

Comparison of Magnesium Sulphate Loading Dose with & without Maintenance Regimen for Management of patients presenting with Eclampsia - Randomized Control Trial

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ABSTRACT

Aim: To compare the frequency of recurrence of convulsions with Magnesium Sulphate loading dose versus loading dose plus maintenance regimen for management of patients presenting with eclampsia.

Methods: In this Randomized Controlled Trial, 240 pregnant female admitted in department of Obstetrics & Gynaecology, LGH, Lahore. Half In group A, females were given MgSO₄ in a single bolus dose i.e. 4 grams intravenously diluted in 100ml normal saline over 20 minutes and 10grams intramuscularly, while in group B, females were given complete standard regime according to the Pritchard i.e. 14 grams loading dose followed by 5gm intramuscularly every 4 hours on alternate buttock for 24 hours after the last episode of convulsion or delivery of the fetus whichever comes later.

Results: In this study recurrence of convulsion was significantly higher in patients who were given MgSO₄ loading dose as compared to patients who were given MgSO₄ loading + maintenance regimen i.e. Group-A: 15.8% vs. Group-B: 5.8%, (p-value 0.013). The frequency of recurrence of convulsion was significantly higher in women who were given loading dose alone as that of women who were given MgSO₄ loading + maintenance regimen but Age, gestational age and parity status of women although did not show any significant association..

Conclusion: Loading dose plus maintenance regimen had low frequency of recurrence convulsion when compared with loading dose of MgSO₄ only.

Keywords: Eclampsia, loading dose, Recurrence of convulsions, Magnesium Sulphate, Maintenance regimen

INTRODUCTION

Hypertensive disorders in pregnancy major cause of maternal and perinatal mortality and morbidity world-wide, 10-25% of maternal deaths in middle income countries happen due to eclamptic seizure.¹ The occurrence of eclamptic convulsion/Seizures reduces to minimal among pre eclampsia patients treated with magnesium sulfate (MgSO₄). Magnesium sulfate decreases the calcium intra as well as extra-cellularly and helps in decreasing cerebral edema formation. It also inhibits the glutamate receptors, such as the N-methyl-d-aspartate (NMDA) receptor, which contributes in NMDA induces seizures²

A cross sectional study conducted in Sindh, Pakistan reveals that the eclampsia was common among young female with primigravida and most of the subjects have no awareness about their raised blood pressure before admission³. A randomized control trial conducted in Lady Reading Hospital on severe pre eclampsia pregnant female reveals that Signal loading dose was as effective as standard dose regimen of magnesium sulphate⁴.

The reported evidence of beneficial effect of MgSO₄ loading dose as compared to MgSO₄ standard regimen is debatable. The study was conducted to prove that MgSO₄ loading dose may be beneficial therefore combinations should not be given as they may cause toxic effects on the mother as well as on fetus. So, the conduct study finds whether MgSO₄ loading dose can replace combination of MgSO₄ with standard regimen. This may help us to improve practice and guidelines to manage patients with eclampsia.

SUBJECTS AND METHOD

In this randomized controlled trial conducted in Department of Obstetrics & Gynecology, Lahore General Hospital of Lahore,

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Pakistan from April 10th, 2016 to October 10th, 2016. 240 patients (ante-partum, intra-partum, postpartum) of age 18-40 years, presenting at gestational age after 20 weeks (through ultrasound) presenting with eclampsia (as per operational definition) were included in the study and Patients already treated with MgSO₄ or have history of hypersensitivity to MgSO₄, other causes of convulsions like epilepsy, cerebrovascular accident, meningitis, encephalitis and other metabolic abnormalities which will be assessed by detailed history and examination, Those who are deeply unconscious with CVA, renal failure, massive pulmonary edema, associated massive haemorrhage, DIC and shock (including sepsis) and assessed by detailed history, examination and investigations were excluded from the study.

Data Collection Procedure: Then females were randomly divided in two groups by using lottery method. In group A, females were given MgSO₄ loading dose while females in group B were given MgSO₄ along with maintenance regimen. In group A, females were given MgSO₄ in a single bolus dose i.e. 4 grams intravenously diluted in 100ml normal saline over 20 minutes and 10grams intramuscularly (5gm in each buttock), while in group B, females were given complete standard regime according to the Pritchard i.e. 14grams loading dose (4gm by intravenous route and 10gms intramuscularly) followed by 5gm intramuscularly every 4 hours on alternate buttock for 24 hours after the last episode of convulsion or delivery of the fetus whichever comes later.

Then patients in both groups were followed-up for 24 hours. During 24 hours recurrence of convulsions was assessed (as per operational definition). Recurrence of convulsions in Group A, was managed by giving another intravenous bolus of 2gms of MgSO₄ in 100ml of normal saline over 5 minutes. If recurrence of more than one convulsion in group A, it was managed by shifting of group A to maintenance regimen. All the information was collected on a specially designed proforma. Permission was granted by Institutional Ethical Review Board.

Data Analysis Procedure: Data was entered and analyzed using SPSS version 25. Quantitative data like age and gestational age

was presented as mean and standard deviation. Qualitative data like preeclampsia (present / absent) and recurrence of convulsions was presented as frequency and percentage. Frequency was calculated for parity. Chi-square test was applied to compare both groups taking $p\text{-value} \leq 0.05$ as significant. Data was stratified for age, parity, gestational age and preeclampsia (present / absent) as an effect modifier. Post stratification, Chi-square test was applied taking $p\text{-value} \leq 0.05$ as significant.

RESULTS

Mean age of women of MgSO₄ loading dose without standard regime (**Group-A**) was 29.82±5.93 years and Mean age of MgSO₄ loading dose without standard regime (**Group-B**) was 30.21±6.33 years. Minimum and maximum age of women in both groups was 20 and 40 years respectively. Mean gestational age of women in Group-A was 28.94±5.62 weeks and in Group-B it was 29.37±5.42 weeks. In group A 26 (21.7%) were nulliparous, 38 (31.7%) were prima gravida and 56(46.7%) were multi gravida. In group B, 27 (22.5%) were nulliparous, 37 (30.8%) women's parity was 1, 45(37.5%) women were having parity as 2 and 11 (9.5%) women's parity was 3.

Frequency of pre-eclampsia in Group-A was 53.3% and in Group-B it was 45.8%. The difference was not statistically significant ($p\text{-value}=0.245$) whereas 15.8% of group A and 5.8% of group B have recurrence convulsion. The association between treatment groups and recurrence of convulsion was statistically significant ($p\text{-value} 0.013$)

Women who were diagnosed with eclampsia having proteinuria, among them Recurrence of convulsion was high in Group-A as that of Group-B but it was not statistically significant. i.e. Group-A: 15.6% vs. Group-B: 7.3% ($p\text{-value}=0.159$). However, women who had no proteinuria with eclampsia among them recurrence of convulsion was significantly higher in Group-A women when compared with Group-B women. i.e. Group-A: 16.1% vs. Group-B: 4.6% ($p\text{-value}=0.036$).

Comparison of findings regarding study groups

Study variables	MgSO ₄ loading Dose		p-value	
	Without maintenance regime	With maintenance regime		
Parity	0	26 (21.7%)	27(23.5%)	0.627
	1	38(31.7%)	37(30.8%)	
	2	39(32.5%)	45(37.5%)	
	3	17(14.2%)	11(9.5%)	
Pre-eclampsia	64(53.3%)	55(45.8%)	0.012	
Convulsion	19(15.8%)	7(5.8%)	0.013	

Recurrence of convulsion according to different study variables in treatment groups

	Group-A	Group-B	Chi- Square Test	p-value
Age group				
20-25	6(15.8%)	1(2.9%)	3.38	0.066
26-30	5(17.2%)	1(4%)	2.38	0.123
31-35	4(15.4%)	3(10.3%)	0.31	0.576
	4(14.8%)	2(6.3%)	1.18	0.278
Gestational Age				
20-25 Weeks	4(9.8%)	3(8.8%)	0.02	0.890
26-30 Weeks	7(22.6%)	2(6.7%)	3.07	0.080
31-35 Weeks	2(6.9%)	2(5.6%)	0.05	0.823
>35 Weeks	6(31.6%)	0(0%)	7.46	0.006*
Parity				
0	6(23.1%)	1(3.7%)	4.33	0.037*
1	5(13.2%)	2(5.4%)	1.33	0.249
2	6(15.4%)	4(8.9%)	0.84	0.359
3	2(11.8%)	0(0%)	1.39	0.238
Eclampsia				
With proteinuria	10(15.6%)	4(7.3%)	1.99	0.159
No proteinuria	9(16.1%)	3(4.6%)	4.42	0.036*

Group-A= MgSO₄ loading dose, Group-B= MgSO₄ loading dose + maintenance regimen
*p-value significant at 0.05

DISCUSSION

According to National High Blood Pressure Education Program, blood pressure of more than 140/90 mm Hg using Korto-koff V sounds for diastolic blood pressure is considered as Hypertension.

Among pregnant female the hypertension can be divided into four major classes.⁵ Various studies in the past showed no significant difference between the loading dose and maintenance regimen. The current study was conducted to determine minor difference in terms of recurrence of convulsions. Administration of loading dose only is easy to monitor and toxicity of the drug can be avoided. It was observed in the study that MgSO₄ loading has higher convulsion as compared to patients treated with MgSO₄ loading dose + maintenance regimen.

It was observed in the study that Age, gestational age and parity status of women although did not show any significant association between recurrence convulsion rate and treatment groups still the frequency of recurrence of convulsion was significantly higher in women who were given loading dose alone as that of women who were given MgSO₄ loading dose + maintenance regimen. However, women with and without proteinuria in both these groups, the frequency of recurrence of convulsion was higher in loading dose group.

Literature reveals that the recurrent seizures and maternal deaths reduce among the pregnant female treated with MgSO₄. Even among Severe pre eclampsia i.e. blood pressure of 160/110 mmHg or more reduces to normal among half of the treated subjects.⁶ Loading dose is cost effective as well as considered as safe for long term effectiveness.^{7, 8} Results of the current study were in contrast to Narayan Jana⁹ as it was documented that MgSO₄ loading dose was associated with a lower seizure recurrence whereas in another study no recurrence was found^{10, 11}. On the other hand no recurrent seizures were documented in standard regimen group as compared to 5% patients with recurrent seizure in loading dose group.¹² In contrast, Ranganna et al 2014¹³ found same recurrence in Modified Pritchard's and Loading dose only. During the treatment on patient in each group suffers from fit/seizure.

Loading dose with and without standard regimen is administered to patients in routine practice. And both are found equally effective. Studies conducted in Peshawar by Begum 2000¹⁴, Noor et al. 2004¹⁵ and later by Nasir & Bibi 2019 advocate the effectiveness of single dose as compared to control. Management of pre eclampsia with single dose, omits the suffering of multiple injection after bolus dose.¹⁵ It is found in the literature that additional magnesium sulfate dose can be given to the patients in case of non-controlling of seizures¹⁶.

In those areas of our country where there is no adequate health resources and professionals for proper administration and monitoring of MgSO₄, it's better to give loading dose only for seizure prophylaxis. In this way, we can reduce the seizure activity to a significant extent and later on we can arrange the referral of the patients with eclampsia to the better health centers for further management.

CONCLUSION

Loading dose plus maintenance regimen had low frequency of recurrence convulsion as compared to loading dose of MgSO₄. Although in literature controversial results are reported few studies reported that both regimens are equally effective and others studies have reported the superiority of loading dose but this controversy is clear now.

Conflict of interest: Nil

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