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EFFECT OF MAGNESIUM SULFATE ON DOPPLER INDICES AND FETAL CIRCULATION IN CASES OF SEVERE PRE-ECLAMPSIA

By

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ABSTRACT

Background: In women with severe PE, the use of magnesium sulfate ($MgSO_4$) is indicated for prevention and control of acute convulsions. Several randomized trials have compared the efficacy of $MgSO_4$ with other anticonvulsants in women with eclampsia, and the rates of recurrent seizures and maternal death significantly reduced with $MgSO_4$ as compared with other anticonvulsants.

Objective: To assess the effect of magnesium sulfate injection on Doppler indices and fetal circulation in cases of severe pre-eclampsia.

Patients And Methods: This was a prospective study that conducted on one hundred pregnant women suffering from pre-eclampsia, selected from the Obstetrics and Gynecology Department of Al-Hussein University Hospital from January 2018 to December 2018, evaluated before and after administration of magnesium sulfate, Doppler ultrasound was carried out to measure umbilical artery blood flow.

Results: The results showed that a significant improvement in Doppler measurements and out come with treated groups ($MgSO_4$) group more than the control group.

Conclusion: $MgSO_4$ proved to cause many hemodynamic changes as it has a vasodilator effect on maternal and fetal blood vessels. Doppler indices in the umbilical arteries significantly changed after administration of $MgSO_4$ in patients with severe preeclampsia.

Key words: Magnesium sulfate, Doppler indices, Pre-eclamsia, fetal circulation.

INTRODUCTION

Preeclampsia is an endothelial disorder unique to human pregnancy, with multiple organ involvement; especially kidney lesion, defined as “glomerular endotheliosis”, represents a specific variant of thrombotic microangiopathy characterized by glomerular endothelial swelling with loss of endothelial fenestrae and occlusion of the capillary lumens; the lesion, however, is not specific of pre-eclampsia, as it was found in women with normal pregnancy as well as in both non-proteinuric and proteinuric hypertension and is consequently not, as earlier believed, pathognomonic of pre-eclampsia *(Shah & Khalil, 2015*; *Vieira & Khalil, 2016* and *Bellomo, 2018)*.

The cardinal features of this syndrome are new-onset hypertension (beyond the 20th gestation week) and proteinuria >300 mg/ 24h. Recent classifications may consider a diagnosis of preeclampsia in the absence of proteinuria, when signs of maternal organ or feto-placental

dysfunction are present, *(Magee et al., 2015)*.

The clinical course of severe pre-eclampsia is characterized by the progressive deterioration of both maternal and fetal conditions. Although delivery is still the only definitive treatment, expectant management for early onset severe pre-eclampsia has been shown to have beneficial effects on neonatal outcomes *(Sakae et al., 2017)*.

A widespread consensus exists on the necessity of treating severe hypertension (≥160 mmHg systolic or 100-110 mmHg diastolic). Treatment is directed at achieving a BP around 140 mmHg systolic and 85-90 mmHg diastolic. Over-correction of BP is discouraged as it may lead to maternal-fetal hypoperfusion. Caution is advised when using short-acting nifedipine, as it may cause profound hypotension and may potentiate side effects of $MgSO_4$ given for the prophylaxis or treatment of preeclampsia *(Dennis et al., 2015* and *Too and Hill., 2013)*.

In women with severe PE, the use of magnesium sulfate ($MgSO_4$) is indicated for prevention and control of acute convulsions. Several randomized trials have compared the efficacy of $MgSO_4$ with other anticonvulsants in women with eclampsia, and the rates of recurrent seizures and maternal death were significantly reduced with $MgSO_4$ as compared with other anticonvulsants *(Oliveira et al., 2017)*.

Although, there are a few studies assessing the effect of magnesium sulfate on fetal circulation, their results have showed a reduction in the resistance index, pulsatility index and systolic/diastolic ratio in the uterine and umbilical arteries *(Rezavand et al., 2016)*. Intravenous administration of magnesium sulfate in pregnant women with severe preeclampsia resulted in a decrease in umbilical artery, uterine artery, and fetal middle cerebral artery Doppler indices with reduced resistance to blood flow in these vessels *(Maged et al., 2016)*.

The aim of this study was to assess the effect of magnesium sulfate injection on Doppler indices and fetal circulation in cases of severe pre-eclampsia.

PATIENTS AND METHODS

This was a prospective study that was conducted on one hundred pregnant women suffering from pre-eclampsia, selected from the Obstetrics and Gynecology Department of Al-Hussein University Hospital during the period from Jan 2018 to Dec 2018.

Inclusion criteria:

Severe pre-eclampsia (BlP 160/110 mmHg, Proteinuria), single pregnancy, gestational age 24-34 week, intact membranes and abnormal umbilical artery Doppler wave-form (Absent end diastolic flow).

Exclusion criteria:

Twin pregnancy, chronic hypertension, fetal death, fetal malformation, known intolerance to MgSO4, chronic diseases as anemia and diabetes mellitus, reversed end diastolic flow and all patients were subjected to the following:

- **Complete medical history.**
- **Clinical Examinations.**
- **Laboratory Investigations:** Complete blood picture, urine

analysis "for proteinuria", random blood sugar and kidney function tests including blood urea and serum creatinine.

- **Radiological Investigations:** Doppler ultrasound examination of the pregnant women for detection of: Uterine artery index and umbilical artery index

All patients with severe pre-eclampsia were admitted to the high-risk unit. Participants gave informed consents before management, and approval by ethical committee was obtained.

$MgSO_4$ was given by IV route in a dose of 4 g IV loading dose administered over 15 min followed by 1 g/hour as a maintenance infusion dose. Duration of treatment did not exceed 24 hours. All patients were checked by ultrasound and Doppler examination for uterine artery and umbilical artery index after administration of $MgSo_4$ in therapeutic doses.

Primary outcome: Eclampsia, Fetal or Neonatal death (any death upto 28 day including stillbirth), Severe maternal morbidity (respiratory depression, cardiac arrest, coagulopathy, ICU admission), and Drug side effects.

Secondary outcome: Pre-eclampsia, Maternal mortality, Neonatal morbidity (APGAR score < 7 at 5 min), Admission to neonatal ICU, Mode of delivery for antepartum or intrapartum severe preeclampsia, Post-partum hemorrhage, and Abruptio placenta.

RESULTS

The demographic data of the studied groups showed that the age of group A ranged between 22-32 years with a mean age of 27.44±3.52 years while in group B the age ranged between 23-31 years with a mean age of 28.10±2.72 years there was no statistical significant difference between both groups of the study regarding age. The BMI of group A ranged between 22-41 with a mean BMI of 28.34±3.3 while in group B the BMI ranged between 23-35 with a mean value of 29.14±2.53 there was no statistical significant difference between both groups of the study regarding BMI ($P > 0.05$).

Laboratory findings: The AST in group A ranged from 27-49 with mean value 37.06±4.90 and in group B ranged from 29-46 with mean value 38.08±4.53. ALT in group A ranged from 27-49 with mean value 38.06±4.90 and in group B ranged from 29-46 with mean value 38.08±4.53. There was no statistical significant difference between the two studied groups regarding AST and ALT ($P > 0.05$). The Blood urea in group A ranged from 24-128 with mean value 55.34±15.427 and in group B ranged from 22-46 with mean value 30±6.224. S. creatinine in group A ranged from 0.75-2.1 with mean value 1.2876±0.297 and in group B ranged from 0.325-1.1 with mean value 0.8025±0.213. There was statistical significant difference between the two studied groups regarding blood urea and S. creatinine ($P < 0.05$). The maternal Hb level in group A ranged from 9.9-16.0 with mean value 12.21±1.45 and in group B ranged from 9.7-15.0 with mean value 11.916±1.32. There was no statistical significant difference between the two studied groups regarding Hb conc. ($P > 0.05$) **(Table 1)**.

Table (1): Comparison between the two studied groups regarding laboratory findings

Groups / Laboratory findings	Group A "*Experimental group*"	Group B "*Control group*"	P Value
AST	37.06±4.90	38.08±4.53	> 0.05
ALT	38.06±4.90	38.08±4.53	> 0.05
Blood urea	55.34±15.43	58.88±13.72	> 0.05
S. creatinine	1.2876±0.30	1.3264±0.28	> 0.05
Hb conc	12.214±1.45	11.916±1.32	> 0.05

The systolic blood pressure in experimental group was significantly lower than the control group ($p<0.05$), while the diastolic blood pressure was less than the control but the difference was insignificant **(Table 2)**.

Table (2): Comparison between the two studied groups regarding blood pressure after treatment

Groups / Parameters	Group A "*Experimental group*"	Group B "*Control group*"	t-test P Value
Systolic blood pressure	161.5±9.25	170.2±10.3	< 0.001*
Diastolic blood pressure	120.6±7.65	128.5±8.65	< 0.001*

The umbilical artery Doppler finding on admission showed an increasing in PI, RI and S/D ratio than the normal value, while the PSV showed decrease than the normal value. In comparing the two studied group on admission, it was found that there was no significant difference between the two groups regarding all umbilical Doppler studied parameters. There was a significant decrease in both PI and RI in experimental group less than the control group, while there was a significant increase in PSV in experimental group more than the control group, while S/D ratio show a decrease in experimental group but this decrease was insignificant **(Table 3)**.

Table (3): Comparison between the two studied groups regarding umbilical artery Doppler before and after treatment

Groups / U/A Doppler Before treatment	Group A "*Experimental group*"	Group B "*Control group*"	t-test P Value
PI	1.14±0.095	1.16±0.089	> 0.05
RI	0.64±0.046	0.66±0.051	< 0.05*
S/D ratio	2.95±0.246	2.96±0.269	> 0.05
PSV	38.48±2.960	38.22±2.940	> 0.05
U/A Doppler After treatment			
PI	0.95±0.086	1.15±0.105	< 0.001*
RI	0.59±0.054	0.65±0.046	< 0.001*
S/D ratio	2.61±0.186	2.95±0.227	< 0.001*
PSV	42.9±3.900	38.6±3.217	< 0.001*

The comparison between the two studied groups regarding maternal complications, regarding incidence of eclampsia in group A was 6.0%, while in control group was 24.0%, there was a significant increase in the incidence of eclampsia in control group more than the exponential group, also the HELLP in group B was significantly higher than group A ($p < 0.05$). The incidence of different neonatal complication was higher in group B "control group" more than group A "Experimental group, but this increase was insignificant. The neonatal complications included preterm, IUGR, NICU, still birth and Apgar score less than 7 at 5 min. **(Table 4)**.

Table (4): Comparison between the two studied groups regarding maternal complications and neonatal complications.

Groups / Maternal complications	Group A "*Experimental group*"		Group B "*Control group*"		P Value
	No.	**%**	**No.**	**%**	
Eclampsia					
Yes	3	6.0	12	24.0	0.012
No	47	94.0	38	76.0	
HELLP					
Yes	9	18.0	19	38.0	0.0256
No	41	82.0	31	62.0	
Neonatal complications					
Preterm	4	8.0	8	16.0	> 0.05
IUGR	6	12.0	7	14.0	> 0.05
NICU	4	8.0	9	18.0	> 0.05
Still birth	1	2.0	3	6.0	> 0.05
APGAR <7 at 5 min.	5	10.0	8	16.0	> 0.05

In group "A" 24.0% had normal vaginal delivery, while in group "B" 10.0% only delivered normal, there was an increasing in normal delivery in experimental group but this increasing was insignificant **(Table 5)**.

Table (5): Comparison between the two studied groups regarding mode of delivery

Groups / Mode of delivery	Group A "*Experimental group*"		Group B "*Control group*"		P Value
	No.	%	No.	%	
NVD	12	24.0	5	10.0	> 0.05
C.S.	38	76.0	45	90.0	

DISCUSSION

Our study revealed that there was no significant difference between both groups regarding age and BMI, this results obey the inclusion criteria, with normal distribution of both age and BMI to eliminate the effect of the demographic data on the net results.

Abdelrahman and his Colleagues (2019) found in their study that there was no significant difference between both groups of their study regarding age and BMI that run in line with our results. Liver functions tests "AST and ALT" showed insignificant difference in both studied groups. In agreement with our results, *Peralta et al. (2014)* found no difference in levels of AST, ALT, and total bilirubin between women with preeclampsia and normal control subjects.

Our study revealed a non-significant difference between both groups regarding serum urea and serum creatinine as well as hemoglobin concentration. *Ekun and his Coworkers (2018)* found in their study that there was a significant increase in the serum blood urea and serum creatinine in cases of preeclampsia which may be due to decreased urinary clearance secondary to reduced glomerular filtration rate and increased reabsorption and this findings were conflicting with our results.

Patil and his Colleagues (2016) found a significant elevation of blood urea and serum creatinine in cases of severe preeclampsia than those with mild preeclampsia or controls which disagreed with our study.

In our study, on comparing between the two studied groups regarding blood pressure after treatment, it was found that the systolic blood pressure in experimental group was significantly lower than the control group, while the diastolic blood pressure was less than the control but the difference was insignificant.

In agreement with our study, *Takenaka et al, (2016)* found that systolic and diastolic BPs after administration of magnesium sulfate were significantly lower than those before administration. In most effective cases, BP decreased to the mild level range for at least 2 h after administration. *Belfort et al. (2013)* reported that 45.7% of patients with severe preeclampsia decreased their BPs by loading 4–6 g of magnesium sulfate.

Our study revealed a significant decrease in umbilical artery Doppler parameters including pulsatility index, RI, S/D ratio and PSV in patients with magnesium sulfat administration. *Maged and his Colleagues (2016)* concluded in their study that the use of magnesium sulfat in cases of severe preeclampsia resulted in a decrease in umbilical artery Doppler index with reduced resistance to blood flow in these vessels which run in

lines with our results. *Rezavan and his Colleagues (2016)* found that there was a significant decreasing effect on umbilical artery pulsatility index of women with severe PE.

Dasgupta and his Coworkers (2012) found in a randomized placebo controlled trial after full dosage of prophylactic magnesium sulfate in preeclampsia, reported that post-magnesium sulfate UA (PI) dropped fundamentally in contrast with pre-magnesium sulfate which runs in line with our study. *Rantonen and his Colleagues (2001)* found that the use of $MgSO_4$ resulted in decrease of the uterine artery. Therefore, the hypothesis that the vasodilator effect of the magnesium was more evident where the higher vascular resistance was found confirmed.

In our results, it was found that maternal complications in group A was significantly lower than the complication in group B, which include of eclampsia and HELLP. On the other hand, the neonatal complication which include of preterm, IUGR, NICU, still birth and APGAR <7 at 5 min showed insignificant difference between the two studied groups. Finally the mode of delivery showed a non-significant increase in normal delivery in group A "experimental group" more than the control group.

Oliveira and his Colleagues (2017) concluded in their study that, after the administration of $MgSO_4$, an increase in the impedance to flow in the ophthalmic artery and consequently a reduction in cerebral perfusion after the use of $MgSO_4$. This can explain how $MgSO_4$ protects women with severe PE against cerebral damage and prevents acute convulsions in these patients which results in decrease in complications in preeclamptic patients which inagreement with our results. *Adekanmi and his Colleagues (2019)* concluded that the uterine artery PI is the best predictor of PE, whereas the combinations of uterine and umbilical arteries PSV best predict severity of PE among high-risk pregnant women as well as it has no effect on fetal outcome.

Abdelrahman et al., (2019) found that there was no significant difference between both groups of their study regarding the effect on fetal outcome which disagree with our results. *Sedek (2015)* found that there was a significant decrease in the uterine artery parameters by Doppler (UAPI, RI, S/D) after injection of magnesium sulfate in pre-eclampsia patients which was in agreement with our results. *Souza and his Colleagues (2010)* reported that there was a significant reduction of the RI, PI and S/D of both uterine arteries.

CONCLUSION

We can conclude that $MgSO_4$ proved to cause many hemodynamic changes as it has vasodilator effect on maternal and fetal blood vessels. Doppler indices in the umbilical arteries are significantly changed after administration of $MgSO_4$ in patients with severe preeclampsia so it should be given to all patients with severe preeclampsia.

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تأثير حقن عقار كبريتات الماغنيسيوم على مؤشرات الفحص بالموجات فوق الصوتية والدورة الدموية الجنينية فى حالات تسمم الحمل الشديدة

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خلفية البحث: يشار في النساء المصابات بتسمم الحمل الشديد إلى استخدام كبريتات المغنيسيوم للوقاية من التشنجات الحادة والسيطرة عليها. وقد قارنت العديد من التجارب فعالية كبريتات المغنيسيوم مع مضادات التشنجات الأخرى عند النساء المصابات بتسمم الحمل، وانخفضت معدلات النوبات المتكررة ووفيات الأمهات بشكل كبير مع كبريتات المغنيسيوم مقارنة بمضادات التشنجات الأخرى.

الهدف من البحث: تقييم تأثير حقن كبريتات المغنيسيوم على مؤشرات دوبلر ودورة الجنين في حالات تسمم الحمل الشديد.

المريضات وطرق البحث: كانت هذه دراسة استطلاعية أجريت على مائة امرأة حامل يعانين من تسمم الحمل، تم اختيارها من قسم أمراض النساء والولادة في مستشفى الحسين الجامعي فى الفترة من يناير 2018 إلى ديسمبر 2018، وقد تم تقييم الحالات قبل وبعد اعطاء كبريتات المغنسيوم بواسطة الموجات فوق الصوتية لقياس معدل سريان الدم بالشريان السري.

نتائج البحث: أظهرت النتائج تحسن كبير في قياسات الدوبلر يأتي مع المجموعات المعالجة بكبريتات المغنيسيوم أكثر من المجموعة الضابطة.

الاستنتاج: كبريتات المغنيسيوم له تأثير موسع للأوعية الدموية للأم والجنين. وقد تغيرت مؤشرات دوبلر في الشرايين السرية بشكل ملحوظ بعد إعطاء كبريتات المغنيسيوم في المرضى الذين يعانون من تسمم الحمل الشديد.