

Different protocols of Magnesium Sulfate in Management of Severe Pre-eclampsia

Dr. Ashraf Elshahat Elsayed Ahmed M.B.B. Ch., MSc, MD

Department of Obstetrics and Gynecology, Faculty of Medicine, Al Azhar University, Cairo, Egypt.
Email: ashraf.2380@yahoo.com

Abstract: Background: Preeclampsia is a syndrome of extensive vascular endothelial malfunction and vasospasm that occurs after 20 weeks' gestation. MgSO₄ is the drug of choice for management of women with eclampsia. Protocols for the administration of MgSO₄ have changed over the years, but have not well formally evaluated. **Objectives:** To determine the minimal effective dose of magnesium sulfate in handling cases of severe preeclampsia and prevention of eclampsia and to define whether only loading dose of magnesium sulfate is effective in the prevention of eclampsia. **Material and method:** A randomized controlled study was performed in the Obstetrics & Gynecology Department, El-Hussein and Bab El-Shearya Hospital, Al Azhar University during the period from January 2019 to the end of June 2019 included 300 pregnant women with criteria of severe preeclampsia and was divided into three groups; Group A=100 patients who took an only loading dose of MgSO₄ with no postpartum maintenance sulfate. Group B =100 patients given reduced doses of MgSO₄ (only for 12 hours) in the postpartum period. Group C=100 patients given a full dose of maintenance MgSO₄ (for 24 hours) in the postpartum period. **Results:** Three hundred patients with severe preeclampsia were enlisted in our study, there is a substantial evidence supports the use of magnesium sulfate for the prevention and treatment of eclampsia, there was no significant difference between occurrence of eclampsia in the three groups after either administration of loading dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or maintenance dose for 24 hours in the studied patients. **Conclusion:** In view of the identical effectiveness, rarer side effects, simplicity of monitoring and cost-reduction of the loading dose in the controlling of pre-eclampsia is better to other regimes of administration requiring several doses.

[Ashraf Elshahat Elsayed Ahmed. **Different protocols of Magnesium Sulfate in Management of Severe Pre-eclampsia.** *Stem Cell* 2019;10(3):10-15]. ISSN: 1945-4570 (print); ISSN: 1945-4732 (online). <http://www.sciencepub.net/stem>. 2. doi:[10.7537/marsscj100319.02](https://doi.org/10.7537/marsscj100319.02).

Keywords: Severe preeclampsia, Magnesium sulfate, Loading dose, Abbreviated dose.

1. Introduction

Preeclampsia is one of the leading cause of maternal and fetal morbidity and mortality worldwide. The basic clinical features of the condition are hypertension and proteinuria occurring after 20 weeks' gestation in women who were not previously known to be hypertensive ⁽¹⁾. Pre-eclampsia often affects young and nulliparous women, whereas older women are at great risk of chronic hypertension with superimposed preeclampsia ⁽²⁾.

Magnesium sulfate is extensively used in obstetrics and is a drug of choice in two important complications of pregnancy, preeclampsia and preterm labor. Magnesium sulfate is used to prevent seizures in preeclampsia patients. ⁽³⁾ Regimens for the administration of this drug have changed over the years, but have not yet been formally evaluated. ⁽⁴⁾

At one time, MgSO₄ was given according to Pritchard regime in which 5 grams of magnesium sulfate was administered four-hourly for 24 hours after loading with 14 grams. It was observed that many patients did not receive maintenance therapy due to suspicion of toxicity but they did not convulse any further. On the basis of this observation, many

studies were planned to compare the efficacy of loading dose of magnesium sulfate versus the standard regime in the management of preeclampsia to prevent fits.

Ehrenberg and Mercer studied abbreviated postpartum magnesium administration in 200 women with mild pre-eclampsia. No cases of this study or other studies using the 24-hour magnesium infusion complicated by eclampsia. ⁽⁵⁾

Usage of magnesium sulfate would be reinforced if rules and proposals for practice could be founded on solid proof about the near impacts of alternative regimens. It is therefore relevant to assess the pros and cons of alternative strategies for administration. As the utilization of magnesium sulfate requires ordinary supervision via skilled staff, which is excessive, and higher percentages might be related with a more serious danger of reactions and antagonistic occasions, it is especially critical to evaluate the base powerful dose and span of treatment. ⁽⁶⁾

In our study, we aimed to assess the comparative effects of three regimens for the administration of magnesium sulfate when used for the care of women with severe pre-eclampsia.

2. Methodology

A randomized controlled study that compared three regimens for the administration of MgSO₄ used for the cases of severe preeclampsia that was performed in the Obstetrics & Gynecology Department, El-Hussein and Bab El-Shearya Hospital, Al- Azhar university during the period from January 2019 to the end of June 2019.

The study included 300 pregnant women presenting to the casualty unit diagnosed as a case of preeclampsia with criteria of severity in the form of one or more of the following:-

- Systolic blood pressure \geq 160.
- Diastolic blood pressure \geq 110.
- Proteinuria $>$ +2 by dip stick.
- Presence of alarming symptoms (headache, visual disturbance, epigastric pain, vaginal bleeding).

- Fetal growth restriction (IUGR)

Inclusion criteria: All Pregnant females with

- Gestational age \geq 20 weeks' gestation.
- Criteria of severe pre-eclampsia.
- Single or multi-fetal pregnancy.
- Primigravida or Multigravida.

Exclusion criteria: All Pregnant females with

- History of epilepsy.
- Diabetes mellitus.
- Chronic hypertension.
- Renal disease.
- Mild preeclampsia.
- Eclampsia.
- Gestation age $<$ 20 weeks' gestation.

After obtaining an informed consent the patients were subjected to the following:

- Careful history taking including age, parity, gestational age.

- Complete physical examination and assessment of the blood pressure.

- Urine analysis by dipstick.

- A blood sample was taken from the patient for laboratory investigations in the form of CBC, coagulation profile, liver function tests, and kidney function tests.

- Ultrasound was done for each patient for assessment of fetal wellbeing, liquor, and placenta.

- All women took initial MgSO₄ (6 grams of MgSO₄ on 250 ml ringer solutions over 20 minutes by IV drip).

Procedure: patients were randomized by simple randomization; a table of random numbers, a computer random number generator was used, patients were randomized into three categories: -

- **Group A** \rightarrow 100 patients who took an only loading dose of MgSO₄ (6 grams of MgSO₄ on 250

ml ringer solutions over 20 minutes) with no postpartum maintenance sulfate.

- **Group B** \rightarrow 100 patients given abbreviated doses of MgSO₄ (4 grams of MgSO₄ on 250 ml ringer solution over 4 hours every 4 hours by IV drip only for 12 hours) in the postpartum period.

- **Group C** \rightarrow 100 patients given a full dose of maintenance MgSO₄ (4 grams of MgSO₄ on 250 ml ringer solution over 4 hours every 4 hours by IV drip for 24 hours) in the postpartum period.

Statistical analysis

Data were statistically described in terms of mean \pm standard deviation (\pm SD). (ANOVA) test, Chi-square (χ^2) test was performed. *p* values less than 0.05 was considered statistically significant. Statistical analysis was done using Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA Ver.15 for Microsoft Windows.

3. Results

300 patients with severe preeclampsia were recruited for our study based on their presentation. The mean age of patients was; 27.13 years, SD 4.97. Mean gestational age was; 35.91 weeks, SD 2.23. Mean systolic BP was; 162.03 mmHg, SD 16.91. Mean diastolic BP was; 104.07, SD 13.237. as shown in **Table (1)**.

There was no significant difference between the occurrence of eclampsia in the three groups after either administration of loading dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients as shown in **Table (2)**

There was no significant difference between the occurrence of HELLP syndrome in the three groups after either administration of loading dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients as shown in **Table (3)**

There was highly significant difference between maternal ICU admission in the three groups after either administration of loading dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients where group C showing the highest rate for ICU admission while group A showing the lowest rate for ICU admission as shown in **Table (4)**.

In more detailed analysis of the significant difference between groups, we found that maternal ICU admission was highly significant between Group A and Group C and non significant between Group A & B as Group A shows the lowest percentage in maternal ICU admission while Group C shows the highest maternal ICU admission with *P* value less than .0001 which is highly significant as shown in **Table (5)**.

Table (1): Demographic features of the studied patients.

Group		Age	GA	SBP	DBP
A N= 100	Mean	27.05	35.23	163.00	104.22
	Std. Deviation	4.913	2.364	19.327	10.980
B N= 100	Mean	26.76	35.77	162.70	104.23
	Std. Deviation	4.216	2.25	17.135	10.731
C N= 100	Mean	26.64	35.59	160.21	100.50
	Std. Deviation	5.151	2.680	16.317	11.741
Total N= 300	Mean	27.13	35.91	162.03	104.07
	Std. Deviation	4.97	2.23	16.91	13.237
	P value	.973	.761	.877	.238

Table (2): Comparison between the occurrence of eclampsia after administration of MgSO₄ in the studied patients.

		Group			P-Value	
		A	B	C		
Eclampsia	No	Count	100	99	98	0.931
		% within Group	100.0%	99%	98%	
	Yes	Count	0	1	2	
		% within Group	0.0%	1%	2%	

Data are expressed as mean \pm standard deviation.
P= 0.931 = not significant.

Table (3): Comparison between the development of HELLP syndrome in the studied groups after administration of MgSO₄.

		Group			P-Value	
		A	B	C		
HELLP	No	Count	97	96	95	0.122
		% within Group	97%	96%	95%	
	Yes	Count	3	4	5	
		% within Group	3%	4%	5%	

Data are expressed as mean \pm standard deviation.
P= 0.122= NS= not significant.

Table (4): Comparison between groups regards maternal ICU admission after administration of MgSO₄

		Group			Total	P-Value	
		A	B	C			
MICU	No	Count	90	66	50	189	< 0.0001*
		% within Group	90%	82.5%	62.5%	78.8%	
	Yes	Count	10	14	30	51	
		% within Group	10%	17.5%	37.5%	21.3%	

Data are expressed as mean \pm standard deviation. P* < 0.0001*= highly significant.

Table (5): Comparison between maternal ICU admission in the group A vs group B, group B vs group C and group A vs group C after administration of MgSO₄

		Group			Total	Group			Total	Group		Total
		A	B			B	C			A	C	
MICU	No	Count	73	66	139	66	50	116	73	50	123	
		% within Group	91.3%	82.5%	86.9%	82.5%	62.5%	72.5%	91.3%	62.5%	76.9%	
	Yes	Count	7	14	21	14	30	44	7	30	37	
		% within Group	8.8%	17.5%	13.1%	17.5%	37.5%	27.5%	8.8%	37.5%	23.1%	
p value		0.101			0.005			0.0001				

Data are expressed as mean \pm standard deviation.

There was no significant difference between perinatal mortality in the outcome of pregnancy in the three groups after either administration of loading

dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients as shown in **Table (6)**.

Table (1): Comparison between perinatal mortality in the outcome of pregnancy in the studied groups after administration of MgSO₄

		Group			P-value	
		A	B	C		
Perinatal death	IUFD	Count	5	4	9	0.431
		% within Group	5.0%	4%	9%	
	neonatal mortality	Count	4	5	5	
		% within Group	4%	5.0%	5.0%	
	no	Count	91	91	86	
		% within Group	91%	91%	86%	

Data are expressed as mean \pm SD. P= 0.431 = NS= not significant.

IUFD= Intra-Uterine Fetal Death **NB**: Most cases of IUFD were due to accidental hemorrhage

4. Discussion

Preeclampsia is a major public health problem and one of the most cause of perinatal and maternal morbidity and mortality, which affects nearly 5% of pregnancies ⁽⁷⁾.

Magnesium sulfate for the prevention and treatment of women with eclampsia was enlisted based on strong evidence from many randomized trials ⁽⁸⁾.

The incidence of seizures in untreated pre-eclamptic women is approximately 3-4%, whilst for those receiving magnesium sulfate; the rate is 0.8-1% ⁽⁹⁾.

In our study, we tried to compare three regimens of administration of Magnesium Sulfate where 300 patients were recruited and divided into three groups. Each group contains 100 patients, the first group received only the loading dose of MgSO₄ and the second group received loading dose plus 12 hours'

maintenance dose while the last group received the loading dose and the full maintenance dose of MgSO₄ for 24 hours.

We found that there was no significant difference between the occurrence of eclampsia, HELLP syndrome, maternal side effects or prematurity & perinatal mortality and neonatal ICU admission in the three groups after either administration of loading dose of MgSO₄ only or administration of loading dose with maintenance dose for 12 hours or 24 hours in the studied patients.

However, there was a significant difference between maternal ICU admissions in the three groups (Group A, B & C) with the highest rate in Group C and the lowest rate in Group A.

In agreement with our study **Tabassum et al. (2009)** conducted their study on 100 women, 50 were given only bolus dose of magnesium sulfate and 50 were given the standard regime. All women with

severe pre-eclampsia and impending eclampsia were included in the study. Patients with pregnancy-induced hypertension and mild to moderate pre-eclampsia were excluded. 50 were given only bolus dose of magnesium sulfate and 50 were given the standard regime. They were observed for one week for the number of convulsions. They found that there was no significant difference in the two groups in term of occurrence of seizures, one patient developed to fit with Pritchard regimen. The rate of cesarean section was lower in group A, 12% versus 30% in group B ($p=0.05$).

Omkara Murth et al. (2013) conducted their study on 170 cases divided into two groups. 85 cases in each group. Each group had 50 eclampsia cases and 35 imminent eclampsia cases. The groups were compared with respect to age, gravidity, antihypertensive therapy, gestational age, antenatal care, type of eclampsia, need of, dose of MgSO₄ received, complications during MgSO₄ therapy and finally concluded that Low dose magnesium sulfate is a standard regime with lesser side effects and equally good perinatal outcome. In our study, we consider only cases with severe preeclampsia and we excluded cases with eclampsia⁽¹⁰⁾.

Bhattacharjee et al. (2011) 144 women with eclampsia were divided into a study group and a control group of 72 women each. The study group received 0.75 g/h of magnesium sulfate intravenously after a loading intravenous dose of 4 g and the control group was given the standard intramuscular regimen as advocated by Pritchard. They found that low-dose intravenous magnesium sulfate was found to be as effective as the standard intramuscular regimen while maintaining a high safety margin⁽¹¹⁾.

In Conclusion, the early diagnosis of severe preeclampsia is very important in order to minimize maternal and fetal complications. We must put the risk factors of preeclampsia in our mind when history is taken and during the examination of pregnant females in order not to misdiagnose the cases of preeclampsia. Clinical examination of pregnant females with preeclampsia should be supported and confirmed by laboratory investigations and ultrasonography to detect complications and for assessment of fetal well-being.

Magnesium sulfate proved to cause many hemodynamic changes as it has a vasodilator effect on maternal and fetal blood vessels, however. Magnesium sulfate should be given to all patients with severe preeclampsia. Thinking about the equivalent viability, less side effects, simplicity of observing and cost-adequacy of the loading dose, loading dose of magnesium sulfate in managing the pre-eclampsia is desirable over different protocols of administration requiring numerous dosages.

Recommendations

We recommend the use of loading dose only of MgSO₄ in the antepartum period with no postpartum maintenance doses. If complications occurred, we recommend the abbreviated regimen as an alternative to the standard regimen.

References

1. Lecarpentier E, Fournier T, Guibourdenche J, Tsatsaris V. [Pathophysiology of preeclampsia]. *Presse Med*; 212: 49, 2016.
2. Heshmati A, Mishra G, Koupil I. Childhood and adulthood socio-economic position and hypertensive disorders in pregnancy: the Uppsala Birth Cohort Multigenerational Study. *J Epidemiol Community Health*; 67: 939-946, 2013.
3. Guzein K, Goynumer G, Gokdagli F: The effect of magnesium sulfate treatment on blood biochemistry and bleeding time in patients with severe Preeclampsia. *The Journal of Maternal-Fetal and Neonatal Medicine* 23(5): 399-402, 2010.
4. Dhakal G, Subedi M, Paudel K.: Magnesium sulphate in management of severe pre-eclampsia and eclampsia. *J Nepal Health Res Counc.*; 10(21):113-7, 2012.
5. Dasgupta S, Ghosh D, Seal SL, Kamilya G, Karmakar M, et al. Randomized controlled study comparing effect of magnesium sulfate with placebo on fetal umbilical artery and middle cerebral artery blood flow in mild preeclampsia at ≥ 34 weeks gestational age. *J Obstet Gynaecol Res* 38: 763-771, 2012.
6. Gordon R, Magee LA, Payne B, Firoz T, Sawchuck D, et al. Magnesium sulphate for the management of preeclampsia and eclampsia in low and middle income countries: a systematic review of tested dosing regimens. *J Obstet Gynaecol Can* 36: 154-163, 2014.
7. Filippi V, Chou D, Ronsmans C, Graham W, Say L: Levels and Causes of Maternal Mortality and Morbidity Third Edition (Volume 2), 2016.
8. Duley L, Gulmezoglu AM, Henderson-Smart DJ: Magnesium sulphate and other anticonvulsants for women with preeclampsia. *Cochrane Database Syst Rev.* (2):CD000025, 2010.
9. Duley L, Matar HE, Almerie MQ, Hall DR: Alternative magnesium sulphate regimens for women with pre-eclampsia and eclampsia (Review) 57, 2011 The Cochrane Collaboration, 2011.
10. Omkara Murthy K, Shobha UN, Dhananjaya BS, Sameena Sultana: a comparative study of low

- dose magnesium sulphate regime and pritchard regime for imminent eclampsia and eclampsia. *Int J Biol Med Res.*; 4(2):3001- 3004, 2013.
11. Bhattacharjee N Saha SP, Ganguly RP, Patra KK, Dhali B, et al; A randomised comparative study between low-dose intravenous magnesium sulphate and standard intramuscular regimen fortreatment of eclampsia. *Journal of Obstetrics and Gynaecology*, 2011; 31(4): 298–303, 2011.

8/20/2019