Bangladesh J Obstet Gynaecol, 2015; Vol. 30(2): 67-73

Original Articles

Simplification of Loading Dose of $MgSo_4$ in the Management of Eclampsia

KHAIRUN NESSA[1], FARHANA DEWAN[2], TAHMINA PARVIN[3], TANIA ISLAM CHOWDHURY[4], NOOR-E-NAHRIN[5]

Abstract:

Objective(s): *The aim of this study was to simplify the loading dose of $MgSo_4$ in the management of eclampsia.*

Materials and Methods: *This cross sectional study was conducted in Eclampsia unit of Dhaka Medical College Hospital during the period from April, 2010 to October, 2010. One hundred patients who admitted in the eclampsia ward were the target population for this study.Patients were selected purposively to use either (Group A=50) 10 gm $MgSO_4$, 4 gm IV and 6gm IM or (Group B =50) 8 gm of Nalepsin IV as loading dose. Maintenance dose were given by the same protocol in eclampsia unit of DMCH. Main outcome measures were controlling and recurrence of convulsion.*

Result: *There was no statistically significant difference in terms of recurrent convulsion (p=0.248). There was no significant difference in live birth rate (p=0.564) and birth condition of the baby (p=0.195). But there is a significant difference in NICU transfer of the baby. Twenty-two babies in group A and 30 babies of group B were referred to NICU (p=0.042). Time required to regain consciousness was same in two groups. Maternal conditions during admission were almost same though two patients condition was very poor in group A and those two died. From group A out of 50 patients 22 developed different complications and 8 patients needed referral to ICU and that poor prognostic 2 patients died. In group B 18 patients developed different complications and 6 patients needed referral to ICU and no mother died. There was a significant difference in term of maternal complications (p =0.044) though it is not related to schedule of anticonvulsant.*

Conclusion: *The results of loading dose of 8g of magnesium heptahydrate IV and 10g of $MgSO_4$IV and IM for controlling convulsion in eclampsia is comparable in terms of maternal and foetal outcome. But 8g of magnesium heptahydrate IV as a loading dose is easy to administer and dose not need to dilute the injection. So for convenience of health workers this simple schedule can be introduced for controlling convulsion in eclampsia as it is easy to administer and painful intramuscular injections can be avoided. Moreover, it is more economic and the risk of toxicity is less.*

Introduction:

Everyday, 1500 women die from pregnancy or child birth related complications, of which majority from developing countries. Eclampsia, accounting for 12% of all maternal death worldwide[1]. Until recently, the treatment of eclampsia varied throughout the world. The basic principles of management are (1) general nursing care (2) control of convulsions (3) control of

1. Assistant Professor, Gynae & Obs, Ibn Sina Medical College & Hospital, Dhaka
2. Professor & Head, Gynae & Obs, ShSMCH, Dhaka
3. Registrar, Gynae & Obs, Dhaka Community Medical College & Hospital, Dhaka
4. Consultant, BISH, Dhaka
5. Junior Consultant, Bogra Mission Hospital, Bogra

severe hypertension (4) initiation of obstetrical management. The use of anticonvulsant treatment varies in different parts of the world. A large multi center study has shown that Magnesium Sulphate is the ideal anticonvulsant[2].

In Bangladesh no institution has more experience than Dhaka Medical College Hospital (DMCH), where 500 to 800 eclamptic patients are admitted every year. In DMCH $MgSO_4$ has been used as a routine anticonvulsant from the beginning of 1998 after the commencement of its regular supply from the central medical store. We follow the dose schedule according to the guidelines published by Eclampsia Working Group[3]. The dose schedule is 4 gm intravenous (IV),given in diluted form and 3 gm intramuscular (IM) in each buttock – a total of 10 gm as a loading dose, followed by 2.5 gm IM every 4 hr in alternate buttock until 24 hrs after delivery or the last fit. This is almost half of dose described by the standard Pritchard regimen[4] in which 5 gm of $MgSO_4$ is administered four hourly for 24 hours after loading with 14 grams; as patient would require at least 44 grams of the drug to complete a course. As weight of the average Bangladeshi women is light, this small dose appears to control convulsions effectively as established in different trials[5] and is recommended by Eclampsia Working Group[3].

$MgSO_4$ that we are using in DMCH is an important preparation supplied by CMSD (Central medical store), the supply of which is inadequate many a time. On the other hand, Nalepsin (100 ml of 4% Mg Heptahydrate) marketed by a local pharmaceutical company is available all over the country.

The dose schedule for loading dose of $MgSo_4$ that we are currently using has both IV and IM component. Preparing the IV and IM component is cumbersome. For a loading dose total 4 ampules of drug are required, which is to be divided for IV and IM portion. Health care providers are to be trained for preparing the total schedule. So preparation needs both time and expertise. Moreover, IM component contains 3 gm (6 ml) $MgSo_4$ and this voluminous drug by IM route is very painful, sometimes it may cause abscess formation.

On the other hand schedule of IV inj Nalepsin is different. It includes 4 gm (100 ml) IV running at 60 drops/ m then 2 gm (50 ml) at 12 drops/minute and finally it is to be continued @ 6 drops/minute for 24 hrs.Though it is safe, giving continuous IV drip might bear risk if someone increases the drip inadvertently. We intended to modify the existing loading dose of IV/IM regim to avoid dilution of the drug and intramuscular component of loading dose. In our study we used 2 bag of inj Nalepsin ie total 8 gm of drug IV stat at loading dose. It is much easier to administer only by IV route and less training of health care provider is needed. Moreover, with only IV dose schedule painful IM injection could be avoided.

So purpose of this study was to explore the efficacy of 8 gm mgso4 as loading dose instead of 10 gm to control and prevent recurrence of convulsion in eclampsia.

Materials and methods :

During the period of April to October 2010,from all patients admitted in Eclampsia Unit of DMCH , a total 100 patients (50 $MgSO_4$ group and 50 Nalepsin group) were purposively selected.Only antepartum and intrapartum cases were included. Exclusion criteria were, patients with severe morbidity like CVA, HELLP Syndrome, DIC, renal failure, pulmonary oedema and patients having contraindication for using $MgSO_4$.

Fifty patients were managed by 10 gm $MgSO_4$ loading dose (group A). Dose schedule for group A: 4 gm (8 ml) of $MgSO_4$ dissolved in 12 ml of distilled water given IV and slowly over 20 minutes followed by 3 gm (6 ml) $MgSO_4$ deep IM in each buttock.

Another 50 patients were managed by 8 gm of Nalepsin (Group B).Dose schedule for group B: Injection Nalepsin 4 gm (100 ml of 4% magnesium heptahydrate) IV at a rate of 60 drops per minute over 25 minutes, followed by inj. Nalepsin 4 gm (100 ml) in IV infusion at the rate of 45 drops per minute over 30 mins. So it took 35 minutes more to complete the loading dose. In both groups maintenance dose was given by the same protocol in eclampsia unit of Dhaka Medical College Hospital ie 2.5 gm $MgSo_4$ IM in alternate buttock 4 hourly for 24 hours.

Beside the anticonvulsant, patients of both groups were managed by the same protocol for eclampsia management recommended by the Eclampsia Working Group of Bangladesh.

Student t test and Chi-square test were done as appropriate for test of significance and a p value of <0.05 is considered significant.

Result :

Rate of maternal complication at admission was higher in group A, leaded by pulmonary oedema and

Table-I

Patients' profile on admission

Parameters	Group				p value
	Group A (n=50)		Group B (n=50)		
Age (in year)	Mean ± SD		Mean ± SD		
Mean ± SD	21.36 ± 4.37		22.60 ± 3.48		0.120^{ns}
Gravidity	N	%	N	%	
• Primi	36	72.0	34	68.0	
• Multi	14	28.0	16	32.0	
Socioeconomic condition					
• Lower class	36	72.0	38	76.0	0.467^{ns}
• Lower middle class	2	4.0	4	8.0	
• Middle class	12	24.0	8	16.0	
Antenatal Checkup					
• Irregular	20	40.0	14	28.0	0.205^{ns}
• None	30	60.0	36	72.0	
Gestational age (weeks)	Mean ± SD		Mean ± SD		
	35.16 ± 3.09		35.02 ± 3.01		0.819^{ns}

Chi-square test was done for categorical data and t test was done for quantitative data to measure the level of significance. ns = Not significant.

Table I shows the patients' characteristics, which was similar in both the groups.

Table-II

Physical and laboratory findings on admission

Parameters	Group				p value
	Group A (n=50)		Group B (n=50)		
Conscious level	N	%	N	%	
• Conscious	20	40.0	20	40.0	0.065^{ns}
• Semi conscious	12	24.0	4	8.0	
• Unconscious	18	36.0	26	52.0	
Systolic BP (mm of Hg)	Mean ± SD		Mean ± SD		
	175.60 ± 22.33		178.60 ± 21.67		0.497^{ns}
Diastolic BP (mm of Hg)					
	102.00 ± 9.90		105.40 ± 6.46		0.045*
Lungs	N	%	N	%	
• Clear	22	44.0	24	48.0	0.688^{ns}
• Crepitation	28	56.0	26	52.0	
Knee Reflex					
• Normal	40	80.0	46	92.0	0.084^{ns}
• Brisk	10	20.0	4	8.0	
Respiratory rate (/min)	Mean ± SD		Mean ± SD		
	18.88 ± 3.22		19.04 ± 3.31		0.807^{ns}
Range	14-26		14-25		
Urine Albumin	N	%	N	%	
• ++	2	4.0	4	8.0	0.242^{ns}
• +++	22	44.0	28	56.0	
• ++++	26	52.0	18	36.0	

Chi-square test was done for categorical data and t test was done for quantitative data to measure the level of significance. ns = Not significant, * = Significant.

Baseline parameters of all patients were almost similar and there was no difference between two groups (Table II).

Table-III
Findings related to convulsion

Parameters	Group				p value
	Group A (n=50)		Group B (n=50)		
Number of convulsions before admission	N	%	N	%	
• <5	28	56.0	39	78.0	
• 5-10	22	44.0	9	18.0	
• >10	0	0	2	4.0	
Mean ± SD	4.72 ± 2.37		4.46 ± 2.12		0.564^{ns}
Time Interval between	Mean ± SD		Mean ± SD		
1st convulsion and admission (hour)	6.12 ± 2.90		6.10 ± 2.24		0.969^{ns}
Time Interval between 1st convulsion and treatment (hour)	7.10 ± 2.91		7.08 ± 2.22		0.969^{ns}
Time Interval between 1st convulsion and delivery (hour)	13.34 ± 5.38		13.36 ± 5.39		0.985^{ns}
Recurrence of convulsion	N	%	N	%	
	10	20.0	15	30.0	0.248^{ns}
Time needed to regain	Mean ± SD		Mean ± SD		
consciousness (hours)	36.93 ± 19.01		34.69 ± 14.66		0.627^{ns}

Chi-square test was done for categorical data and t test was done for quantitative data to measure the level of significance.
ns = Not significant.

Number of convulsion, time interval between 1st convulsion and admission, starting of treatment and delivery was same in both the groups (Table III).

Table-IV
Mode of delivery

Mode of delivery	Group				p value
	Group A (n=50)		Group B (n=50)		
	N	%	N	%	
NVD	18	36.0	21	42.0	0.934^{ns}
LSCS	24	48.0	21	42.0	
Forceps	2	4.0	2	4.0	
Ventouse	6	12.0	6	12.0	

Chi-square test was done to measure the level of significance.
ns = Not significant.

The different dose schedule did not effect in mode of delivery, which was similar in both the groups. Normal vaginal delivery and caesarean section is almost equal in both groups and rate of instrumental delivery is very low (Table IV).

Table-V

Fetal outcome

Parameters	Group				p value
	Group A (n=50)		Group B (n=50)		
	N	%	N	%	
Fetal outcome					
• Live birth	44	88.0	42	84.0	0.564^{ns}
• Still birth	6	12.0	8	16.0	
Condition of baby	(n=44)		(n=42)		
	N	%	N	%	
Healthy	32	72.7	25	59.5	0.195^{ns}
Asphyxiated	12	27.3	17	40.5	
Referral to NICU	(n=44)		(n=42)		
	N	%	N	%	
• Yes	22	50.0	30	71.4	0.042*
• No	22	50.0	12	28.6	
Birth weight (in kg)	(n=50)		(n=50)		
	N	%	N	%	
• <2.5	26	59.1	36	85.7	
• ≥ 2.5	18	40.9	6	14.3	
Mean ± SD	2.14 ± 0.59		2.00 ± 0.44		0.221^{ns}
Range	1.2-3.0		1.2-2.9		

Chi-square test was done for categorical data and t test was done for quantitative data to measure the level of significance. ns = Not significant, * = Significant.

Foetal outcome was also similar in both groups in terms of live birth rate 88% vs 84% , good apgar score 72.7% vs 59.5% and mean birth weight 2.14 ± 0.59 vs 2.00 ± 0.44 kg in group A and B respectively. Though low birth weight rate was a bit higher in group B, which is not significant. So NICU referral was also higher in group B 71.4% and 50% in group A (Table V).

Table-VII

Maternal outcome

Parameters	Group				p value
	Group A (n=50)		Group B (n=50)		
	N	%	N	%	
Complications at admission	22	44.0	18	36.0	0.044
ICU required	8	16.0	6	12.0	0.564
Maternal Death	2	4.00	0	00	0.153

Chi-square test was done to measure the level of significance.

shows significance difference. Two patients died from group A, though it might not be related to dose schedule as number of convulsion was not very different and there was no recurrent convulsion. Both of them were poor prognostic with pulmonary oedema. Though complication rate shows significant difference, death rate did not show the same.

Discussion:

Eclampsia is a multisystem disorder with complex pathogenesis, which is not completely understood. Control of convulsion and prevention of recurrence is one of the most important parts of management of eclampsia. There is now conclusive evidence that the best available anticonvulsant for women who have had an eclamptic fit is magnesium sulphate[6-8].

Bangladesh is a developing country where the incidence of eclampsia is very high, and eclampsia remains the leading cause of death in large tertiary level hospitals such as Dhaka Medical College Hospital (DMCH) for many years. $MgSO_4$ is being used as a routine anticonvulsant in different obstetric centers of Bangladesh since 1998, but the dose that is recommended by Bangladesh Eclampsia Working Group is much lower than that used in the Eclampsia Collaborative Trial (10gm loading dose compared to 14gm loading dose). The lower dose is chosen considering the smaller size of Bangladeshi women and concerns about toxicity in circumstances in which measuring serum magnesium levels would be difficult. Its efficacy in controlling convulsions and preventing recurrences has been established in many prospective studies. Studies showed that half of the standard dose of $MgSO_4$ appeared to be sufficient to control convulsion effectively and serum level of $MgSO_4$ remained lower than levels which produced toxicity[2,5]. A randomized controlled trial compared the effect of only loading dose and standard regimen for controlling of convulsion and showed the similarity of both the regimes in terms of controlling convulsion and recurrent convulsion rate. Recurrent convulsion rate was almost the same in both groups (3.96% in loading vs 3.51% in standard regime). Conclusion of the study was that only loading dose of $MgSO_4$ can control convulsion in eclampsia and it is as effective as standard regime.[5]

Cosidering the result of this study 8 gm loading dose is not under dose where maintenance dose is continued

So this study was conducted with a view to use 8 gm of Magnesium Heptahydrate (only IV) as a loading dose in the management of convulsion in eclamptic patients, and the observations were compared with those of 10 gm of $MgSO_4$ (both IV and IM). This has the advantages of being more simplified administration and need of less efficiency of healthcare providers. Moreover, painful IM injection can be avoided and it is more economic and can reduce the risk of toxicity.

None of the parameters were statistically significant. The mean time interval between 1st convulsion and treatment was 7.10 ± 2.91 versus 7.08 ± 2.22 hours. The mean time interval between 1st convulsion and delivery was 13.34 ± 5.38 versus 13.36 ± 5.39 hours. Only 10 percent patients of group A and 15 percent of group B experienced recurrent convulsion.

Mode of delivery, mean birth weight of the baby, birth asphyxia were similar in both groups. Low birth weight rate was higher in group B and NICU referral was also higher in that group though it has got no relationship with dose schedule. Table VI showed time required to regain consciousness. There was no statistically significant difference in regaining consciousness which was 36.93 ± 19.01 versus and 34.69 ± 14.66 hours in group A and Group B respectively.

Table VII shows the maternal outcome. There was statistically significant difference in term of maternal complications in group A and group B. P value was 0.044. The most commonest complication was pulmonary oedema. Two patients of pulmonary oedema from group A died and the death was not related to dose schedule as number of convulsion was comparable with group B and there was no recurrent convulsion. Even then there was significant difference in death rate between groups.

In conclusion it can be said that existing loading dose can be changed to 8 gm IV from 10gm IV and IM as there is no difference in treatment outcome. Rather it can avoid voluminous (6ml) painful intramuscular injection. However, a large scale study needs to be conducted to reach to a definitive conclusion.

References:

1. Maternal Mortality in 2005 estimates developed by WHO UNICEF UNFPA and the World Bank. Geneva World Health Organization 2007.

2. The Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995; 345: 1445-1463.

3. Eclampsia Working Group. Eclampsia in Bangladesh: A review of guideline. Bangladesh journal of Obstetric and Gynaecology. 1997; 12: 1-27.

4. Prichard JA, Cunninghum FG, Prichard SA. The Parkland Memorial Hospital Protocol for treatment of eclampsia, evaluation of 245 cases. Am J Obstet Gynaecol 1984; 148: 954-963.

5. Begum MR, Begum A, Quadir E. Loading dose versus standard regime of magnesium sulphate in the management of aclampsia: A randomized trail. J Obstet Gynaecol Res 2002; 28: 154-59.

6. Duley L, Henderson-Smart DJ, Walker GJA, Chou D. Magnesium sulphate versus diazepam for eclampsia. Cochrane Database of Systematic Reviews 2010;Issue 12. Art. No.: CD000127; DOI: 10.1002/14651858.CD000127.

7. Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database of Systematic Reviews 2010;Issue 10. Art. No.: CD000128; DOI: 10.1002/14651858.CD000128.

8. Duley L, Gülmezoglu AM, Chou D. Magnesium sulphate versus lytic cocktail for eclampsia. Cochrane Database of Systematic Reviews 2010;Issue 9. Art. No.: CD002960; DOI10.1002/14651858.CD002960.