

Intramuscular Loading Dose versus Combined Intravenous and Intramuscular Loading Dose of Magnesium Sulphate in the Management of Eclampsia

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Abstract

Background: Eclampsia is a common obstetrical emergency, remains a leading cause of maternal and perinatal morbidity and mortality in Bangladesh. Combined Intramuscular (IM) and Intravenous (IV) regime of $MgSO_4$ is commonly used in the treatment of eclampsia. However, IM loading dose of $MgSO_4$ could be a suitable alternative for community intervention of the management of eclampsia. This study aimed to compare the efficacy of the loading total IM regime of injection $MgSO_4$ with the standard loading combined IV and IM regime for prevention of recurrent convulsions in the treatment of eclampsia.

Materials and methods: An open labeled randomized clinical trial was conducted in the Department of Obstetrics and Gynaecology, Chittagong Medical College Hospital, Bangladesh from January 2017 to December 2017 including 120 patients with eclampsia. Patients were randomly allocated to either of the two groups: one group received standard loading combined IV and IM regime and other group received loading IM regime. The primary outcome measure was the rate of recurrent convulsions.

Results: Both the groups were comparable in terms of their baseline demographic, obstetric and clinical characteristics. The recurrent convulsion rate was similar in two groups (15% vs. 13.3%, $p=0.756$). The mean number of recurrent convulsion was 1.67 ± 0.71 and 1.88 ± 1.12 in IM and IM+IV group, respectively ($p=0.65$). Maternal mortality was 1.7% in both groups. Live birth rate was 85% in IM and 80% in IM+IV group ($p=0.542$) and low APGAR score at 5 minutes was found in 60.8% and 62.5% of the neonates in IM and IM+IV group, respectively ($p=0.558$).

Conclusions: Loading total IM regime of $MgSO_4$ was found equally effective to the loading combined IV and IM regime in terms of prevention of recurrent fits in eclampsia. So it could be used by the field level workers before referral.

Key words: Eclampsia; Magnesium sulphate; Recurrent convulsion.

INTRODUCTION

The United Nations Sustainable Development Goal 3.1 aims to reduce the global Maternal Mortality Ratio (MMR) to less than 70 per 100,000 live births by 2030.¹ However, a steady decline in global maternal mortality, preeclampsia and eclampsia remains one of the most common reasons for maternal deaths.² The preeclampsia/eclampsia-specific MMR decreased from 77 per 100 000 live births in the 2001 Bangladesh Maternal Mortality and Health Care Surveys (BMMSs) to 40 per 100 000 live births in the 2010 BMMS, yet halted in the 2016 BMMS at 46 per 100 000 live births.³

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Death from eclampsia is challenging to prevent. However, the earliest intervention by in. $MgSO_4$ in the community could prevent convulsion and recurrence of fit and give better maternal-fetal outcomes.⁴ There are three $MgSO_4$ regimes available for practice. The popular one is the combined IV and IM regime, known as the Pritchard regime, used in Bangladesh, the IVs Zuspan regime and the IM regime.^{5,6} The eclampsia working group had tailored the Pritchard regime in Bangladesh. It had recommended a loading dose of 4 gm IV and 3 gm IM injection in each buttock, a total of 10 (Instead of 14 gm of Pritchard regime) followed by 2.5gm IM every 4 hourly in alternate buttocks as maintenance dose until 24 hours of delivery or the last fit (instead of 5gm IM of Pritchard regime).⁷ Though not practiced in our country presently, the total IM regime is 10 gm $MgSO_4$ IM as loading dose. This is followed by 2.5 gm IM every four hours in alternate buttocks as the maintenance dose until 24 hours of delivery or the last fit. WHO also recommended using IM $MgSO_4$ where IV loading dose is impossible.⁸

Nevertheless, great hesitation existed in using $MgSO_4$ at Bangladesh's primary health care level. This is because the two popular regimens, Pritchard and Zuspan, have an IV route of administration of their loading dose, and the initially thought safety margin is narrow. It has, however, been reported that $MgSO_4$ toxicity is not as expected and that clinical monitoring of women is sufficient.⁹ Therefore, the only limitation to introducing this evidenced-based treatment to the primary health care level is the route of administration of the loading dose. The present randomized clinical trial has been conducted to remove the constraints of preparing and using IV loading doses of $MgSO_4$ by field-level workers in rural areas. The study compared the efficacy of the total IM regime with the combined loading of IV and IM regimes in preventing recurrent convulsion, adverse effects and other fetomaternal outcomes in treating eclampsia.

MATERIALS AND METHODS

This open label randomized clinical trial was conducted at the Department of Obstetrics and Gynecology of Chittagong Medical College Hospital (CMCH) from January 2017 to December 2017. CMCH is the second largest public tertiary care teaching and training institute located at the southeastern Bangladesh. The study was approved by the ethical review committee of CMC. As informed written consent requires a sound mind, consent was obtained from the next to kin usually the husband because many patients were unconscious or confused.

Women with either antepartum or intrapartum eclampsia with gestational age ≥ 32 weeks were included in this study. Women with severe complication of eclampsia and women having known medical diseases like diabetes mellitus, heart disease, Jaundice, blood dyscrasia etc were excluded. In addition,

women with contraindication of magnesium therapy (eg. oliguria, renal failure, absent knee-jerk, respiratory rate $< 14/\text{min}$) and those who received $MgSO_4$ or other anticonvulsant outside the hospital were also excluded.

Patients were randomly allocated in to two equal group by simple lottery method. One group received 10gm of $MgSO_4$ by IM route, 5gm (10 ml) in each buttock (IM group) and the patients in the other group received $MgSO_4$ 4gm (8ml dissolved in 12 ml distilled water) IV slowly for 5-10 minutes then 3gm IM in each buttock (IV+IM group). For both groups if recurrence of convulsion occur within 4 hours of loading dose, repeat dose of 2.47gm (5 ml) $MgSO_4$ IV slowly was given over 5 minutes. In this study inj. G-MAG SULPH (2.47gm Magnesium Sulphate $7H_2O$ BP) batch number 185-149-29, manufactured by Gonoshasthaya Pharmaceuticals Ltd was used. Prior to initiation of $MgSO_4$ therapy presence of patellar reflex, respiratory rate more than 14/min and urine output more than 30 ml/hour was documented.

All patients were monitored by pulse, BP, respiratory rate, level of consciousness, knee jerk, auscultation of lungs, urine output hourly up to delivery then 4 hourly for next 24 hours. Besides anticonvulsant, patient of both groups were managed by giving supportive care. Antihypertensive therapy with inj. Labetolol was given to women whose blood pressure were above 150/100 mm of Hg. Complications (HELLP syndrome, renal failure, abruption placenta, pulmonary oedema) were treated accordingly. After control of convulsion irrespective of gestational age, termination of pregnancy was done according to obstetric indication and Bishop scoring within limited time for patient with eclampsia. Then they were followed up till discharge or death (Which was earlier).

Rate of recurrence of convulsion was the primary outcome measure. Secondary outcomes were time taken to regain consciousness, side effects and toxicities, maternal and neonatal complications. Recurrence of convulsion was defined when convulsion recurs within 4 hours of giving the loading dose and regain of Consciousness was defined as Glasgow Coma Score is 11 or more.¹⁰

Data were analyzed using SPSS version 23.0. Quantitative data were expressed as mean \pm SD and compared between groups by Independent sample t test. Categorical data were expressed as frequency and percentage and compared between groups by Chi-square or Fisher's Exact test. Statistical significance was defined as $p < 0.05$.

RESULTS

Sociodemographic characteristics of the patients are described in Table I, which shows that both the groups were comparable in terms of their mean age, economic condition and occupation ($p > 0.05$).

Table I Baseline sociodemographic characteristics of the patients

Characteristics	Assigned Group				p value
	IM (n=60)		IM+IV (n=60)		
	n	%	n	%	
Age, in years	22.30	± 4.27	21.63	± 3.86	0.327*
Income status					
□ Poor	36	60.0	32	53.3	0.422†
□ Lower middle class	23	38.3	28	46.7	
□ Upper middle class	1	1.7	0	0.0	
Occupation					
□ House wife	58	96.7	55	91.7	0.22†
□ Day labourer	0	0.0	2	3.3	
□ Garments worker	0	0.0	2	3.3	
□ Others	2	3.3	1	1.7	

Data were expressed as mean ±SD or frequency and per cent. †: Chi-square test, Independent sample t test.

Most of the patients were primi and was on irregular ante natal checkup in both groups without any significant difference. Both the groups were comparable in terms of referral site, distance from home to hospital, referring person and pre hospital treatment. Most of the patients came to the hospital either directly from home or from Upazila Health Complex (UHC). Most of the patients (77.5%) were admitted with antepartum eclampsia. Baseline characteristic of the patients in terms of GCS, blood pressure, oedema, and albuminuria at presentation are described in Table II. There was no significant difference between two groups regarding the disease severity patterns (p>0.05). Both groups were comparable in terms of the time interval to reach the hospital, number of convulsion before hospitalization, time to initiate the treatment after reaching the hospital, onset of convulsion to delivery interval and time taken to regain consciousness (p>0.05).

Table II Baseline clinical characteristics of the patients

Characteristics	Assigned Group				p value
	IM (n=60)		IM+IV (n=60)		
	n	%	n	%	
Gravidity					
□ Primi	44	73.3	41	68.3	0.688†
□ Multi	16	26.7	19	31.7	
Gestational age, in weeks	36.35	± 2.40	36.35	± 2.40	0.671*
Eclampsia type					
□ Antepartum	47	78.3	46	76.7	0.827†
□ Intrapartum	13	21.7	14	22.5	
GCS					
□ 15	2	3.3	2	3.3	0.971†
□ 14 – 8	48	80.0	47	78.3	
□ <8	10	16.7	11	18.3	
DBP, mmHg	107.58	± 14.48	106.08	± 9.66	0.506*
SBP, mmHg	161.17	± 18.05	160.67	± 13.26	0.863*
Oedema	53	88.3	52	86.7	0.472†
Albuminurea	56	93.3	57	94.9	0.744†

Data were expressed as mean ±SD or frequency and per cent. †: Chi-square test, Independent sample t test.

Respectively, 9 (15%) and 8 (13.3%) patients in the IM and IM+IV group had recurrent convulsion in this study. The mean number of recurrent convulsion was 1.67±0.71 and 1.88±1.12 in IM and IM+IV group, respectively (p=0.65). Figure 1 shows that there was no significant difference between the groups in respect to number of recurrent convulsion (p=0.756).

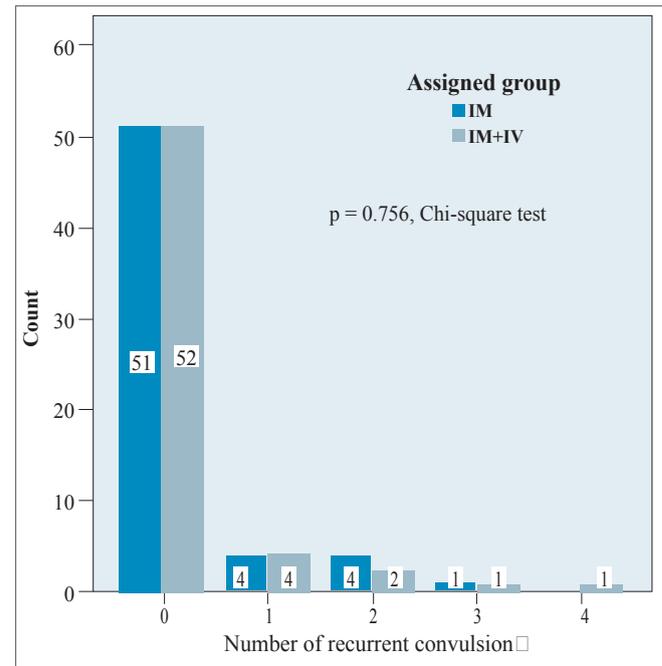


Figure 1 Number of recurrent convulsion between two groups

Most of the patients, 48 (80%) and 50 (83.3%) in IM and IM+IV group, respectively needed cesarean section for delivery. In respect to delivery mode both the groups are comparable as there was no significant difference in terms of delivery mode (Figure 2).

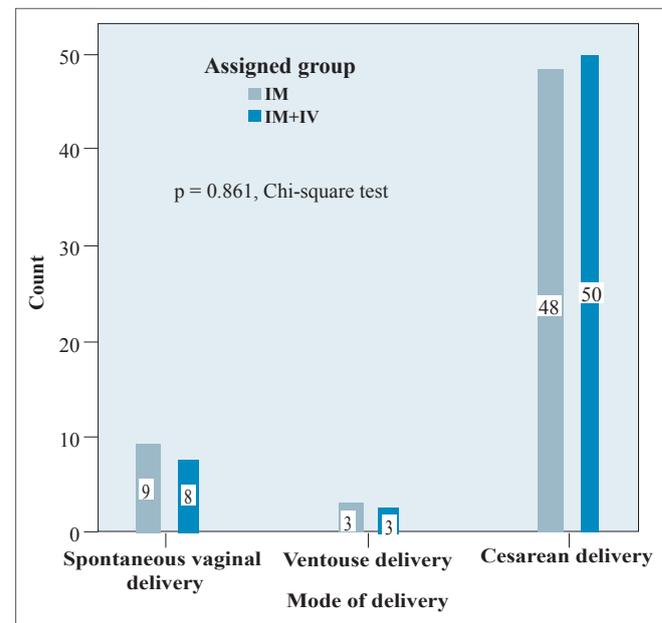


Figure 2 Mode of delivery between two groups

Maternal and neonatal outcomes were compared in Table III. Obstetric complications as shown in Table 9 during labour and delivery (Like PPH and abruption, CVA, Heart failure, HELLP) were almost similar in both groups. Case fatality rate was 1.7% in both groups. The average duration of hospital stay was about a week in both groups. A higher live birth was observed in IM group than in the IM + IV (85% in IM 80% in IM+IV) but it was insignificant. APGAR Scores in 5 minutes and rate of admissions in neonatal intensive care unit were also similar in both groups (p>0.05).

Table III Comparison of maternal and neonatal outcomes between two groups

Characteristics	Assigned Group		p value		
	IM (n=60)	IM+IV (n=60)			
	n	%	n	%	
Intranasal complication					
□ Abruptio placenta	7	41.7	5	58.3	0.38†
□ PPH	2	66.7	1	33.3	
Postnatal complications	3	5.0	2	3.3	0.659†
Length of hospital stay	7.22 ± 1.31		7.03 ± 1.52		0.477*
Maternal mortality	1	1.7	1	1.7	
APGAR score <7 at 5 minutes	31	60.8	30	62.5	0.558†
Live birth	51	85.0	48	80	0.542†
NICU admission	32	62.7	22	54.2	0.091†

Data were expressed as mean ±SD or frequency and per cent.†: Chi-square test, Independent sample t test.

DISCUSSION

This study was conducted to find out whether the total IM loading dose of MgSO₄ is effective and comparable with the combined loading IV and IM regime in termination of convulsion and prevention of its recurrence in eclampsia patients. This randomized control trial demonstrated that IM loading dose of MgSO₄ was as effective as IM+IV dose in eclampsia.

Mean age of the study patients was around 22 years and most of the patients were nulliparous, came from poor socioeconomic group and house wife in profession. (96.7% and 91.7% respectively). So this study was done between two groups of almost similar types of patients and the result was not affected by the minor variations. The results were also found comparable to the other studies.¹¹⁻¹³ Other obstetric and clinical characteristics of the patients were similar with other studies conducted in other hospitals in and around Bangladesh.^{11,14,15}

In the current study the loading total IM regime appears to be equally effective like the loading combined IV and IM regime in preventing recurrence of convulsions in the treatment of Eclampsia. After receiving the loading dose, 15% and 13.3% of the patients in IM and IM+IV group, respectively, developed recurrent convulsions. The recurrent convulsion rates vary in different studies from 0% to 25% with different regimen of

MgSO₄.^{11,15-17} These differences in the recurrent convulsion rate might be attributed to the interval between onset of convulsion and initiation of MgSO₄ therapy and differences in BMI of the enrolled patients.

One patient (1.7%) died in both group, which was 4.2% with IM MgSO₄ regime in Okusanya et al. study.⁶ Common maternal morbidities observed in this study were abruptio placenta, PPH, CVA, cardiac failure and HELLP syndrome. No significant difference was seen between both groups. A similar finding was seen in other study.¹⁷

In this study we evaluated the impending signs of toxicity clinically by observing patellar reflex, urine output, respiratory rate and local site infection and no patient developed any sign of toxicity in either group. Ekele et al. suggested that, clinical assessment of knee jerk, respiration and urine output is adequate to monitor maternal magnesium toxicity without the need to determine actual maternal serum levels.⁹

In this study perinatal death is about 15% in each group which was comparable with the study of Rouf et al. (20%).¹¹ Low Apgar score at 5 minutes was recorded in 39.2% and 37.5%, respectively, in IM and IM+IV group. Repeated convulsion at home before reaching hospital and anticonvulsant therapy with diazepam are very likely contributors to fetal depression and low Apgar score at birth.

From these above perspective it can be inferred that the loading total IM regime is found as effective as the loading combined IV and IM regime in terms of control of convulsions and prevention of recurrence and seems to be at least equally effective in terms of managing pregnancy outcome and preventing case fatality if not better than IV and IM combined regime. In our country MgSO₄ is available as 2.47 gm/5 ml in 50% solution. For giving 4 gm IV as loading dose it has to be diluted by taking 8 ml of MgSO₄ and 12 ml distilled water and it should be given slowly for 5-10 minutes. This calculation and preparation is difficult for field level workers. On the other hand most of the field level workers in our country are unfamiliar with the use of IV cannula but they can administer IM injections. So, only some educational and motivational measures will enable them to ensure the loading total IM regime of MgSO₄ at the domestic level. This method also needs minimum man power to manage the case.

LIMITATIONS

The study was done in hospital setting to make recommendation for community level, which was the main limitation of the study. In addition, instead of measuring serum magnesium level magnesium toxicity was assessed by clinical parameters.

CONCLUSION

The present study concluded that loading dose of MgSO₄ is as effective as combined IV and IM regimen in controlling seizures in eclampsia. The recurrent seizure rate was comparable in both group. Feto-maternal outcomes were also similar in both groups.

ECOMMENDATION

On the basis of findings of the study IM loading dose of mgso₄ could be recommended as a pre-referral treatment for eclampsia at the field and primary health care level. IM loading dose can be used in those situations where IV access is difficult

such as obesity and anasarca. Nevertheless, a larger randomized control trial, preferably at the community level is desirable to further evaluate the prospects of the use of MgSO₄ at primary health care delivery facilities.

DISCLOSURE

All the authors declared no competing interest

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