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Doppler Indices "UAI" Enfluence by $MgSO_4$ and Fetal Circulation in Cases of Severe Pre-Eclampsia

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Abstract

Background: Preeclampsia, is development of new onset hypertension with proteinuria and leads to endothelial disorder with multiple organ involvement in pregnant women. Severe pre-eclampsia is characterized by the progressive deterioration of both mothers and fetus. The use of $MgSO_4$ is beneficial in severe PE.

Aim of Study: This study aimed 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 comparative study conducted on 50 pregnant female with severe pre-eclampsia, selected from the Obstetrics and Gynecology Department of Damanhour Teaching Hospital during the period from Jan 2019 to Dec 2020 and were classified into group (A) and (B) each included 25 women (A) treated by ordinary management with $MgSO_4$ (I.V) and (B) with ordinary treatment of preeclampsia only. Doppler is used to assess the UA for follow-up.

Data were fed to the computer using IBM SPSS software package version 20.0.

Results: Our results revealed a non-significant statistical difference between both groups regarding demographic data of women, investigations done except AST and ALT there was a significant elevation in group B; also, there was significant decrease in UAI, UARI and systolic diastolic ratio of UA.

In our study there was no difference between both groups regarding post-therapy complication either fetal or maternal.

Conclusion: We can conclude that $MgSO_4$ when used decreases the incidence of complications in severe PE as well as reduces the uterine artery indices with beneficial effect on fetus.

Key Words: *Uerine Artery Index: UAI – Intrauterine Fetal Death: IUFD – PE: Preeclampsia.*

Introduction

Preeclampsia, formerly known as toxemia of pregnancy, can be defined as new onset hypertension, after the 20th week of gestation, associated with proteinuria and/or other signs of end-organ damage. The term eclampsia refers to the occurrence of seizures that cannot be attributed to other causes in a woman with pre-eclampsia **[1]**.

The incidence of pre-eclampsia is estimated to range between 2.5 and 5% **[2]**. Pre-eclampsia complicates about 3% of pregnancies in the USA, and Scandinavian countries **[3]**. Higher incidence rates have been observed, such as 8.7% in a study from Canada **[2]**. Such wide variations are probably related to intrinsic characteristics of the populations studied and to the diagnostic criteria adopted **[1]**.

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 **[1,4,5]**.

The cardinal features of this syndrome are new-onset hypertension (beyond the 20th gestation week) and proteinuria >300mg/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 **[6]**.

According to ACOG guidelines, features of severe pre-eclampsia include any of the following: (1) Hypertension: systolic >160mmHg or diastolic >110mmHg on two occasions at least 4h apart

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while the patient is on bed rest; (2) Thrombocytopenia (platelet count <100,000); (3) Impaired liver function, severe persistent right upper quadrant (RUQ), or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses or both; (4) New development of renal insufficiency; (5) Pulmonary edema; and (6) New-onset cerebral or visual disturbances **[7]**.

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 **[8]**.

A widespread consensus exists on the necessity of treating severe hypertension (≥160mmHg systolic or 100-110mmHg diastolic). Treatment is directed at achieving a BP around 140mmHg systolic and 85-90mmHg 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 **[9,10]**.

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 **[11]**.

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 **[12]**. 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 **[13]**.

This study aimed to assess the effect of Magnesium sulfate injection on Doppler indices and fetal circulation in cases of severe pre-eclampsia.

Patients and Methods

This is a prospective comparative study carried out on fifty pregnant women suffered from pre-eclampsia selected from the Obstetrics and Gynecology Department of Damanhour Teaching Hospital during the period from Jan. 2019 to Dec. 2020.

The following females (1) Severe pre-eclampsia (BP >160/110, proteinuria) Singleton fetus (2) Singleton full term fetus as diagnosed from LMP and 1^{st} trimester ultrasound examination, (3) Intact membranes; (4) Abnormal umbilical artery Doppler wave-form (absent end-diastolic flow) all were included in the study. Women with (1) Twin pregnancy, (2) Chronic hypertension, (3) Fetal death; (4) Fetal malformation; (5) Known intolerance to $MgSO_4$; (6) Chronic disorders as DM, Anemia, (7) Reversed end-diastolic flow of umbilical artery were excluded from this study.

All cases signed a well-informed written consent to declare their agreement to be enrolled in the study as agreed upon by the ethical committee.

All cases in this study will subjected to; (1) history taking "personal, present, past, menstrual, obstetric histories"; (2) complete clinical "general, local and gynecological examination including pelvic and rectal" examination and fundus examination for papilledema; (3) investigations [routine "urinanalysis, random blood sugar, kidney function tests as urea and creatinine" and ultrasonographic examination "assess last menstrual period and gestations age and uterine artery index"].

$MgSO_4$ was given by IV route in a dose of 4gm IV loading dose administered over 15min followed by 1gm/hour as a maintenance infusion dose. Duration of treatment should not normally exceed 24 hours.

All patients will be checked by ultrasound and Doppler examination for uterine artery and umbilical artery index after administration of $MgSO_4$ in therapeutic doses.

Data were analyzed using IBM SPSS software package version 20.0 (Belmont, Calf, 2013). Data were collected in tables then analyzed in regarding to Chi square (x^2) and *p*-value less than 0.05 were considered significant.

Results

This was a prospective study that was conducted on one hundred pregnant women selected from the Obstetrics and Gynecology Department of Damanhour Teaching Hospital during the period from Jan. 2019 to Dec. 2020.

Cases of the study were classified into two groups one of them was given the ordinary therapy of pre-eclampsia while the second group was given the ordinary pre-eclampsia in addition to magnesium sulfate by injection to assess the effect of Magnesium sulfate injection on Doppler indices and fetal circulation in cases of severe pre-eclampsia.

The age of group A ranged between 22-35 years with a mean age of 29.38±3.26 years while in group B the age ranged between 19-34 years with a mean age of 30.1±2.6 years and the statistical analysis revealed that there was no statistical significant difference between both groups of the study regarding age (p=0.902) (Table 1).

The BMI of group A ranged between 21-39 with a mean BMI of 26.55±3.3 while in group B the BMI ranged between 20-35 with a mean value of 28.4±2.6 and the statistical analysis revealed that there was no statistical significant difference between both groups of the study regarding BMI (p=0.180) (Table 1).

Table (1): Demographic data of both groups of the study.

Variable	Group A	Group B	p-value
Age:			
Range	22-35	19-34	0.902
Mean ± S.D	29.38±3.26	30.1±2.6	(NS)
BMI:			
Range	21-39	20-35	0.180
Mean ± S.D	26.55±3.3	28.4±2.6	(NS)

All cases of both groups A and B had lower limb edema (25/25, 100%), proteinuria (25/25, 100%) and elevated blood pressure (25/25, 100%) and the statistical analysis revealed that there was no significant difference between both groups regarding these variable (p=1.0).

AST of patients of group A ranged between 27-49IU/dL with a mean value of 36.06±4.2IU/dL while in group B it ranged between 26-48IU/dL with a mean value of 38.08±4.5IU/dL and the statistical analysis revealed that there was a statistical significant increase in AST level in patients of group B than those of group A (p=0.035) (Table 2).

ALT of patients of group A ranged between 26-42IU/dL with a mean value of 37.1±3.8IU/dL while in group B it ranged between 24-47IU/dL with a mean value of 36.5±4.2IU/dL and the statistical analysis revealed that there was a statistical significant increase in ALT level in patients of group B than those of group A (p=0.031) (Table 2).

Serum urea of patients of group A ranged between 33-125mg/dL with a mean value of 53.8± 12.7mg/dL while in group B it ranged between 28-95mg/dL with a mean value of 50.88±11.7mg/dL and the statistical analysis revealed that there was no statistical significant difference between both groups regarding serum blood urea level (p=0.228) (Table 2).

Serum creatinine of patients of group A ranged between 0.71-2.3mg/dL with a mean value of 1.24±0.23mg/dL while in group B it ranged between 0.85-2.1mg/dL with a mean value of 1.33± 0.28mg/dL and the statistical analysis revealed that there was no statistical significant difference between both groups regarding serum creatinine level (p=0.499) (Table 2).

Hemoglobin concentration of patients of group A ranged between 10-15.5gm/dL with a mean value of 13.1±1.4gm/dL while in group B it ranged between 9.2-14.8gm/dL with a mean value of 12.2±1.3gm/dL and the statistical analysis revealed that there was no statistical significant difference between both groups regarding hemoglobin concentration (p=0.273) (Table 2).

Table (2): Laboratory data of both groups of the study.

Variable	Group A	Group B	p-value
AST			
Range	27-49	26-48	0.035
Mean ± S.D	36.06±4.2	38.08±4.5	(S)
ALT:			
Range	26-42	24-47	0.031
Mean ± S.D	37.1±3.8	36.5±4.2	(S)
Blood urea:			
Range	33-125	28-95	0.228
Mean ± S.D	53.8±12.7	50.88±11.7	(NS)
Serum creatinine:			
Range	0.71-2.1	0.85-2.1	0.499
Mean ± S.D	1.24±0.23	1.33±0.28	(NS)
Hb concentration:			
Range	10-15.5	9.2-14.8	0.273
Mean ± S.D	13.1±1.4	12.2±1.3	(NS)

Uterine artery pulsatility index in group A ranged between 1-3.3 with a mean value of 2.91± 0.68 while in group B it ranged between 1.25-2.55 with a mean value of 1.74±0.28 and the statistical analysis revealed that there was a significant decrease in UAI in group B than group A (p=0.034) (Table 3).

Uterine artery resistant index in group A ranged between 1-3.05 with a mean value of 1.78±0.54 while in group B it ranged between 0.95-2.3 with a mean value of 1.33±0.43 and the statistical analysis revealed that there was a significant decrease in resistant index in group B than group A (p= 0.01) (Table 3).

Systolic diastolic ratio during uterine artery Doppler in group A ranged between 4.2-5.1 with a mean value of 4.93±1.31 while in group B it ranged between 4.05-4.88 with a mean value of 3.98±1.21 and the statistical analysis revealed that there was a significant decrease in S/D ratio in group B than group A (p=0.01) (Table 3).

Table (3): UAI of both groups of the study.

UAI	Group A	Group B	p-value
UAPI:			
Range	1-3.3	1.25-2.55	0.034
Mean ± S.D	2.91±0.68	1.74±0.28	(S)
RI:			
Range	1-3.05	0.95-2.3	0.01
Mean ± S.D	1.78±0.54	1.33±0.43	(S)
S/D:			
Range	4.2-5.1	4.05-4.88	0.01
Mean ± S.D	4.93±1.31	3.98±1.21	(S)

Seven cases of group A (7/25, 28%) developed complications in the form of eclampsia (three cases 3/25, 12%) and IUFD (four cases 4/25, 16%) and the remaining cases of group A passed normal without complications (18/25, 72%) while in group B eight (8/25, 32%) developed complications in the form of eclampsia in four cases (4/25, 16%) and IUFD in four cases (4/25, 16%) and the statistical analysis revealed that there was no significant statistical difference between both groups of the study regarding complications either for mothers or for fetus (p=0.231 and 1.0 respectively) (Table 4).

In ten of cases of group A (5/25, 20%) the pregnancy terminated by NVD while 20 cases (80%) the pregnancy was terminated by CS while in group B three cases (3/25, 12%) the pregnancy terminated by NVD while 22 cases (88%) the pregnancy was terminated by CS and the statistical analysis revealed that there was a significant statistical increase in NVD in group A than in group B (p=0.04) while there was no statistical significant difference between both groups of the study regarding termination of pregnancy by CS (p=0.783) (Table 4).

Table (4): Follow-up data of both groups of the study.

Variable	Group A		Group B		p-value
	No.	%	No.	%	
Mother outcome:					
Complicate	3	12	4	16	0.231
Normal	22	88	21	84	(S)
Fetal outcome:					
IUFD	4	16	4	16	1.0
Normal	21	84	21	84	(NS)
Termination of pregnancy:					
NVD	5	20	3	12	0.04 (S)
CS	20	80	22	88	0.783 (NS)

Discussion

Preeclampsia (PE) is one of the most important causes of maternal death and the acute cerebral complications in women with PE are responsible for at least 75% of these deaths. Although both vasospasm and cerebral over-perfusion may be associated with eclamptic seizures, in most cases, the cerebral damage in women with PE is associated to cerebral over-perfusion rather than ischemia **[11].**

Preeclampsia, especially in severe cases, is one of the important causes of perinatal morbidity and mortality. Fetal effects of preeclampsia like fetal distress which caused by hypoxia is identified in preeclampsia. The most likely cause of hypoxia and distress is blood disorders **[12].**

Preeclampsia (PE) is a multi-system disorder of widespread vascular endothelial malfunction and vasospasm, characterized by new onset of hypertension and either proteinuria or end-organ dysfunction or both after 20 weeks of gestation in a formerly normotensive woman. Albeit most influenced pregnancies convey at term or close term with adverse maternal and fetal outcome, these pregnancies are at expanded danger for maternal and fetal mortality or morbidity worldwide **[14].** Preeclampsia is further sub classified into, mild and severe, early onset and late-onset syndrome **[7,15].**

Magnesium sulfate is one of the most commonly used obstetric drugs, and it is also known ASA standard therapy in women with severe preeclampsia. This drug prevents maternal complications of severe preeclampsia, while it affects the fetal nervous or perfusion system. As mentioned by P. Vigil-De and Sibai BM, magnesium sulfate is applied for the treatment of fetal distress and intrauterine fetal resuscitation. On the other hand,

several studies have confirmed Doppler sonography in the evaluation of vascular status of the fetus **[12].**

This prospective study was conducted on 100 cases of preeclampsia classified into two groups each contains 50 cases one of them subjected to ordinary therapeutic protocols and the second group subjected to the same protocol in addition to magnesium sulfate.

Our study revealed that there was no significant difference between both groups regarding age and BMI or clinical symptoms and signs.

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 **[15].**

Ekun and his coworkers, (2018), found no significant difference between both groups of their study regarding age which was in agree with our results **[16].**

Liver functions tests "AST and ALT" showed a significant increase in both groups groups. Ekun and his coworkers, (2018), found in their study that there was a significant increase in the serum level of of liver enzymes (AST and ALT) in cases of preeclampsia which was in agree with our results **[16].**

Patil and his colleagues, (2016), in their study found a significant elevation of liver enzymes (AST and ALT) in cases of severe preeclampsia which was inagreement with our study **[17].**

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 may be due to decreased urinary clearance secondary to reduced glomerular filtration rate and increased reabsorption and this findings were conflicting with our results **[16].**

Patil and his colleagues, (2016), in their study found a significant elevation of blood urea and serum creatinine in cases of severe preeclampsia than those with mild preeclampsia or controls which disagree with our study **[17].**

Rezavand and his colleagues, (2016), found in their study that there was no significant effect of injecting $MgSo_4$ on the hemoglobin concentration of the mother with severe preeclampsia which runs in line with our results **[12].**

Our study revealed a significant increase in uterine artery pulsatility index in patients with protocol that added to it magnesium sulfat than the ordinary protocols.

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 uterine artery index as a Doppler index with reduced resistance to blood flow in these vessels which run in lines with our results **[13].**

Rezavand and his colleagues, (2016), found in their study that there was a significant decreasing effect on uterine pulsatility index of women with severe PE which agree with our results **[12].**

Dasgupta's 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 and MCA (PI) dropped fundamentally in contrast with pre-magnesium sulfate which runs in line with our study **[18].**

Rantonen and his colleagues, (2001), found in their study 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 was confirmed which was in agreement with our results **[19].**

In spit of increase the rate of maternal complications in group A but this was significantly differs while fetal outcome and the termination of pregnancy also didn't show significant difference between both groups.

Oliveira and his colleagues, (2017), concluded in their study that after the administration of MgSO4 reflect 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 **[11].**

Jamileh in his study documented that Rantonen and his colleagues, (2001), found in their study the decrease rate of complications with the use of

$MgSO_4$ in severe pre-eclamptic pregnant women was in agreement with our results **[19,20].**

Rezavand and his colleagues, (2016), found in their study that there was no significant effect of injecting $MgSo_4$ on fetal parameters and has no effect on fetal outcome which was in agreement with our results **[12].**

Adekanmi and his colleagues, (2019), concluded in their study 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 and this run in line with our results; in addition they found that more women with severe PE (45.6%) had operative delivery through caesarean section. All the women who had abortion, before GA of 28 weeks, were women with PE and this disagree with our results [21].

Abdelrahman and his colleagues, (2019), found in their study that there was no significant difference between both groups of their study regarding the effect on fetal outcome which disagree with our results **[15].**

Sedek, (2015), found in his study 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 [22].

Souza and his colleagues, (2010), reported in their study that there was a significant reduction of the RI, PI and S/D of both uterine arteries **[23].**

Conclusion:

We can conclude that Vitamin D supplementation during pregnancy is essential to help in normal development of the fetus and prevent fertal growth retardation (FGR). So, we recommend vit-D supplementation for pregnant women to prevent these events.

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قياس مدى تأثر مؤشرات الدوبلر بتركيز سلفات الماغنسيوم والدورة الدموية الجنينية فى حالات ارتفاع ضغط الدم الشديدة مع الحمل (تسمم الحمل)

الخلفية العلمية : تسمم الحمل، هو تطور ارتفاع ضغط الدم الجديد مع البيلة البروتينية ويؤدى إلى اضطراب بطانى مع تورط أعضاء متعددة فى النساء الحوامل. يتميز تسمم الحمل الحاد بالتدهور التدريجى لكل من الأمهات والجنين. استخدام $MgSO_4$ مفيد فى PE الشديد.

الهدف من البحث : هدفت هذه الدراسة إلى تقييم تأثير حقن كبريتات المغنيسيوم على مؤشرات دوبلرو الدورة الدموية الجنينية فى حالات تسمم الحمل الشديد.

المرضى وطرق البحث : كانت هذه دراسة مقارنة استشرافية أجريت على ٥٠ امرأة حامل مصابة بتسمم الحمل الحاد، تم اختيارهن من قسم أمراض النساء والتوليد فى مستشفى دمنهور التعليمى خلال الفترة من يناير ٢٠١٩ إلى ديسمبر ٢٠٢٠ وتم تصنيفهن إلى المجموعة (أ) و (ب) شملت كل منهم ٢٥ امرأة (أ) عولجت من قبل الإدارة العادية باستخدام $MgSO_4$ I.V و (B) مع العلاج العادى لتسمم الحمل فقط : يستخدم دوبلر لتقييم AU للمتابعة تم تغذية البيانات إلى الكمبيوتر باستخدام حزمة برامج IBM SPSS الإصدار ٢٠٠٠.

النتائج :وكشفت نتائجنا عن وجود فرق إحصائى غير ذى دلالة بين المجموعتين فيما يتعلق بالبيانات الديموغرافية للنساء، وكانت التحقيقات التى أجريت باستثناء AST وALT هناك ارتفاع كبير فى المجموعة باء، أيضاً، كان هناك انخفاض كبير فى UAI و UARI ونسبة الانبساطى الانقباضى من UA فى دراستنا لم يكن هناك فرق بين كلتا المجموعتين فيما يتعلق بمضاعفات ما بعد العلاج سواء الجنين أو الأم.

الخلاصة : يمكننا أن نستنتج أن $MgSO_4$ عند استخدامه يقلل من حدوث مضاعفات فى PE الشديد وكذلك يقلل من مؤشرات الشريان الرحمى مع تأثير مفيد على الجنين.