

# Comparison of Efficacy and Safety of Intra-Muscular MgSO<sub>4</sub> with Low Dose Intra-Venous Regimen in Treatment of Eclampsia

Aqsa Ikram Ul Haq<sup>1</sup>, Ulfat Naseem<sup>2</sup>, Nadia Sadiq<sup>3</sup>, Syeda Maryam Batool, Tahira Khalid<sup>5</sup>, Shama Bashir<sup>6</sup>

<sup>1,6</sup> Senior Registrar Gynae/Obs,  
Holy Family Hospital, Rawalpindi.  
<sup>2</sup> Post-Graduate Trainee Gynae/Obs  
Holy Family Hospital, Rawalpindi  
<sup>3</sup> Woman Medical Officer,  
Holy Family Hospital, Rawalpindi.

<sup>4</sup> Associate Professor of Gynae/Obs,  
Combined Military Hospital, Rawalakot.  
<sup>5</sup> Associate Professor Gynae/Obs,  
Federal Medical & Dental College, Islamabad.

## Author's Contribution

<sup>1,2</sup> Conception of study  
<sup>1,2</sup> Experimentation/Study conduction  
<sup>1,2,3,4,5,6</sup> Analysis/Interpretation/Discussion  
<sup>3,4</sup> Manuscript Writing  
<sup>1,3</sup> Critical Review  
<sup>4,5,6</sup> Facilitation and Material analysis

## Corresponding Author

Dr. Aqsa Ikram Ul Haq  
Senior Registrar  
Gynae/Obs  
Holy Family Hospital  
Rawalpindi  
Email: dr.aqsa81@gmail.com

## Article Processing

Received: 10/02/2022  
Accepted: 28/09/2022

**Cite this Article:** Aqsa Ikram ul Haq, Ulfat Naseem, Nadia Sadiq, Syeda Maryam Batool, Tahira Khalid, Shama Bashir. Comparison of efficacy and safety of intramuscular magnesium sulphate with low dose intravenous regimen in treatment of eclampsia.

<https://www.journalrmc.com/index.php/JRMC/article/view/1901>  
DOI: <https://doi.org/10.37939/jrhc.v26i4.1901>

**Conflict of Interest:** Nil  
**Funding Source:** Nil

## Abstract

**Introduction:** Hypertensive disorders and its complications contribute maximum in maternal morbidity and mortality worldwide especially in developing countries. Multiple drugs have been under trial for a long period of time in means of their efficacy and safety profile. Out of all drugs MgSO<sub>4</sub> made its place as one of the treatment of choice in eclamptic patients. It has multiple advantages although its not without side effect, if not used appropriately and with caution.

**Objective:** To compare the efficacy and safety of intramuscular versus low dose intravenous magnesium sulphate in treatment of eclampsia.

**Study Setting:** The study was conducted at Gynecology and Obstetrics Department unit II, Holy Family Hospital, Rawalpindi, from June 20, 2020 to December 20, 2020. Study design was Randomized Controlled Trial.

**Materials and Methods:** Patients were randomly distributed into two groups, group-A (IM Group) and group-B (IV Group). Group-A patients received a loading dose of 4 gm IV MgSO<sub>4</sub> over 5-10 minutes+10 gm MgSO<sub>4</sub> deep intra-muscular injection (5 gm in each buttock) and a maintenance dose of 5 gm MgSO<sub>4</sub> deep intramuscular injection in alternate buttock every 4 hourly. Group-B patients received MgSO<sub>4</sub> 4 gm slow IV over 5-10 minutes as loading dose and 1 gm MgSO<sub>4</sub> per hour as continuous intravenous maintenance infusion. Clinical response to therapy for both drugs was calculated in terms of efficacy and safety. All the data were entered & analyzed by using SPSS v25.0. Both the groups were compared in terms of efficacy and safety by using Chi-Square test. A p-value less than 0.05 were taken as significant.

**Results:** A sample size of 160 eclamptic patients was taken in our study. We divided the patients in two groups: Group A (IM MgSO<sub>4</sub>) and Group B (IV MgSO<sub>4</sub>). Group A shows: 45(56.3%) in 18-30 years age group and 35(43.8%) in 31-40 years age group, while in group-B, there were 48(60.0%) in 18-30 years age group and 32(40.0%) in 31-40 years age group. In IM MgSO<sub>4</sub> group, prevention from recurrence of seizure was noted in 74(92.5%) and 78(97.5%) in IV MgSO<sub>4</sub> group, which is insignificant statistically with a p-value of 0.147.

**Conclusion:** MgSO<sub>4</sub> proved itself as one of the best drug for control of convulsions in eclamptic patients. The difference of routes has an effect in means of toxicity which was slightly more in intramuscular route; toxicity was manifested by loss of knee jerk in eclamptic patients. Although there was no profound difference in control of recurrence of seizures in both routes.

**Keywords:** Eclampsia, Intramuscular MgSO<sub>4</sub>, Intravenous MgSO<sub>4</sub>.

## Introduction

Eclampsia is a term used for tonic clonic fits in pregnant patients with uncontrolled hypertension or having severe pre-eclampsia.<sup>1</sup> Eclampsia has proved to be one of the severe complications of pregnancy and made its place as 2<sup>nd</sup> most common cause of maternal morbidity and maternal mortality in developing countries.<sup>2</sup>

It contributes for deaths of pregnant females to 11% in developing countries and 9% in Asia.<sup>3-4</sup> The developed nations quote an incidence of 1.6-2/1000 deliveries while in developing nations it is 6-157/1000 deliveries.<sup>5</sup>

The pathogenesis of eclamptic convulsions remains unknown.<sup>6</sup> Efficient antenatal care can prevent from the worst consequences of this disease. But there is low utilization of both antenatal and intra-partum care in low resource countries such as Pakistan, especially in rural areas where patients present to the hospital only as a last resort.<sup>7</sup>

Ideal management of eclampsia includes control of seizures at top most priority. Management includes Anticonvulsants, anti-hypertensives, fluid and electrolyte balance and termination of pregnancy.<sup>8</sup>

Magnesium sulphate is a life-saving drug required for control of convulsions in eclamptic patients and played a significant role in lowering fatal outcomes secondary to eclampsia. It is one of the evidence based drug used for prevention and treatment of eclampsia.<sup>9</sup> Different dosage and route of administration were successfully tried. Rationale of study is to compare the efficacy and safety of intramuscular versus low dose intravenous magnesium sulphate in treatment of eclampsia. Safety refers to the frequency of adverse effects that are treatment emergent from a drug. Efficacy is a measure of the ability of a drug to treat whatever condition it is indicated for.

Dose related toxicity is a major concern especially in clinical environments of tertiary care hospitals of our setups where one to one patient monitoring is not possible. Widely accepted regimens used for treatment of eclampsia are Zuspan and Pritchard regimens.<sup>9</sup>

Intravenous route of MgSO<sub>4</sub> is used in Zuspan regimen whereas intramuscular route is used in Pritchard regimen. Both regimens have their own advantages and disadvantages. Intravenous route of Zuspan regimen is more frequently used in developed countries where one to one care is not a problem. Pritchard regimen is more commonly used in developing countries because of ease of administration

although there are significant cases of pain and infection at the injection site.<sup>9-10</sup>

Previously conducted studies have compared the efficacy of different MgSO<sub>4</sub> regimens in treatment of eclampsia. Sing S and Singh RK in their study found that the patients in which intramuscular regimen is used, 6% patients developed seizures after treatment in comparison to intravenous regimen in which only 4% patients developed seizures after treatment with MgSO<sub>4</sub> with p-value 0.646. The toxicity in means of loss of knee jerk was also calculated which was profoundly high in IM group as compared to IV group i-e, 14% vs 2% with p-value of 0.027.<sup>11</sup>

In another study, Kanti V et al in which they compare IM and IV MgSO<sub>4</sub> regimens with regard to efficacy and safety. Overall magnesium toxicity (safety) was observed in 29.5% eclamptic patients in IM group while it was present in 17.7% of patients in IV group.<sup>12</sup> Lost knee reflex found in 11.8% of patients in both groups. Decreased urine output was 11.8% and 5.9% in IM vs IV group respectively. Low respiratory rate was only observed in IM group (5.9%). Their study results revealed that recurrence of convulsion was found to be similar 5.88% in IV and IM group.<sup>13</sup> No statistical difference was found in means of maternal death between the groups with p value of 0.314. The calculated impending toxicity considered by loss of patellar reflex was statistically higher with p value of 0.034 in IM group.<sup>14</sup>

## Materials and Methods

The study was conducted at Gynecology and Obstetrics Department, Holy Family Hospital, Rawalpindi from June 20, 2020 to December 20, 2020. Study design was Randomized Controlled Trial. Sample technique was Probability Consecutive Sampling. The sample size was calculated by using WHO sample size calculator. Sample size was total 160 pregnancies with eclampsia (80 in each group). Study was conducted after approval and permission from ethical committee of hospital. An informed written consent was taken by the researcher from the patients. Participants fulfilling the inclusion criteria were enrolled for the study. Detailed clinical history was obtained and all records of antenatal visits and prescriptions regarding any antihypertensive treatment were thoroughly checked. History of blurring of vision, epigastric pain, number of convulsions at home or on the way to the hospital, preeclampsia in previous and present pregnancy was asked in detail. General examination included pulse,

blood pressure, pallor, icterus and edema and systemic examination included respiratory system examination, cardiovascular system examination, obstetric pelvic examination, neurological examination and fundal examination was done.

If systolic blood pressure more than 160 mm of Hg or diastolic blood pressure more than 110 mm of Hg was observed, it was treated with Inj. Labetalol 20 mg IV and repeated when required. Routine investigation included complete blood count, liver function test, renal function test, serum electrolytes were advised.

Patients were randomly distributed into two groups, group-A (IM Group) and group-B (IV Group). Group-A patients received a loading dose of 4 gm IV MgSO<sub>4</sub> over 5-10 minutes+10 gm MgSO<sub>4</sub> deep intra-muscular injection (5 gm in each buttock) and a maintenance dose of 5 gm MgSO<sub>4</sub> deep intramuscular injection in alternate buttock every 4 hourly.

Group-B patients received MgSO<sub>4</sub> 4 gm slow IV over 5-10 minutes as loading dose and 1 gm MgSO<sub>4</sub> per hour as continuous intravenous maintenance infusion. Clinical response to therapy for both drugs was calculated in terms of efficacy and safety as per our operational definition. Data were recorded on a pre-designed proforma (attached).

All the data were entered & analyzed by using SPSS v25.0. Mean and standard deviation was calculated for quantitative variables like age, gestational age and BMI. Frequency and Percentages were calculated for qualitative variables like efficacy, safety, knee jerk reflex, low respiratory rate and low urine output. Both the groups will be compared in terms of efficacy and safety by using Chi-Square test. A p-value less than 0.05 were taken as significant. Effect modifiers like age, gestational age and BMI were controlled by stratification. Post-stratification, chi-square test was applied and p-value less than 0.05 were taken as significant.

## Results

Total sample size calculated includes 160 patients with eclampsia. We divided patients into two groups i.e. Group A (IM MgSO<sub>4</sub>) and Group B (IV MgSO<sub>4</sub>). Group A showed 45(56.3%) in 18-30 years age group and 35(43.8%) in 31-40 years age group, while in group-B, there were 48(60.0%) in 18-30 years age group and 32(40.0%) in 31-40 years age group.

In group-A, 40(50.0%) had gestational age between 20-26 weeks and 40(50.0%) >26 weeks, while in group-B, 42(52.5%) had gestational age between 20-26 weeks and 38(47.5%) >26 weeks.

In group-A, 55(68.8%) had normal BMI, while 23(28.7%) and 2(2.5%) were overweight and obese respectively, while in group-B, 57(71.3%) had normal BMI, while 22(27.5%) and 1(1.3%) were overweight and obese respectively.

In IM MgSO<sub>4</sub> group, prevention from recurrence of seizure was noted in 74(92.5%) and 78(97.5%) in IV MgSO<sub>4</sub> group, which is statistically insignificant with a p-value of 0.147.

According to safety comparison between groups, loss of knee jerk was observed in 2(2.5%) in IM MgSO<sub>4</sub> group versus 0(0.0%) in IV MgSO<sub>4</sub> group, while low respiratory rate (0% vs. 0%) and low urine output (1.25% vs. 1.25%) were compared between IM MgSO<sub>4</sub> versus IV MgSO<sub>4</sub>.

**Table 1: Comparison of efficacy between groups**

Efficacy	Groups		Total	p-value
	Intramuscular MgSO <sub>4</sub>	Intravenous MgSO <sub>4</sub>		
Yes	74	78	152	0.147
	92.5%	97.5%	95.0%	
No	6	2	8	5.0%
	7.5%	2.5%	5.0%	
Total	80	80	160	100.0%
	100.0%	100.0%	100.0%	

**Table 2: Comparison of safety between groups**

Safety	Groups		Total	p-value
	Intramuscular MgSO <sub>4</sub>	Intravenous MgSO <sub>4</sub>		
Yes	77	79	156	0.311
	96.3%	98.8%	97.5%	
No	3	1	4	2.5%
	3.8%	1.3%	2.5%	
Total	80	80	160	100.0%
	100.0%	100.0%	100.0%	

## Discussion

One of the jarring truths of eclampsia is its contribution in maternal mortality in all developing countries. Data collected from developing countries showed a very high incidence of eclampsia with a continued increment that put a question mark in antenatal care provided in developing countries. Studies conducted in our neighbouring countries by

Singh S et al in India and by Begum MR and Begum M in Bangladesh quoted the incidence of eclampsia from 3.2-9%, respectively.<sup>14,15</sup>

MgSO<sub>4</sub> made its place as a drug of choice in prophylaxis and treatment of severe pre-eclampsia and eclampsia. There is lack of evidence in routine use of MgSO<sub>4</sub> in milder cases of preeclampsia because of paucity of data regarding its side effects.

MgSO<sub>4</sub> toxicity and overdose leading to maternal morbidity and mortality can be overcome with close monitoring and giving calculated dose at controlled rate. This sort of monitoring and calculated dose is more supported in IV route by evidence.<sup>16</sup> Although IV route is preferred but centers with a lot of patient burden, lack of one to one care and low resourced still prefer IM regimen of MgSO<sub>4</sub>. This preference is based on need of less monitoring and also cost effective.

In our study maximum patients of both groups falls in age group of 18-30 years although patients range from 18-40 years. These findings correlated with study of Singh VK et al<sup>17</sup> who included 80 eclamptic patients that also fall in age group of 15-40 years.

Recurrence of convulsions after using different regimens is different. Studies done by Sibai and Pritchard quoted it 16% and 11% respectively.<sup>18</sup> One of the biggest trial done for its assessment was collaborative eclampsia trial<sup>19</sup> which gave a figure of 5.7-13.2% with IM Pritchard regimen. In another study done by Coetzee et al.<sup>20</sup> a recurrence of convulsions rate of 0.3% was found in severe cases of pre-eclampsia with Zuspan regimen.

Clinical assessment of loss of knee jerk and suppressed respiration has its own independent place in assessment of MgSO<sub>4</sub> toxicity without measuring maternal magnesium serum levels. This concept was also supported by Chinayon P and Ekele.<sup>21</sup> In our study results 3.75% patients had lost knee jerk in IM MgSO<sub>4</sub> group as compared to no patient found in IV MgSO<sub>4</sub> group. Depressed respiration rate was 2.5 and 1.25% in IM and IV group, respectively. Although Chissell S<sup>22</sup> study gave us contradictory results in comparison to ours as they gave a figure of 12.5% cases with MgSO<sub>4</sub> toxicity in IV group and no patient in IM group.

In another study, Kanti V et al, a comparison was done between IV and IM MgSO<sub>4</sub> regimens in regard of safety and efficacy. Overall magnesium toxicity (safety) was observed in 29.5% eclamptic patients in IM group while it was present in 17.7% of patients in IV group.<sup>23,24</sup>

Lost knee reflex was found in 11.8% of patients in both groups, while decreased urine output was more in IM

MgSO<sub>4</sub> (11.8%) as compared to IV MgSO<sub>4</sub> (5.9%). Low respiratory rate was only observed in IM group (5.9%). Their study results revealed that recurrence of convulsion was found to be similar 5.88% in IV and IM group.<sup>25</sup>

## Conclusion

There is no doubt in well played role of MgSO<sub>4</sub> in control of convulsions in eclamptic patients. Route of MgSO<sub>4</sub> exert its effects by means of difference in toxicity. Although no statistical difference was found in control and recurrence of convulsions in both routes. So, MgSO<sub>4</sub> can be used effectively by any route for treatment.

## References

1. Agrawal S, Walia GK, Staines-Urias E, Casas JP, Millett C. Prevalence of and risk factors for eclampsia in pregnant women in India. *Fam Med Community Health*. 2017;5:225-44.
2. Mohanapu S, Raveendran S, Murugaiah Y, SenInt M. A comparative study of low dose magnesium sulphate therapy with standard pritchard's regime in the management of eclampsia. *J Reprod Contracept Obstet Gynecol*. 2016;5:2939-43. DOI: <https://dx.doi.org/10.18203/2320-1770>.
3. Sunitha HB, Parikh S, Waikar MR, Panchgar V, Shetti AN. Comparison of single loading dose magnesium sulphate regimen with low dose magnesium sulphate regimen in the treatment of eclampsia. *Indian J Obst Gynecol Res*. 2017;4:338-42.
4. Say L, Chou D, Gemmill A. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014;2:323-33.
5. Saeed G, Wajid R, Dar AY. Maternal mortality in eclampsia after cesarean section versus vaginal delivery. *Ann King Edward Med Uni*. 2017;23:451-5. <http://dx.doi.org/10.21649/journal.akemu/2017/23.4.451.455>
6. Sunitha HB, Parikh S, Waikar MR, Panchgar V, Shetti AN. Comparison of single loading dose magnesium sulphate regimen with low dose magnesium sulphate regimen in the treatment of eclampsia. *Indian J Obst Gynecol Res*. 2017;4:338-42.
7. Kathawadia KK, Patel PC, Vaishnav SB. Outcome of Low Maintenance Dose MgSO<sub>4</sub> in Eclampsia Patients of a Tertiary Care Hospital of Gujarat, India- A Prospective Study. *Int J Med Res*. 2016;6:199-203.
8. Kumari CK, Anuragamayi Y, Lakshmi DR, Syamala. A Comparative Study of Low Dose Magnesium Sulphate Regime vs Standard Dose Pritchard Regime in the Management of Eclampsia in Indian Scenario. *J Evol Med Dent Sci*. 2014;3:9931-9.
9. Gordon R, Magee LA, Payne B, Firoz T, Sawchuck D, Tu 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*. 2014;36:154-63.
10. Pratt JJ, Niedle PS, Vogel JP, Oladapo OT, Bohren M, Tunçalp Ö, et al. Alternative regimens of magnesium sulfate for treatment of preeclampsia and eclampsia: a systematic review of non-randomized studies. *Acta Obstet Gynecol Scand*. 2016;95:144-56. DOI: 10.1111/aogs.12807

11. Singh S, Singh RK. Comparison of IM magnesium sulfate and IV magnesium sulfate for control of convulsion in eclamptic patients. *J Evid Med Healthcare*. 2015;2:8605-10.
12. Kanti V, Gupta A, Seth S, Bajaj M, Kumar S, Singh M. Comparison between intramuscular and intravenous regimen of magnesium sulfate in management of severe preeclampsia and eclampsia. *Int J Reprod Contracept Obstet Gynecol*. 2015;4:195-201.
13. Mattar, F, and B M Sibai. "Eclampsia. VIII. Risk factors for maternal morbidity." *American journal of obstetrics and gynecology* vol. 182,2 (2000): 307-12. doi:10.1016/s0002-9378(00)70216-x
14. Warrington JP. Placental ischemia increases seizure susceptibility and cerebrospinal fluid cytokines. *Physiol Rep*. 2015. doi: 10.14814/phy2.12634
15. Reddy, Aparna et al. "Maternal circulating levels of activin A, inhibin A, sFlt-1 and endoglin at parturition in normal pregnancy and pre-eclampsia." *PloS one* vol. 4,2 (2009): e4453. doi:10.1371/journal.pone.0004453
16. Banerjee, Subhasis et al. "Mouse models for preeclampsia: disruption of redox-regulated signaling." *Reproductive biology and endocrinology: RB&E* vol. 7 4. 15 Jan. 2009, doi:10.1186/1477-7827-7-4
17. Cooray, Shamil D et al. "Characterization of symptoms immediately preceding eclampsia." *Obstetrics and gynecology* vol. 118,5 (2011): 995-999. doi:10.1097/AOG.0b013e3182324570
18. Nerenberg, Kara A et al. "Long-term Risk of a Seizure Disorder After Eclampsia." *Obstetrics and gynecology* vol. 130,6 (2017): 1327-1333. doi:10.1097/AOG.0000000000002364
19. Brewer, Justin et al. "Posterior reversible encephalopathy syndrome in 46 of 47 patients with eclampsia." *American journal of obstetrics and gynecology* vol. 208,6 (2013): 468.e1-6. doi:10.1016/j.ajog.2013.02.015
20. "Committee Opinion No 652: Magnesium Sulfate Use in Obstetrics." *Obstetrics and gynecology* vol. 127,1 (2016): e52-e53. doi:10.1097/AOG.0000000000001267
21. Anjum, Shaheen et al. "Maternal outcomes after 12hours and 24hours of magnesium sulfate therapy for eclampsia." *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* vol. 132,1 (2016): 68-71. doi:10.1016/j.ijgo.2015.06.056
22. Al-Safi, Zain et al. "Delayed postpartum preeclampsia and eclampsia: demographics, clinical course, and complications." *Obstetrics and gynecology* vol. 118,5 (2011): 1102-1107. doi:10.1097/AOG.0b013e318231934c
23. Vadillo-Ortega, Felipe et al. "Effect of supplementation during pregnancy with L-arginine and antioxidant vitamins in medical food on pre-eclampsia in high risk population: randomised controlled trial." *BMJ (Clinical research ed.)* vol. 342 d2901. 19 May. 2011, doi:10.1136/bmj.d2901
24. Latika Sahu, Shubhra Singh, Anjali Tempe, B. C. Koner. A randomized comparative study between low-dose magnesium sulphate and standard dose regimen for management of eclampsia. *Int J Reprod Contracept Obstet Gynecol*. 2014;3(1):79-86.
25. Bangal VB, Purushottam A. Giri, Satyajit P. Gavhane. A study to compare the efficacy of low dose magnesium sulphate regime with Pritchard regime in eclampsia. *Int J Biomed Adv Res*. 2012;3(1):53-7.