

# Single loading dose of magnesium sulphate in severe preeclampsia and eclampsia-is it effective? a randomized prospective study

## Abstract

**Introduction:** Magnesium sulphate ( $MgSO_4$ ) is the most effective anticonvulsant in preventing and controlling convulsion in severe preeclampsia and eclampsia. We tried to compare the efficacy of single dose of  $MgSO_4$  with standard Pritchard regime.

**Objectives:** To compare between single loading dose of  $MgSO_4$  and standard Pritchard regime in terms of efficacy and outcomes.

**Methods:** In a comparative, prospective, randomized study carried out from July 2010 to December 2012 in the Department of Obstetrics and Gynecology, Medical College, Kolkata, we included antenatal women with severe pre-eclampsia and eclampsia after 34 weeks of gestation, who were randomized in two groups. The study group (A) received single loading dose of  $MgSO_4$  and the control group (B) received the standard Pritchard regime. The results were analyzed by standard statistical methods.

**Results:** Total 500 women were included, of which 150 belonged to group A (50 severe preeclampsia, 100 eclampsia) and 350 to group B (150 severe preeclampsia, 200 eclampsia). The incidence of appearance or recurrence of convulsions, pulmonary edema, maternal mortality, Caesarean section and post-partum hemorrhage did not vary significantly in between two groups. However, in group A, the incidence of magnesium toxicity was significantly lower ( $p$ -value  $<0.005$ ) than group B. The mothers in group A took significantly less time to return to post natal wards and also to return home with involvement of significantly less number of health care staffs in their care ( $p$  value  $<0.0001$ ). The perinatal outcomes were similar in between two groups.

**Discussion:** Women receiving single dose  $MgSO_4$  had similar clinical course to those receiving standard regime, while having significantly less incidence of magnesium toxicity. It was associated with fewer burdens on health care delivery system.

**Conclusion:** Single loading dose  $MgSO_4$  is a cost-effective and safe therapy in developing countries with low average body-weight and limited resources.

**Keywords:** pregnancy, preeclampsia, eclampsia, magnesium-sulphate, loading dose, pritchard regime

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**Abbreviations:** BMI, body mass index; BP, blood pressure; CCU, critical care unit; CNS, central nervous system; CTG, cardiotocography; CVA, cerebrovascular accident; DBP, diastolic blood pressure; GNI, gross national income; IEC, institutional ethics committee; IM, intramuscular; IV, intravenous; LDH, lactate dehydrogenase; LMIC, low and medium income countries; MAGPIE, magnesium sulphate for prevention of eclampsia;  $MgSO_4$ , magnesium sulphate; NHBPEP, National high blood pressure education program; PPH, postpartum hemorrhage; SBP, systolic blood pressure; SGOT, serum glutamate oxaloacetate transferase; SGPT, serum glutamate pyruvate transferase; SNCU, sick neonatal care unit; WHO, World Health Organisation

## Introduction

Hypertensive disorders in pregnancy are the diseases of major concern among the obstetricians. It is a major cause of maternal and perinatal mortality and morbidity world-wide, especially in low and middle income countries where they account for 10-25% of maternal deaths. The major cause of maternal deaths in these cases is eclamptic seizure.<sup>1</sup>

The Working Group of the National High Blood Pressure Education Program (NHBPEP) [2] defined hypertension as blood pressure (BP)  $\geq 140/90$  mm Hg using Korotkoff V sound for diastolic blood pressure. The same Working Group classified hypertensive disorders in pregnancy into four groups

1. Gestational Hypertension;
2. Preeclampsia and Eclampsia syndrome;
3. Superimposed preeclampsia on chronic hypertension;
4. Chronic hypertension.<sup>2</sup>

Preeclampsia is defined as presence of hypertension and proteinuria (300mg or more in 24 hour urine). It may again be mild or severe.<sup>2</sup> Eclampsia, on the other hand is the sudden onset grand mal seizure in a woman with pre-eclampsia that cannot be attributed to other causes. The management of eclampsia and severe pre-eclampsia include initial stabilization, rational use of antihypertensives, anticonvulsants and planning for delivery to achieve "cure". Anticonvulsant is essential in eclampsia to control seizure and also in severe pre-eclampsia to prevent eclamptic convulsion.

Various anticonvulsants had been used in the past but it is only the Magnesium Sulphate ( $MgSO_4 \cdot 7H_2O$ ) that withstood the taste of time. The superiority of  $MgSO_4$  as an anticonvulsant in patients with eclampsia, when compared with diazepam and phenytoin was determined in a multicentric randomized control trial.<sup>3</sup> Recurrent seizures and maternal deaths both were significantly lower in women receiving  $MgSO_4$ . On the other hand, even in severe preeclampsia, use of prophylactic  $MgSO_4$  can significantly reduce the risk of eclamptic convulsion by 58% compared to placebo, as shown in a large multicentric trial- the MAGPIE trial.<sup>4</sup> The long term safety as well as the cost-effectiveness especially in low gross national income countries (GNI) have been proved by two subsequent studies.<sup>5,6</sup>

$MgSO_4$  can be given as per Zuspan or Pritchard regime. Although continuous intravenous (IV) infusion (4g of 50% solution IV loading dose followed by 20% solution 1g/hour IV infusion) is more commonly used worldwide; limited availability of infusion pump, lack of adequate manpower and the associated cost made it less popular in developing countries of Indian subcontinent where Pritchard regime seems to be more useful. The standard regime consists of loading dose of total 14g; 4g of 20% solution IV and 10g 50% solution intramuscularly (IM). It is followed by maintenance dose of 5g 50% solution IM every 4 hours, provided the knee jerk is maintained, urine output is 30 ml/hour or 100 ml per 4 hours and respiratory rate is more than 14 per minute. It is continued up to 24 hours after delivery or 24 hours after the last convulsion, whatever is the later.

However, the above mentioned dose regimen is based mainly on the Western women. The average body weights of Indian women are far less than their Western counterparts. Again, hypertensive disorder is a very common obstetric complication in low resource country,<sup>7</sup> mainly due to lack of adequate antenatal care, inadequate access to health care facilities, lack of awareness among common people and also poor socio-economic conditions. On the other hand, the health-care provider to patient ratio is not optimum in most of the institutes, even in tertiary care hospitals. Again because of associated side effects of the therapy,  $MgSO_4$  administration needs proper monitoring, which may not be always possible in a busy labor ward. On the other hand, it is not uncommon to withhold  $MgSO_4$  after one or two doses due to signs of magnesium toxicity or oliguria and surprisingly most of the time there is no episode of repeated seizure.

In a Cochrane review Duley et al.<sup>8</sup> included four randomized controlled trials of comparing the standard dose with the alternative dose of  $MgSO_4$  from India and South Africa and they concluded that those trials were too small to draw any conclusion.<sup>8</sup> Gordon et al.<sup>9</sup> in their systematic review, analyzed that in LMIC (low and middle income countries), modified forms of standard Zuspan or Pritchard regimes were commonly used, either by decreasing the dose in grams (for only loading dose, for only maintenance dose or for both) or by decreasing the total duration of therapy. They explained that the reasons behind those dosing modifications on were concern about  $MgSO_4$  toxicity (mainly because of smaller size of women and others), inconsistent supply of drugs, cost-effectiveness, lack of resources for monitoring and difficulties with repeated IM injections for the patients.<sup>9</sup> They also observed that  $MgSO_4$  is underutilized in LMIC (low and middle income countries), thus emphasizing the need of policy changes to ensure the widespread availability of the drug and its use.<sup>9,10</sup>

Keeping all these in mind, we tried to study the efficacy of single loading dose of  $MgSO_4$  in antenatal women with severe preeclampsia and eclampsia, by comparing it with the standard practice.

## Aims and objectives

- To find the efficacy of single loading dose of  $MgSO_4$  (14gram-4g 20% solution IV + 10g 50% solution IM) compared to standard Pritchard regimen of  $MgSO_4$  (loading dose as mentioned above + 4 hourly maintenance dose of 5g 50% solution 24 hours after delivery).
- To compare the maternal outcomes, perinatal outcomes, patient satisfaction (in terms of hospital stay) and the load on health care staffs in between these two groups

## Material and methods

A comparative, prospective randomized study was carried out from July 2010 to December 2012 in pregnant women attending the Emergency and the Out Patient Department of the Department of Obstetrics and Gynecology, Eden Hospital, Medical College and Hospital, Kolkata. Severe pre-eclampsia and eclampsia were defined as per NHBPEP criteria. Antenatal women with severe pre-eclampsia and eclampsia after 34 weeks of gestation with live fetus who deserved active management and who did not receive any prior anticonvulsant were included in the study. Excluded were women having contraindications to  $MgSO_4$  (like myasthenia gravis), mild pre-eclampsia, gestational hypertension, chronic hypertension without superimposed pre-eclampsia, gestational age <34 completed weeks, women already having intrauterine fetal death, women undergoing conservative management, women receiving prior anticonvulsants and women presenting in post-partum period.

After getting clearance from the Institutional Ethical Committee (IEC), informed consent was obtained from all the participants. Detailed history taking and systemic and obstetric examination were done. Women with severe pre-eclampsia were treated with antihypertensives (as applicable), antenatal corticosteroids (as indicated), monitoring of clinical (BP, proteinuria, signs and symptoms of severe pre-eclampsia) and laboratory parameters (complete blood count including platelets, liver enzymes, serum creatinine) and fetal monitoring (cardiotocography- CTG, Doppler, Ultrasound) as appropriate, as per the World Health Organization (WHO) recommendations.<sup>11</sup> Eclamptic women were initially stabilized by general measures, along with control of blood pressure, in accordance with WHO.<sup>11</sup> All of these women were assessed to make the plan for delivery- induction of labor, augmentation of labor or caesarean section as appropriate. As all of those two categories of women deserved  $MgSO_4$  (prophylactic or therapeutic), they were randomized to two groups by lottery.

### The study group:

- received only single loading dose of  $MgSO_4$  and the control group
- received the standard Pritchard regime of  $MgSO_4$  (loading plus 4 hourly maintenance unless signs of magnesium toxicity or oliguria appeared).

All the women were carefully followed up to note control of BP, development or recurrence of eclamptic seizure, other central nervous system (CNS) manifestations (sensorium, cerebrovascular accidents- CVA, visual disturbances), pulmonary edema, oliguria, admission to Critical Care Unit (CCU). Signs of magnesium toxicity was also monitored (absent knee jerk, decreased respiratory rate and others) every 4 hourly in all of the women. The labor events, mode of delivery, blood loss at delivery, time to return to post-natal ward,

duration of hospital stay and number of health care staffs involved in maternal care were all noted. Regarding perinatal parameters, fetal hypoxia, Apgar score, admission to SNCU (Sick Neonatal care Unit) and mortality were also studied.

The results were analyzed by standard statistical methods like two sample 't' test (both tailed or one tailed accordingly) and 2-proportion test and p value <0.05 was considered to be significant.

## Results

Total 500 women were studied, of which 150 belonged to group A (50 severe preeclampsia and 100 eclampsia) and 350 (150 severe preeclampsia and 200 eclampsia) to group B. Owing to obvious differences in terms of prognosis, results were classified in two different parts depending on whether the women presented with severe pre-eclampsia or eclamptic convulsion. The first part comprised of the patients who fulfilled the criteria for severe pre-eclampsia. In this part, 50 women (A1) received only loading dose and 150 (B1) received the standard Pritchard regime.

Women in both the groups were comparable in terms of maternal age, gravid, gestational age and body weight (Table 1). There was no significant difference in between these two groups regarding the clinical and laboratory parameters, like systolic and diastolic blood pressure (SBP and DBP respectively), proteinuria, platelet count, serum LDH (lactate dehydrogenase), SGOT (Serum glutamate oxaloacetate transferase), SGPT (Serum glutamate pyruvate transferase) and serum creatinine levels (Table 2).

**Table 1** Demographic variables of women with severe preeclampsia

	A1 (n=50)	B1 (n=150)	p-value
	Mean±SD	Mean±SD	
Maternal Age (years)	24.52±3.54	24.07±4.24	0.49
Gravida	1.2 ±0.71	1.21±0.71	0.796
Gestational Age (weeks)	34.7±3.07	34.5±3.31	0.707
BMI (Kg/m <sup>2</sup> )	24.63±4.86	23.92±5.31	0.404

**Table 2** Clinical and laboratory parameters of the women with severe preeclampsia

	A1 (n=50)	B1 (n=150)	p-value
	Mean±SD	Mean±SD	
SBP (mm Hg)	168±1.95	167.5±1.41	0.051
DBP (mm Hg)	98±7.42	100±7.07	0.089
Proteinuria	3±1.22	2.95±1.41	0.823
Platelet Count (lac/ cmm)	1.85±0.01	1.94±1.36	0.641
Serum LDH (IU/L)	444±189.50	503.2±185.7	0.054
SGOT (IU/L)	112.56±94.80	152.80±134.87	0.052
SGPT (IU/L)	104.14±96.36	138.97±123.86	0.071
Serum Creatinine (mg/dl)	0.63±0.35	0.61±0.39	0.748

SBP, systolic blood pressure; DBP, diastolic blood pressure; LDH, lactate dehydrogenase; SGOT, serum glutamate oxaloacetate transferase; SGPT, serum glutamate pyruvate transferase

While carefully analyzing the outcomes, we found that, two women in group A1 developed convulsions even after receiving MgSO<sub>4</sub>, compared to four women in group B1; all these patients being managed with 2g of 20% solution of MgSO<sub>4</sub> given IV. The incidences of CVA, pulmonary edema, CCU admission and maternal mortality

were not significantly different between two groups (p value <0.05 was considered significant). However, the incidence of oliguria was significantly higher in the A1 group. Absent knee jerk was seen in one woman of A1 as against 11 of B1 (p-value 0.029) and decreased respiratory movement in two of A1 and 16 of B1 (p-value 0.036). Thus incidence of magnesium toxicity was significantly lower in A1 as against B1. However, the incidences Caesarean section rates, uterine inertia and post-partum hemorrhage (PPH) did not show statistically significant differences between two groups. The mean time taken to return to post-natal ward was 13±1.41 hours in A1 while that was 25.5±2.12 hours in B1, with p-value <0.0001 (significant). Similarly the duration of hospital stay and the number of health care staffs involved in care of the women were significantly higher in group A1 compared to group B1. Regarding perinatal outcomes, the incidence of fetal hypoxia (as defined by CTG) and neonatal Apgar score taken after 5 minutes of birth were not showing any significant differences in between two groups. However the admission to SNCU and perinatal mortality were similar between the two groups (Table 3).

**Table 3** Follow up results of women with severe preeclampsia

	A1 (n=50)	B1 (n=150)	p-value
Convulsions	2	4	0.631
Other CNS Symptoms	11	0	0.082
Pulmonary Edema	1	1	0.412
Oliguria <sup>2</sup>	6	4	0.009*
CCU Admission	5	5	0.061
Maternal Death <sup>3</sup>	2	3	0.435
Absent Knee Jerk	1	194	0.029*
Decreased Respiratory Rate <sup>5</sup>	2	234	0.036*
Caesarean Section	27	83	0.873
Uterine Inertia <sup>6</sup>	9	14	0.097
PPH <sup>7</sup>	3	4	0.267
Return to Post-natal ward (hours) (Mean±SD)	13±1.41	25.5±2.12	<0.0001*
Duration of Hospital stay (days) (Mean±SD)	4.3±1.69	5.8±1.93	<0.0001*
Number of Health Care staffs(Mean±SD)	4.3±1.43	6±1.67	<0.0001*
Fetal Hypoxia <sup>8</sup>	5	7	0.168
Apgar score (5 min) (Mean±SD)	8±1.27	7.84±2.83	0.6995
SNCU Admission	11	23	0.276
Perinatal Mortality <sup>9</sup>	1	0	0.082

CNS, central nervous system; CCU, critical care unit; PPH, postpartum hemorrhage; SNCU, sick neonatal care unit

<sup>1</sup>One case of cerebral hemorrhage.

<sup>2</sup>Defined as urine output <30ml/hour or <100ml/4 hour

<sup>3</sup>Two mothers died of coagulopathy, one of renal failure, two of embolism

<sup>4</sup>MgSO<sub>4</sub> was withheld in those cases after observation of these side effects

<sup>5</sup><14/minute

<sup>6</sup>Uterine contractions <3/10 minutes, each lasting <40 seconds

<sup>7</sup>>500ml in vaginal and >1000ml in Caesarean delivery

<sup>8</sup>Defined by non-reassuring fetal heart rate pattern in CTG

<sup>9</sup>Include still birth (>28 weeks of gestation and early neonatal (<7 days) death

\*Significant p-value

The second part comprised of the patients having eclamptic seizures. In this case, 100 women received only loading dose (A2) and 200 received the standard Pritchard regime (B2). Women in both the groups were comparable in terms of maternal age, gravid, gestational age and body weight (Table 4).

**Table 4** Demographic variables of women with eclampsia

	A2 (n=100)	B2 (n=200)	p-value
	Mean±SD	Mean±SD	0.715
Maternal Age (years)	22.98±4.88	23.09±4.24	0.732
Gravida	1.21±0.09	1.21±0.78	1
Gestational Age (weeks)	34.85±0.77	35±0.78	0.116
BMI (Kg/m <sup>2</sup> )	24.93±5.47	24.06±6.29	0.383

Now, we compared the outcomes in between these two groups. 12 women in group A2 had repeat convulsions after the loading dose, compared to 23 women in group B2. All of them responded to IV 2g of 20% MgSO<sub>4</sub> given at the time of repeated convulsion. Incidences of other CNS disturbances (altered sensorium, CVA, visual blurring), pulmonary edema, oliguria, CCU admission and maternal mortality did not vary significantly in between these two groups. Absent knee jerk was seen in three women of A2 as against 25 of B2 (p value 0.008) and decreased respiratory movement in four of A2 and 22 of B2 (p value 0.042). Clearly, the incidence of magnesium toxicity was significantly lower in A2 as against B2. The rate of Caesarean section, uterine inertia and PPH did not show significant difference in these two groups. The patients in the group A2 took significantly more time in return to post-natal ward and also in total duration hospital stay with p-value in both cases <0.0001 (significant). The mothers in A2 group needed involvement of more health care staffs compared to B2 and that difference was also statistically significant (p value<0.0001). Regarding perinatal factors, although the 5 minute Apgar score was significantly better in babies in group A2, the incidences of fetal hypoxia, admission to SNCU and perinatal mortality did not vary significantly in these two groups (Table 5).

**Table 5** Follow up results of women with eclampsia

	A2 (n=100)	B2 (n=200)	p-value
Recurrent Convulsions <sup>1</sup>	12	23	0.897
Other CNS Symptoms	8	13	0.631
Pulmonary Edema	8	7	0.091
Oliguria <sup>2</sup>	9	11	0.25
CCU Admission	6	10	0.719
Maternal Death <sup>3</sup>	5	7	0.535
Absent Knee Jerk	3	254	0.008*
Decreased Respiratory Rate <sup>5</sup>	4	224	0.042*
Caesarean Section	68	143	0.529
Uterine Inertia <sup>6</sup>	17	39	0.603

Table Continues...

	A2 (n=100)	B2 (n=200)	p-value
PPH <sup>7</sup>	12	27	0.719
Return to Post-natal ward (hours) (Mean ± SD)	18±2.98	29.99±3.25	<0.0001*
Duration of Hospital Stay (days) (Mean ± SD)	6.89±0.76	8.54±1.09	<0.0001*
Number of Health Care Staffs involved (Mean ± SD)	6.79±1.24	8.53±2.39	<0.0001*
Fetal Hypoxia <sup>8</sup>	8	11	0.401
Apgar score (5 min) (Mean ± SD)	8.5±0.04	6.89±2.35	<0.0001*
SNCU Admission	26	59	0.529
Perinatal Mortality <sup>9</sup>	3	5	8.03

CNS, central nervous system; CCU, critical care unit; PPH, postpartum hemorrhage, SNCU, sick neonatal care unit

<sup>1</sup>Defined as convulsion occurring after start of MgSO<sub>4</sub> loading dose

<sup>2</sup>Defined as urine output <30ml/hour or <100ml/4 hour

<sup>3</sup>Five mothers died of CVA, three of pulmonary embolism, two of renal failure, one of coagulopathy, one had intra-operative cardiac arrest.

<sup>4</sup>MgSO<sub>4</sub> was withheld in those cases after observation of these side effects

<sup>5</sup><14/minute

<sup>6</sup>Uterine contractions <3/10 minutes, each lasting <40 seconds

<sup>7</sup>>500ml in vaginal and >1000ml in Caesarean delivery

<sup>8</sup>Defined by non-reassuring fetal heart rate pattern in CTG

<sup>9</sup>Include still birth (>28 weeks of gestation and early neonatal (<7 days) death

\*Significant p-value

## Discussion

There is no doubt about efficacy of MgSO<sub>4</sub> in management of hypertensive disorders in pregnancy; for control of convulsions in eclampsia and prevention of convulsions in severe preeclampsia. The question is what should be the ideal dose. Due to heavy load on health care system and limited number of health-care providers, regular and frequent monitoring of the women receiving MgSO<sub>4</sub> is not always possible.

Body mass index (BMI) is important factor determining the efficacy and toxicity of MgSO<sub>4</sub>, as seen in the study carried by Tudela et al.<sup>12</sup> Jana et al.<sup>13</sup> in their study carried out in Burdwan, India found that low dose MgSO<sub>4</sub> (8g loading- 3g IV and 5g IM; followed by 2.5gIM 4 hourly) was safe and effective for eclamptic women having light weight.<sup>13</sup> They even found that the low dose regime was associated with lower incidence of seizure recurrence and lower maternal mortality compared with the Collaborative Eclampsia Trial.<sup>13</sup> In our study also the participating women had lower body weight than their Western counter-parts, giving rise to a concern about the magnesium toxicity. We indeed, found that in both severe preeclampsia and eclampsia women receiving only loading dose of MgSO<sub>4</sub> had significantly lower incidence of side effects (like absent knee jerk and decreased respiratory rate) than women receiving the standard Pritchard regime.

So, the concern about magnesium toxicity led many investigators to look into the possibility of abbreviated regime of MgSO<sub>4</sub>. Ehrenberg & Mercer<sup>14</sup> in their study on abbreviated post-partum MgSO<sub>4</sub> therapy in preeclampsia found that women receiving MgSO<sub>4</sub> for 12 hour post-partum had the clinical course similar to that of 24-hour group.<sup>14</sup>

Another study carried out by Darnagawn et al.<sup>15</sup> in Christian Medical College, Vellore showed that in case of severe preeclampsia a shortened (6-hour) MgSO<sub>4</sub> regime was as effective as the 24-hour regime with significant benefits in terms of cost and morbidity.<sup>15</sup> A recent study in Brazil by Maia et al.<sup>16</sup> showed that abbreviated exposure (12 hour) to MgSO<sub>4</sub> in severe preeclampsia was associated with decreased drug exposure and reduced time-gap to contact newborn after delivery but similar outcomes.<sup>16</sup>

Several studies investigated the role of only single loading dose of MgSO<sub>4</sub> in managing hypertensive disorders in pregnancy.<sup>17-22</sup> All of them were carried out in low resource countries like Pakistan,<sup>17,18</sup> Bangladesh,<sup>19</sup> Nepal,<sup>20</sup> Nigeria<sup>21,22</sup> and Egypt.<sup>23</sup> Noor et al.<sup>17</sup> conducted a study on MgSO<sub>4</sub> in women with eclampsia and preeclampsia at Peshawar, Pakistan in which majority of the patients received only loading dose and 5g intramuscular dose was repeated only if the patient had convulsions.<sup>17</sup> They found that initial loading dose was adequate for most of the women to prevent convulsions. In our study, the convulsion rates were similar in the mothers receiving single dose and those receiving standard therapy.

El-Khayat et al.<sup>23</sup> conducted a study of loading IV MgSO<sub>4</sub> versus standard IV regime in postpartum severe preeclampsia in Egypt and concluded that the former could be a promising alternative regime.<sup>23</sup> In their quasi-experimental study, Shoaib et al.<sup>18</sup> of Jinnah Postgraduate Medical Centre, Karachi (2009) showed that single loading dose of MgSO<sub>4</sub> was preferred to standard Pritchard regime in pre-eclampsia to prevent convulsion in terms of equal effectiveness, ease of monitoring and cost-effectiveness.<sup>18</sup> In our study on women with preeclampsia (group A1 and B1), single loading dose of MgSO<sub>4</sub> had similar efficacy as standard Pritchard regime, as evident by maternal and neonatal morbidity and mortality.

Perhaps, the more encouraging results came from the randomized control trial conducted in Dhaka Medical College by Begum et al.<sup>19</sup> They randomized eclamptic women to either single loading dose or standard dose of MgSO<sub>4</sub> and found that the former is quite effective to control eclamptic convulsion. In our study also on the eclamptic women (group A2 and B2), those receiving single dose of MgSO<sub>4</sub> had similar clinical course (in terms of complications of eclampsia-like CNS symptoms, oliguria, pulmonary edema, CCU admission, caesarean section rate, uterine inertia, PPH and mortality) to those receiving standard MgSO<sub>4</sub> regime.

Some authors even used lower amount of drug in loading dose. In a randomized controlled trial on women with eclampsia or severe preeclampsia carried out at Nigeria, a loading dose of 10g IM (without the 4g IV) was compared with the standard Pritchard regimen (of loading and maintenance dosing) and the authors did not find any significant difference in the episode of eclamptic seizure after starting the therapy.<sup>22</sup>

Therefore, both in severe preeclampsia and eclampsia, single dose MgSO<sub>4</sub> seems to be a promising alternative. The results of our study can be extrapolated to the setting where referral of the mothers with hypertension to the higher centre is needed. In that case, loading dose of MgSO<sub>4</sub> before referral could lower down the morbidity significantly, as seen in a community-based study carried out in Bangladesh.<sup>7</sup>

Single loading dose of MgSO<sub>4</sub> therapy should be considered cost-effective in management of both severe preeclampsia and eclampsia.<sup>18</sup> In our study mothers receiving only loading dose of MgSO<sub>4</sub> took significantly less time to return to post-natal wards and the duration of hospital stay were also shorter. This is of particular importance

considering the poor socio-economic background of the women participating in our study. The number of healthcare staffs involved in maternal care was also significantly lower in mothers receiving single dose therapy compared to standard therapy, because the former group needed monitoring for less frequency and duration. Again, this is helpful in better utilization of the limited number of manpower in a busy obstetric ward in developing countries like India with sub-optimum care-giver to patient ratio.

The positive aspect of our study lies in demonstration of safety and efficacy of single dose MgSO<sub>4</sub> in head to head comparison with the standard Pritchard regime. But the study has its limitations. We could not carry out the economic analysis in between these two groups and also the pharmacokinetic profile of single dose MgSO<sub>4</sub> could not be taken care of.

## Conclusion

Single loading dose of MgSO<sub>4</sub> is quite effective and safe both in severe pre-eclampsia and eclampsia, as prophylactic and therapeutic anticonvulsant respectively. It is particularly suitable in developing countries where average body weight is low, monitoring is difficult and resource-availability is limited. It is also associated with significant patient satisfaction in terms of quicker return to postnatal wards and shorter hospital stay. On the other hand, it involves relatively less number of health care professionals to take care of women, leading to more effective utilization of manpower and resources. It should be considered as alternative to standard Pritchard regime in women who deserves MgSO<sub>4</sub> therapy but 1:1 monitoring is difficult. However, multicentric randomized controlled studies involving more number of participants should be conducted before using it in routine practice.

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## Conflicts of interest

The authors declare there is no conflict of interests.

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