in 24 hours collected urine sample with 1+ or greater on urine dipstick test) after 20 weeks of gestation (*Pallavee and Nischintha, 2015*).

Preeclampsia often affects young and nulliparous women, whereas older women are at great risk of chronic hypertension with superimposed preeclampsia (*Lawlor et al., 2010*).

Preeclampsia is considered severe if one or more of the following blood pressure: systolic ≥ 160 mmHg or diastolic ≥ 110 mm HG on two occasions at least 4 hours apart while the patient is on bed rest, thrombocytopenia: platelet count $< 100,000$ / microliter, impaired liver function: doubling of liver transaminases, severe persistent right upper quadrant or epigastric pain unresponsive to medications and not accounted for by alternative diagnoses, new-onset renal insufficiency: serum creatinine > 1.1 mg/dl or doubling of serum creatinine in the absence of other renal disorders, pulmonary edema and new-onset cerebral or visual disturbances (*ACOG, 2014*).

In normal pregnancy, the spiral arteries in the placental bed are invaded by trophoblast, which becomes incorporated into the vessel wall and replaces the endothelium, muscular layer and neural tissue. These physiological changes convert the spiral arteries from narrow muscular vessels to wide non-muscular channels independent of maternal vasomotor control. Pre-eclampsia is thought to be the consequence of impaired trophoblastic invasion of the maternal spiral arteries (*Poon et al., 2012*).

As a result of impaired utero-placental blood flow, manifestations of preeclampsia may be seen in fetal placental unit. These include intra uterine growth restriction (IUGR), oligohydraminos, placental abruption, and non-reassuring fetal status found on antepartum surveillance by Doppler ultrasound (*ACOG, 2010*).

Indirect evidence for impaired placental perfusion in pregnancies designed to develop preeclampsia has been provided by Doppler studies of the uterine arteries which showed increased pulsatility index (PI) during the second trimester and also in the first trimester of pregnancy (*Plasencia et al., 2011*).

High flow resistance in the capillaries of terminal villi leads to a low end-diastolic velocity in the umbilical artery and a subsequent hypoxia (*Weiner et al., 2010*). During chronic fetal hypoxia, there is a continuous reduction of cerebral vascular resistance resulting in decrease Middle cerebral artery resistance index values gradually (*Mimica et al., 2010*).

Magnesium sulphate is widely used in obstetrics and is a drug of choice in two important complications of pregnancy,

preeclampsia and preterm labor. Magnesium sulphate is used to prevent seizures in preeclampsia patients (*Guzin et al., 2010*).

Fetal circulation has long been studied by Doppler sonography, which can provide valuable information regarding neonatal prognosis and fetal well-being in compromised pregnancies. Doppler sonography has also been used for evaluation of various drugs on Doppler blood waveforms (*Sayin et al., 2010*).

The hemodynamic effects of magnesium sulphate are highly heterogeneous. While some studies have found a significant reduction in blood pressure and in Doppler parameters of uterine, umbilical and fetal middle cerebral arteries, it is important to determine the hemodynamic effects of this treatment on uterine arteries and on the umbilical and fetal middle cerebral arteries using Doppler flow velocity in women with severe preeclampsia. This knowledge may further consolidate the use of magnesium sulphate and contribute to defining a better procedure for fetal monitoring in these pregnant women (*Souza et al., 2010*).

The aim of the present work was to evaluate changes in Doppler velocimetry parameters (resistance index [RI], pulsatility index [PI] and systolic/diastolic [S/D] ratio) of the umbilical artery before and after loading dose of magnesium sulphate administration in pregnant women with severe preeclampsia, and the possible effects of these changes on mode of delivery and neonatal outcome.

PATIENTS AND METHODS

A prospective observational cohort study was conducted at the Obstetrics and Gynecology Department, Al-Galaa Teaching Hospital. Cases were recruited from the emergency unit during the period from November 2019 to July 2020. One hundred women with severe preeclampsia were included in the study. Assessment of umbilical artery Doppler velocimetry parameters (RI, PI, S/D) were performed before, and 20 minutes after intravenous administration of 6 grams of magnesium sulfate.

Inclusion criteria:

- Singleton pregnancy.
- Primigravida or Multigravida.
- Pregnant females ≥ 37 weeks of gestation.
- Diagnosed as severe preeclampsia by the following criteria:
 - Blood pressure: Systolic ≥ 160 mmHg or diastolic ≥ 110 mm HG on two occasions at least 4 hours apart while the patient is on bed rest.
 - Thrombocytopenia: Platelet count $< 100,000$ / microliter.
 - Impaired liver function: Doubling of liver transaminases, severe persistent right upper quadrant or epigastric pain unresponsive to medications and not accounted for by alternative diagnoses.
 - New-onset renal insufficiency: Serum creatinine > 1.1 mg/dl or doubling of serum creatinine in the absence of other renal disorders.
- Pulmonary edema.

- New-onset cerebral or visual disturbances (ACOG, 2014).

Exclusion criteria:

- Multifetal pregnancy.
- History of epilepsy.
- Patients with diabetes.
- Patients with renal disease.
- Fetuses with congenital anomalies.
- Patients receiving anticoagulants e.g. heparin (unfractionated or low molecular weight).
- Patients with severe IUGR.
- Patients with accidental hemorrhage.

All patients were subjected to the following:

1. Detailed History Taking.
2. Complete Physical Examination.
3. Investigations:
 - Doppler Studies.
 - Real-time ultrasonography for biophysical profile.

Blood pressure was measured according to the following methodology:

- Patient was placed in the sitting or semi sitting position.
- Using a cuff of appropriate size.
- Cuff placed at the level of the heart.
- Kortokoff phase V was used to determine the diastolic blood pressure.

Regimen of magnesium sulphate:

The magnesium sulfate was given according to the regimen of 6 grams

intravenous over 20 minutes as a loading dose.

Technique of umbilical artery Doppler studies:

All patients were placed in a semi recumbent position with a left lateral tilt, and then the uterine content are scanned to select an area of amniotic cavity with several loops of cord. Then using a pulsed wave Doppler on a free loop of cord, the characteristic sound and shape of the umbilical artery were identified. When the screen showed at least 3 consecutive wave forms of similar height, the image was frozen and umbilical artery Doppler velocimetry parameters (Resistance index, pulsatility index and systolic/diastolic ratio) were estimated. A minimum of 3 separate readings were averaged before the final values were obtained. Umbilical artery Doppler studies were avoided during fetal activity and fetal breathing because of effect of fetal breathing movements on waveform variability; recording was performed during fetal apnea.

Neonatal assessment:

Was performed by assessment of:

- APGAR score at 10 minutes.
- The need for neonatal ICU admission.
- Neonatal death.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative

percentages. Quantitative data were expressed as mean ± SD (Standard deviation). t-test was used to compare between two independent groups of

normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Mean age of patients was; 31.41 years, SD ± 3.87, mean gestational age was

37.85 weeks, SD± 0.67, and mean BMI was; 28.20, SD ± 2.64 (**Table 1**).

Table (1): Demographic features of the studied patients

Values	Mean (± SD)	Range
Age	31.41 ± 3.87	23 – 38
Gestational age	37.85 ± 0.67	21.8 – 33.7
BMI	28.20 ± 2.64	36.3 – 39.6

The loading dose of MgSO4 elicited a slight reduction in umbilical artery RI from before taking it and 20 minutes after (0.69 ± 0.05 vs 0.65 ± 0.05), in PI from

before taking it and 20 minutes after (1.24 ± 0.18 vs 1.14 ± 0.18), in S/D ratio from before taking it and 20 minutes after (3.14 ± 0.44 vs 2.93 ± 0.41) (**Table 2**).

Table (2): Comparison between umbilical artery RI, PI and systolic/diastolic (S/D) ratio before & 20 minutes after administration of the loading dose of MgSO4

Values	Mean (± SD)	Range	P value
RI before MgSO4	0.69 ± 0.05	0.59 – 0.76	<0.001
RI 20 minutes after MgSO4	0.65 ± 0.05	0.54 – 0.75	
PI before MgSO4	1.24 ± 0.18	0.88 – 1.75	<0.001
PI 20 minutes after MgSO4	1.14 ± 0.18	0.86 – 1.77	
S/D before MgSO4	3.14 ± 0.44	2.33 – 3.86	<0.001
S/D 20 minutes after MgSO4	2.93 ± 0.41	2.25 – 3.66	

Neonatal assessment using Apgar score at 10 minutes showed that 77% of neonates had an Apgar score > 7, while 23 % had an APGAR score < 7. Throughout

this study there, were 7 cases of neonatal deaths comprising 7% of the studied population (**Table 3**).

Table (3): Apgar score at 10 minutes and neonatal deaths

Values	Frequency	Percent
Apgar Score at 10 minutes	<7	23
	>7	77
Neonatal death	Yes	7
	No	93
Total	100	100

DISCUSSION

In our study, it was revealed that the loading dose of magnesium sulphate has caused a statistically highly significant reduction in Doppler velocimetry indices of the umbilical artery in pregnant women with severe preeclampsia.

These results went hand in hand with the study done by *Souza et al. (2010)* who reported a reduction of umbilical artery Doppler velocimetry indices (RI, PI, S/D) in pregnant women with severe preeclampsia after intravenous administration of magnesium sulphate.

Likewise, *Houlihan et al. (2010)* showed that magnesium sulphate leads to a decrease in vascular resistance of the umbilical artery with a consequent vasodilatory effect.

On the other hand, *Belfort et al. (2010)*, assessing pregnant women with preeclampsia, there was no significant reduction in the vascular resistance of the umbilical artery as measured by the pulsatility index (PI). These contradictory results could be explained by the fact that, in such study, women were not stratified according to severity and most cases were of women suffering from non-severe preeclampsia. However, in our study, only pregnant women with severe preeclampsia were recruited.

These results went hand in hand with *Singh et al. (2016)* who showed that there was a significant reduction in the percentage of CTG traces with accelerations 1 hour after administration of the loading dose of magnesium sulphate. However, there were no significant changes after 15 minutes.

In our study, 33% of the studied population was delivered vaginally, while 67% were delivered by cesarean section due to failed progress, CPD, and fetal distress or previous cesarean section.

On assessing the neonates born to the women with preeclampsia involved in our study, we observed that magnesium sulphate did not have a significant effect on neonatal outcome. Additionally, all neonatal deaths encountered in the current study occurred in patients had increased umbilical artery Doppler indices and fetal distress before administration of loading dose of magnesium sulphate, and could therefore be attributed to severe preeclampsia rather than magnesium sulphate administration.

The confounding circumstances, that were associated with maternal MgSO₄ treatment, were more likely to increase the likelihood of respiratory depression immediately after birth, thus leading to increased delivery room resuscitation, NICU admission and possible neonatal deaths rather than MgSO₄ itself. These findings went hand in hand with *Riaz et al. (2010)* stated that MgSO₄-exposed infants had a higher incidence of hypotonia and lower median Apgar scores than control infants. However, there was no association between adverse outcomes and maternal serum magnesium concentrations at delivery, duration of treatment, or dose of MgSO₄. This study differs from our study in the presence of the control group, the assessment of serum magnesium concentrations; duration of exposure to magnesium sulphate and all studied population had full term pregnancy in our study.

Study by Weisz *et al.* (2015) found significantly fewer MgSO₄-exposed infants required intensive resuscitation. However, after adjustment for confounders, this difference was no longer significant.

The current study has shown improvement of the umbilical artery Doppler indices after administration of the loading dose of magnesium sulphate. This was evidenced by the fact that only 4% of the patients had an emergency CS after 20 minutes of administration of the loading dose of magnesium sulphate due to foetal distress. 77% of neonates had an Apgar score > 7 at 10 minutes. There were only 7 neonatal deaths and all occurred in patients with increase umbilical artery Doppler indices before administration of loading dose of magnesium sulphate, and could therefore be attributed to severity rather than magnesium sulphate administration.

CONCLUSION

- Doppler indices in the umbilical artery significantly improved after administration of magnesium sulphate in patients with severe preeclampsia.
- Magnesium sulphate did not affect the neonatal Apgar score and the need for resuscitation and neonatal ICU admission.
- Umbilical artery Doppler parameters are considered a better indicator of the current foetal status and as a predictor of neonatal outcome.

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التغيرات الطارئة على دوبلر الشريان السري بعد الجرعة الابتدائية من سلفات الماغنسيوم في مرضى تسمم الحمل الشديد

كريم حسام الدين أحمد شلبي، محمد محمد إبراهيم جبريل، محمد محمد إبراهيم فرحات

قسم التوليد وأمراض النساء، كلية الطب، جامعة الأزهر

E-mail: k.shalaby@gmail.com

خلفية البحث: تسمم الحمل هو مرض يتطور بشكل شائع خلال النصف الثاني من الحمل، وكانت هناك محاولات عديدة لاختبار مجموعة متنوعة من العلامات البيولوجية والكيميائية الحيوية والفيزيائية الحيوية للتنبؤ بحدوث المرض ولكن حتى الآن لا توجد اختبارات فحص موثقة لذلك فضلا عن عدم وجود تدابير وقائية يمكن أن تكون فعالة للمرض. تعتبر الموجات فوق الصوتية دوبلر من أهم الأدوات لتقييم صحة الجنين من خلال تطبيق دراسات قياس سرعة الدوبلر على الشريان السري.

الهدف من البحث: المقارنة بين مؤشرات دوبلر للشريان السري (مؤشر المقاومة، مؤشر النبض ونسبة الانقباضي / الانبساطي) قبل وبعد استخدام جرعة تحميل من كبريتات المغنيسيوم أكثر من 20 دقيقة في النساء الحوامل المصابات بمقدمات الارتعاج الشديدة، والتأثيرات المحتملة لهذه التغييرات على الوضع من الولادة ونتائج حديثي الولادة.

المريضات وطرق البحث: تم إجراء دراسة استطلاعية جماعية على 100 امرأة حامل في قسم أمراض النساء والولادة بمستشفى الجلاء التعليمي. وتم إختيار الحالات من وحدة الطوارئ خلال الفترة من نوفمبر 2019 إلى يوليو 2020. وخضعن للتصوير بالموجات فوق الصوتية دوبلر للشريان السري قبل وبعد الحقن الوريدي لـ 6 جم من كبريتات المغنيسيوم (جرعة التحميل) على مدى 20 دقيقة. وكانت المتغيرات المدروسة هي معلمات قياس السرعة الدوبلرية للشريان السري. وتم إجراء مقارنة الوسائل بين القياسات (قبل وبعد) لكل فرد.

نتائج البحث: كان هناك فرق كبير بين مؤشر مقاومة الشريان السري قبل 20 دقيقة بعد إعطاء جرعة التحميل من $MgSO_4$. وقد أدت جرعة التحميل من $MgSO_4$ إلى انخفاض طفيف في مؤشر مقاوم في الشريان السري قبل تناوله وبعد 20 دقيقة. وكان هناك فرق ذو دلالة إحصائية عالية بين مؤشر نبض الشريان السري قبل 20 دقيقة بعد إعطاء جرعة التحميل من $MgSO_4$. وكان هناك فرق ذو دلالة إحصائية عالية في مؤشرات دوبلر الشريان السري بعد كبريتات المغنيسيوم. ولم تؤثر كبريتات المغنيسيوم على درجة أبغار الوليدية والحاجة إلى الإنعاش وقبول وحدة العناية المركزة.

الاستنتاج: أدى إعطاء كبريتات المغنيسيوم عن طريق الوريد عند النساء الحوامل المصابات بمقدمات الارتعاج الشديدة إلى انخفاض مؤشرات دوبلر الشريان السري مع انخفاض المقاومة لتدفق الدم في هذه الأوعية.

الكلمات الدالة: إرتفاع ضغط الدم، الشريان السري، الموجات فوق الصوتية دوبلر، تسمم الحمل، كبريتات المغنيسيوم.