

COMPARISON BETWEEN THE EFFICACY OF SINGLE LOADING DOSE REGIMEN AND STANDERED DOSE REGIMEN OFMAGNESIUM SULPHATE IN PATIENTS WITH SEVERE PRE ECLAMPSIA

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ABSTRACT

Objective: check comparison between the efficacy of single loading dose regimen and standered dose regimen of magnesium sulphate in patients with severe pre eclampsia.

Material and Methods: This research study was coordinated at Department of Gynecology and Obstetrics, Lady Reading Hospital Peshawar-Pakistan. The period of this study was one year from April 2016 to April 2017. Study design was randomized control trial in which a total of 256 patients in each group, taking proportion of efficacy of loading dose 85% and efficacy of standered dose 92%2, 5% level of significance, 80% power of test and 95% confidence interval. Moreover, all patients with severe pre eclampsia, gestational age > 20 weeks, patients age 20-40 years,with patients having singleton pregnancy while mild to moderate pre eclampsia, gestational age < 20 weeks, multiple pregnancy were excluded. In this study the total patients were divided into two groups, group A: receiving loading dose magnesium sulphate therapy and group B: receiving standard magnesium sulphate therapy. Gestation was confirmed by early available ultrasound in the first trimester or by her last menstrual period date. Good blood pressure control was a key step in both groups. All women in both groups were followed after receiving magnesium sulphate maintenance therapy to detect the occurrence of fits.

Results: In this mean age in Group a (loading dose regimen of magnesium sulphate) was 24.1 ± 3.24 while mean age in Group B (standered dose regimen of magnesium sulphate therapy) was 24.96 ± 3.79 . More over in this study loading dose regimen of magnesium sulphate was effective in all the 256 patients while standeaed dose regimen of magnesium sulphate therapy was also effective in all the 256 patients.

Conclusion: Associated with similar efficacy in controlling convulsions, the use of loading dose magnesium sulphate protocols is a viable alternative to standard dose therapy. Further studies are requied to support its routine clinical use.

Keywords: Efficacy, pre eclampsia, loading dose, MgSo4.

This article may be cited as: Nasir S, Bibi K. Comparison between the efficacy of single loading dose regimen and standered dose regimen ofmagnesium sulphate in patients with severe pre eclampsia. *J Med Sci* 2019 Oct;27(4):344-49.

INTRODUCTION

Pre eclampsia and eclampsia are still a leading cause of maternal mortality throughout the world¹. Pre eclampsia, considered as a syndrome that can affect any organ system, is seen in 5-8% of all pregnancies². Convulsions in pre eclampsia that cannot be attributed

to any other factor defined as eclampsia. Incidence of seizures in untreated pre eclampsia is 3-4 %, while those receiving MgSo4 is 0.8-1%¹.

It has been set up that magnesium sulphate is the anticonvulsant of decision for both counteractive action and treatment of eclmpsia, however routine 24 hours organization of upkeep portion of mgso4 subsequent to stacking portion has not been exposed to logical examination^{3,4,5}. The therapeutic range of mgso4 is 2-4mmol/L or 4-8mg/dl.sincethe complication is related to the blood levels of magnesium. Convulsions are almost always prevented by plasma magnesium levels of 4-7 meq/l. At 10meq/l patellar reflex is lost which is followed by respiratory depression at higher levels². It

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Date Received: April 12, 2019

Date Revised: September 13, 2019

Date Accepted: November 20, 2019

is observed that plasma magnesium level of 4-7 meq/l required for fits control can be achieved by giving less then 20 grams of mgso4 dose that is 54.5% less then the standered dose⁶. So current study shows that seizures can be safely controlled in women with eclampsia with a lower dose of mgso4 with the advantage of lower magnesium toxicity. The very fact that there is no single standardization protocol in world, gives scope for tailoring the mgso4 regimen according to the local needs. In the past decade, researchers from the developing countries were constantly striving to steadily decrease the dosage of both the loading and maintenance doses of mgso4 regimen, to suit the local conditions⁷.

In a study in India conducted publish in international journal of gynae and obstetrics to assess the efficacy of low dose mgso4 for eclampsia, the low dose regimen was associated with a lower seizure recurrence (6.1% Vs 9.7%; $P=0.02$) and a slightly lower maternal mortality (2.7%Vs 3.2%; $P=0.6$) compared with the collaborative eclampsia trial⁸. Similarly in a study conducted in university of Maiduguri teaching hospital, where total dosage of mgso4 reduced by 40% in postpartum eclamptic patients and found that shortened postpartum course of mgso4 is as effective as standerd Pritchard regimen in management of eclampsia⁹. Padhar regimen (a low dose mgso4) used in Indian women appeared to control and prevent convulsions effectively¹⁰. The stacking portion routine is alluring for some reasons. In the 1st place, it limits the danger of poisonous quality since most patients would not require the upkeep portion. Clinical observing for magnesium sulphate poisonous quality as by evoking patellar reflexes, checking respiratory rate and estimating urinary yield could be religiously attempted at tertiary emergency clinics, where there are satisfactory labor, offices and supervision. Be that as it may, labor specifically is a test at a local emergency clinics, and essential social insurance focuses of many creating nations. Secondly the cost of treatment using loading dose only is about a third of standereddose regimen and this would be a welcome development in resource poor countries³. So the present study is designed to determine the efficacy of low dose mgso4 therapy in tems of fits prophylaxis as it is quite possible that higher doses will increase the hazards without increasing its benefits. The results of this study can be used as first hand local evidence for futures recommendations and involving higher authorities in promoting low dose mgso4 therapy in order to decrease the work load of HDA and to decrease the mgso4 hazards in case the efficacy is proved to be significant in our study.

MATERIAL AND METHODS

This study was conducted at Department of Gynecology and Obstetrics, Lady Reading Hospital Peshawar-Pakistan. Study period was one year April 2016 to April 2017. Study design was randomized control trial in which a total of 256 patients in each group taking

proportion of efficacy of loading dose 85% and efficacy of standered dose 92%², 5% level of significance, 80% power of test and 95% confidence interval. More over all patients with severe pre eclampsia, gestational age > 20 weeks, patients age 20-40 years with patients having singleton pregnancy while mild to moderate pre eclampsia, gestational age < 20 weeks, Multiple pregnancy were excluded. Patients were divided into two groups, group A: receiving loading dose magnesium sulphate therapy and group B: receiving standard magnesium sulphate therapy. Gestation was confirmed by early available ultrasound in the first trimester or by her last menstrual period date. Good blood pressure control was a key step in both groups. All women in both groups were followed after receiving mgso4 maintenance therapy to detect the occurrence of fits. Strictly exclusion criteria had followed to control con-founders and bias in the study results. The specially designed proforma was used to record the data. Extreme care was practiced under supervision of an expert obstetrician fellow of CPSP. Mean and standard deviation was calculated for age, parity, gestation age, weight, height. Frequency and percentage was calculated for efficacy. Efficacy was stratified among age, gestational age, and parity to see the effect modifier. chi square test was applied in which P-value < 0.05 was considered as significant value. All the results were presented in the form of tables and charts.

RESULTS

Age distribution among two groups was analyzed as in Group A (loading dose regimen of mgso4) 141(55%) patients were in age range 20-30 years and 115(45%) patients were in age range 31-40 years. Mean age was 24.1 ± 3.24 . Where as in Group B (standered dose regimen of mgso4 therapy) 148(58%) patients were in age range 20-30 years and 108(42%) patients were in age range 31-40 years. Mean age was 24.96 ± 3.79 . Status of parity among two groups was analyzed as in Group A (loading dose regimen of mgso4) 166(65%) patients were primi para and 90(35%) patients were multi para. Where as in Group B (standered dose regimen of mgso4 therapy) 159(62%) patients were primi para and 97(38%) patients were multi para.

Period of gestation among two groups was analyzed as in Group A (loading dose regimen of mgso4) 26(10%) patients had POG range 20-25 weeks, 51(20%) patients had POG range 26-30 weeks, 102(40%) patients had POG range 31-35 weeks, 77(30%) patients had POG range 36-40 weeks. Mean POG was 34.22 ± 3.24 . Where as in Group B (standered dose regimen of mgso4 therapy) 23(9%) patients had POG range 20-25 weeks, 51(20%) patients had POG range 26-30 weeks, 100(39%) patients had POG range 31-35 weeks, 82(32%) patients had POG range 36-40 weeks. Mean POG was 34.25 ± 4.12 .

Weight among two groups was analyzed as in Group A (loading dose regimen of mgso4) 184(72%) patients were 45-65 Kg, 72(28%) patients were 66-85 Kg. Mean weight was 82.54 ± 12.9 . Where as in Group B (standered dose regimen of mgso4 therapy) 179(70%) patients were 45-65 Kg, 77(30%) patients were 66-85 Kg. Mean weight was 82.34 ± 10 . Height among two groups was analyzed as in Group A (loading dose regimen of mgso4) 246(96%) patients had height range 5.00 to 5.99 feet, 10(4%) patients had height range 6.00 to 6.99 feet. Mean height was 34.22 ± 3.24 . Where as in Group B (standered dose regimen of mgso4 therapy) 241(94%) patients had height range 5.00 to 5.99 feet, 15(6%) patients had height range 6.00 to 6.99 feet. Mean height was 34.25 ± 4.12 . Efficacy among two groups was analyzed as Group A (loading dose regimen of mgso4) was effective in all the 256 patients while Group B (standered dose regimen of mgso4 therapy) was all so effective in all the 256 patients. Stratification of efficacy with age, gestational age and parity.

Table 1: Period of Gestation (n= 512).

Period of gestation in weeks	Group A	Group B
20-25	26(10%)	23(9%)
26-30	51(20%)	51(20%)
31-35	102(40%)	100(39%)
36-40	77(30%)	82(32%)
Total	256(100%)	256(100%)
Mean and SD	34.22 ± 3.24	34.25 ± 4.12

GROUP A: loading dose regimen of mgso4

GROUP B: Standered dose regimen of mgso4 therapy.

Chi Square test was applied in which P value was 0.047

Table 2: Weight and Height (n= 512).

Weight	Group A	Group B
45-65 Kg	184(72%)	179(70%)
66-85 Kg	72(28%)	77(30%)
Total	256(100%)	256(100%)
Mean and SD	82.54 ± 12.9	85.34 ± 10
HEIGHT	Group A	Group B
5.00-5.99 Feet	246(96%)	241(94%)
6.00-5.99 Feet	10(4%)	15(6%)
Total	256(100%)	256(100%)
Mean and SD	34.22 ± 3.24	34.25 ± 4.12

GROUP A: loading dose regimen of mgso4

GROUP B: Standered dose regimen of mgso4 therapy.

Chi Square test was applied in which P value was 0.047

Table 3: Efficacy (n= 512).

Efficacy	Group A	Group B
Effective	256(100%)	256(100%)
Not effective	00(00%)	00(00%)
Total	256(100%)	256(100%)

GROUP A: loading dose regimen of mgso4

GROUP B: Standered dose regimen of mgso4 therapy.

Chi Square test was applied in which P value was 0.000

Table 4: Stratification of Efficacy with age, Parity and Period of Gestation (n= 512).

AGE		Group A	Group B	P value
20-30 years	Effective	141	148	0.000
	Not effective	0	0	
31-40 years	Effective	115	108	0.000
	Not effective	0	0	
PARITY		Group A	Group B	P value
Primi para	Effective	166	159	0.000
	Not effective	0	0	
Multi para	Effective	90	97	0.000
	Not effective	0	0	
POG		Group A	Group B	P value
20-25 weeks	Effective	26	23	0.000
	Not effective	0	0	
26-30 weeks	Effective	51	51	0.000
	Not effective	0	0	
31-35 weeks	Effective	102	100	0.000
	Not effective	0	0	
36-40 weeks	Effective	77	82	0.000
	Not effective	0	0	

GROUP A: loading dose regimen of mgso4

GROUP B: Standered dose regimen of mgso4 therapy.

DISCUSSION

Pre eclampsia still a noteworthy reason for maternal death muddling 5 - 8 % of pregnancy. In the period that contamination and draining can be dealt with, preeclampsia remains an issue that isn't preventable and treatable past strong measures and conveyance. In contrast to preeclampsia, considering the wide hole in the frequency rates, eclampsia is viewed as a preventable condition. Current conventions for the utilization of magnesium sulfate are basically founded on spearheading report of Jeffrey M, et al¹¹² Pritchard that included 245 instances of eclampsia. Viability of magnesium sulfate in anticipation and treatment of eclamptic spasms is tried and true and bolstered with an assortment of concentrates. However, conventions and portion of magnesium sulfate are not proof based and restricted restorative list and poisonous quality is as yet a noteworthy worry in clinical use¹². Magnesium sulfate is cleared by kidneys and toxicity is avoided by ensuring urine output, at least 30 mL/hour. Convulsions are almost always prevented by plasma magnesium levels of 4-7 mEq/L. At 10 mEq/L patellar reflex is lost which is followed by respiratory depression on higher levels. Therefore, low dose regimens, might significantly improve the safety. Moreover, low dose MgSO₄ might be used in cases with mild renal impairment which is usually present in these patients. Recent studies revealed supportive evidence about the neuroprotective effect of MgSO₄¹².

Begum MR et al¹³ had shown that the efficacy of MgSO₄ in prevention and treatment of eclamptic convulsions is time tested and supported with a variety of studies. However, protocols and dose of MgSO₄ are not evidence based and narrow therapeutic index and toxicity is still a major concern in clinical use. We have shown that in patients with pre eclampsia loading dose of magnesium sulphate is as effective as standard regime in controlling fits. In our study no patient had a convulsion in both groups while in study by Regmi MC et al¹⁴ patients had convulsion in dose reduction women with small body size. Within recommended the in loading dose group while no patient had convulsion in standard regime group. However the difference was not statistically significant. ($p = 0.184$). A study by Shoaib

T et al¹⁵ showing loading dose to be 100% effective in controlling fits versus standard regime to be 98%. Another study conducted by Begum R et al¹⁶ at Dhaka Medical College Hospital, recurrent seizures were 4.0% in loading dose group and 3.5% in standard regime group. Similarly another study by Seth S et al¹⁷ loading dose to be less effective in controlling fits as compared to standard regime (effectiveness 85% versus 92.3%) but was not statistically significant. Similarly another study by Ekele B et al¹⁸ showed loading dose to be 92% effective in controlling convulsions in eclamptic patients.

The idea of victimisation simply the loading dose of metallic element salt to regulate and forestall fits in toxemia was steered by Souza As et al¹⁹ however the primary comprehensive study was printed in 2002. It absolutely was shown in this study that the repeated convulsion rate was virtually a similar (3.96% versus three.52%) between the cluster that had solely a loading dose of ten grams (4 gram endovenous and six gram intramuscular) and also the management group that had each the loading dose and the maintenance doses of two⁵. grams four-hourly for twenty-four hours. However, one amongst the restrictions of the study was that it absolutely was not test with the likelihood of allotment bias.

The results of the study show comparable admission characteristics of both the study groups i.e., age, parity & gestational age at time of admission. These characteristics were similar to a study carried out by Regime MC et al¹⁴. Another study performed by Seth S et al¹⁷ shows similar characteristics in both groups. Why would small doses or associate ultra-short regime of metallic element salt be effective in eclamptics? We have a tendency to don't have an evidence however some employees have instructed atiny low body mass index. My study shows difference in weights of women in 2 groups. The mean weight in group A was 82.5 ± 12 versus 85.3 ± 10 in group B. Okusanya BO et al²⁰ found that mean serum magnesium levels were significantly lower in women having a weight >70kg than the level observed in patients with a body weight <70kg. Similarly Okusanya BO et al²⁰ also suggested a dose adjustment according to patients' weight or body mass index.

The present study suggested that loading dose of magnesium sulphate is as effective as standard regimen in controlling seizures in eclampsia. The recurrent seizure rate was comparable in both group. Providing only loading dose to the patients reduces painful intramuscular injections and also definitely reduces the cost. So loading dose only regimen is suitable of our group of patients. The stacking in utilized in this examination study is drawing in for a few reasons. Inside the underlying spot, it limits the peril of lethality since most patients wouldn't might want the upkeep portions. Clinical looking for nuclear number 12 sulfate lethality as endorsed by inspiring sesamoid bone reflexes, count rate and mensuration urinary yield can be religiously embraced at tertiary emergency clinics any place there are satisfactory faculty, offices and the board. Anyway work force particularly could be a test at the region clinics and first human services focuses of the many creating nations. We have also confirmed that in certain patients with toxemia of pregnancy, the profound ligament reflexes can be made a decision about ambiguous or missing even before the inception of nuclear number 12 sulfate restorative guide if there's a decision to direct the medication; along these lines ligament reflexes can't be totally depended upon as AN early indication of harmfulness underneath such a situation. Besides, the estimation of treatment abuse the radical short arrangement is two or three third of the quality routine and this can be an appreciated improvement in asset poor nations.

CONCLUSION

Related with comparative adequacy in controlling convulsions the utilization of stacking portion magnesium sulfate (MgSO₄) conventions is a suitable option in contrast to standard portion treatment.

RECOMMENDATIONS

Further examinations are required to help routine clinical utilize low portion conventions & it would help obstetrician to use more effective regimen as well as decrease work load in tertiary care hospitals.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Nasir S: Conceptualization, Data Collection, Manuscript Writing.

Bibi K: Data analysis Manuscript writing, Proof Reading.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.