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Original Article

# Modified Low Dose Magnesium Sulfate Regime: Is it Efficient to Control Eclampsia?

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## Abstract

**Background:** Eclampsia, the occurrence of a seizure in association with pre-eclampsia, is rare but potentially life-threatening. Magnesium sulfate is the drug of choice for treating eclampsia. It has the added advantage of reducing maternal and neonatal morbidity along with controlling seizures. Low therapeutic index of $MgSO_4$ is a cause for concern.

**Materials and Methods:** There were 50 patients and 200 blood samples after the investigation and clinical examination patients were enrolled in the study. A preloading serum magnesium (0 h) samples were taken from the peripheral vein. A modified magnesium sulfate regime was used in the management of eclamptic convulsions in which a loading dose of 4 g magnesium sulfate intravenously diluted in normal saline was administered over 20 min slowly followed by 8 g deep intramuscular magnesium sulfate 4 g in each buttock. A maintenance dose of 4 g of intramuscular magnesium sulfate was then administered every 8 hours on alternate buttocks for 24 h of the last convulsion or delivery. Venus blood sample was collected before loading dose and at mid-point, that is, at 4 h before each maintenance dose.

**Conclusion:** Serum magnesium levels in these were within the therapeutic range, therefore routine estimation of these cations is not necessary. The low-dose regime appears to control and prevent convulsions effectively in Indian women.

**Key words:** mgso4, Bp, UNICEF, MMR

## INTRODUCTION

Preeclampsia and eclampsia, the hypertensive disorders complicating pregnancy are affecting significantly more women in developing countries like India.[1] The minimum criteria for classification as preeclampsia as per the working group definition are: Blood pressure being 140/90 mmHg or more after 20 weeks' gestation; proteinuria of 300 mg or more over 24 h or + on dipstick test. Increased certainty of preeclampsia is considered at blood pressure 160/110 mmHg or more; proteinuria 2 g or more over 24 h or ++ or more on dipstick test; serum creatinine >1.2 mg/dL unless known to be previously elevated; platelets <1 lacs/μL; microangiopathic hemolysis with increased LDH; elevated serum transaminase levels –ALT or AST; persistent headache or other cerebral or visual disturbance; persistent epigastric pain. Eclampsia is an occurrence of seizures in a pregnant woman with preeclampsia that cannot be attributed to other causes.[2] Preeclampsia and eclampsia contribute to around 9% of the deaths in Asia and Africa.[3] The pregnant women with severe gestational hypertension are recommended to be treated with antihypertensive drugs based on clinician's experience and judgment. However, magnesium sulfate is recommended to prevent eclampsia in women having a severe form of preeclampsia.[4] The role of magnesium sulfate has been established for the prevention and treatment of eclampsia. However, there is a recent rationale that the Indian and Asian population on account of low body mass index needs less dose of magnesium sulfate to achieve therapeutic effects. Systematic review on the subject has emphasized the need for the study on low-dose regimens of magnesium sulfate.[5] The present study evaluates the low-dose regimen of magnesium sulfate in the

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management of preeclampsia and eclampsia at an inpatient hospital at the Jalna district of Maharashtra in India.

## MATERIALS AND METHODS

The present hospital-based observational study was done at Jalna Mission Hospital from January 1st, 2010 to September 30th, 2011, involving 50 women admitted with eclamptic fits, which received magnesium sulfate therapy and delivered at the institute during the study period. Inclusion criteria were: Eclampsia with a verifiable history of fits at home, on the way to the hospital, or inside the hospital, systemic symptoms like breathlessness/dyspnea, headaches, diplopia, right hypochondrial pain, signs such as raised blood pressure, edema, proteinuria, and exaggerated reflexes. The study excluded all cases of epilepsy, encephalopathy, tetanus, and meningitis. Patients with hypoglycemia, ketoacidosis, known cases of significant respiratory disease, known cases of heart disease, and patients having already received any anticonvulsant outside this institute were also excluded from the study. Informed consent was taken from all the participants and the ethics and scientific committee of the institute approved the study protocol (No: JMH/12/2009 dated December 21, 2009).

### Clinical Examination of the Patients

On admission, each patient was subjected to a clinical examination which included the history of the present pregnancy and its management. The gestational age was usually calculated from the last normal menstrual period and confirmed by ultrasound at about 18–22 weeks of gestation. Relevant past obstetric, medical, surgical, drug, social, and family histories were reviewed. Physical examination included general health of the patient, blood pressure estimation with Korotkoff phase 4 for the diastolic blood pressure, examination of the gravid uterus for a fetal lie and presentation, and measurement of uterine height to exclude intrauterine growth restriction.

Every patient had initial baseline investigations such as complete blood count for hemoglobin and hematocrit, white blood cells and platelets, renal function tests including electrolytes, urea, creatinine, uric acid, liver function tests for elevated aspartate transaminase, alanine transaminase and lactate dehydrogenase coagulation profile (prothrombin time, partial thromboplastin time and fibrinogen degradation products), 24-h urine for creatinine clearance and total amount of protein in the urine, and serum magnesium level. Continuous fetal monitoring was carried out in every patient. After the investigation and clinical examination patients are enrolled in the study.

### Protocol for Administration of Magnesium Sulfate

Preloading serum magnesium (0 h) sample was taken from peripheral veins. A modified magnesium sulfate regime was used in the management of eclamptic convulsions in which a loading dose of 4 g magnesium sulfate intravenously diluted in normal saline was administered over 20 min slowly. This was followed by 8 g of deep intramuscular magnesium sulfate (4 g in each buttock).

A maintenance dose of 4 g intramuscular magnesium sulfate was then administered every 8 h on alternate buttocks for 24 h of the last convulsion or delivery.

Venous blood sample was collected before the loading dose and at mid-point, that is, at 4 h before each maintenance dose. Non-hemolyzed serum samples separated through centrifugation were assayed for total serum magnesium.

### Monitoring

Magnesium sulfate therapy was aggressively monitored by measuring urinary output 30–35 mL/24 h as the lower limit or 120 mL in 4 h, a respiratory rate of more than 18–20/min, deep tendon reflexes, that is, patellar reflex, ankle jerk reflex. Serum magnesium levels were also monitored.

Magnesium sulfate toxicity was indicated by

- Loss of tendon reflexes
- Drowsiness
- Poor urine output and respiratory rate <16/min
- High serum magnesium levels more than 3.5 mmol/L.

**Magnesium level monitoring**

| Serum magnesium | | | Effect |
|---|---|---|---|
| mmol/L | mEq/L | mg/dl | |
| 2–3.5 | 4–7 | 5–9 | Therapeutic range |
| >3.5 | >7 | >9 | Loss of patellar reflexes |
| >5 | >10 | >12 | Respiratory paralysis |
| >12.5 | >25 | >30 | Cardiac arrest |

The protocol for the treatment of magnesium sulfate toxicity was

1. Stop magnesium sulfate therapy
2. Use of antidote: An infusion of 10 mL of 10% calcium gluconate.

Prichard intramuscular regimen is standard of care in resource-limited settings. It is delivered as: Loading dose: 4 g (20%) IV slowly in 20 cc normal saline plus 5 g (50%) IM in each buttock (Total: 14 g). Maintenance dose: 5 g deep IM in alternate buttock every 4 h for 24 h after the last convulsion.[6]

The dose and regime used in our study was: Loading dose: 4 g (20%) IV slowly in 20 mL normal saline; plus 4 g (50%) IM

in each buttock (Total of 12 g). Maintenance dose was given after 8 h of loading dose as 4 g (50%) deep IM in alternate buttocks 8 hourly up to 24 h of last convulsion or delivery.

## RESULTS

### Statistical Analysis

The data were entered using MS Excel-2007 and analyzed using SPSS-16 software. The data were summarized using Mean±Standard deviation (For numerical data) and frequency/percentage (for categorical data). Repeated measures ANOVA test was used for comparison of serum magnesium level over the time taking 0 h as baseline. Following statistical tests of significance are used.

| Statistics | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Age | Gest age | RR | SMg0 | SMg4 | SMg12 | SMg20 |
| n | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Mean | 23.02 | 36.84 | 21.52 | 2.084 | 2.728 | 3.062 | 3.576 |
| Standard deviation | 4.023 | 2.923 | 2.002 | 0.3899 | 0.4233 | 0.4998 | 0.6859 |
| Minimum | 18 | 28 | 16 | 1.6 | 2.1 | 2.4 | 2.3 |
| Maximum | 35 | 42 | 26 | 3.2 | 4.4 | 4.5 | 5.3 |

### Age Distribution

The age distribution of studied patients was from 18 years to 35 years with a mean age of 23 years.

### Religion

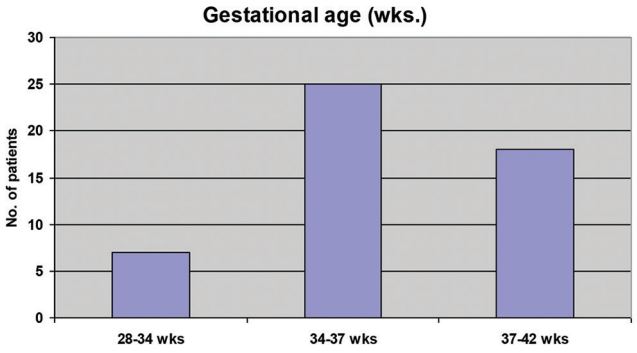
The distribution of patients according to religion showed 66% Hindus, 22 % Muslims, 10 % Christians, and 2 % Sikh.

According to the parity of the patients, when data were analyzed, it showed that the majority of patients, that is, 32 patients (64%) were primigravidas. Eight patients, that is, 16% were second gravidas, six patients, that is, 12% were multigravidas.

### Gestational Age

50% of patients Studied were in the 34–37 week gestational age 38% were in 37–40 weeks, and 14 % of patients were from 28 to 34 weeks.

Maximum patients were seen in the 34–37 weeks.




According to the mode of delivery lower segment cesarean section was required in 21 patients out of 50, that is, 42%.

Sixteen patients, that is, 32% had a normal delivery. Assisted vaginal deliveries in the form of forceps delivery and vacuum extraction delivery were required in two patients out of 50, that is, 4%, and 11 patients, that is, 22%, respectively.

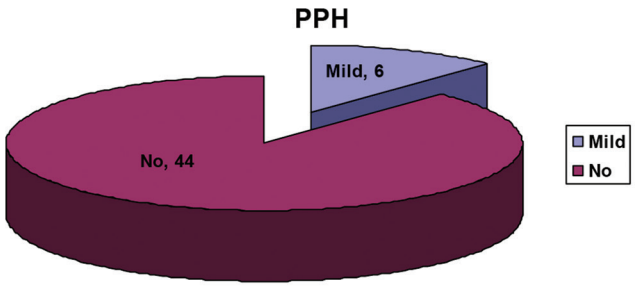
*Result of labor: LSCS was more in the study group for indications such as*

1. No progress in labor, failed induction of labor 40%
2. One patient for abruption and fetal distress in 10%
3. Others for malpresentation and position.

*Postpartum hemorrhage*

| PPH | Frequency | Percent |
|---|---|---|
| Mild | 6 | 12.0 |
| Nil | 44 | 88.0 |
| Total | 50 | 100.0 |

PPH: Postpartum hemorrhage




Postpartum hemorrhage (PPH) was observed in six patients. The patient had mild PPH which was managed medically. These six out of fifty patients, that is, 12% of patients were managed medically, and no surgical intervention was required.

*Pregnancy outcome of 50 patients*

| Outcome | Frequency | Percent |
|---|---|---|
| Post-term | 1 | 2.0 |
| Preterm baby | 9 | 18.0 |
| Preterm IUGR | 2 | 4.0 |
| Preterm twin babies | 2 | 4.0 |
| Stillborn | 2 | 4.0 |
| Term baby | 33 | 66.0 |
| Term baby IUGR | 1 | 2.0 |
| Total | 50 | 100.0 |

IUGR: Intrauterine growth restriction

When we studied the outcome of babies, it was found that in 66% of babies delivered at term, Intrauterine growth restriction occurred in 3/50 (6%) of the women. While 24% of babies were preterm out of which two (4%) twin preterm babies were delivered, and one baby was preterm intrauterine growth restricted (2%). Two fetuses (4%) were stillborn.

### *APGAR score*

| APGAR Score | Frequency | Percent |
|---|---|---|
| <7 | 17 | 34.0 |
| >7 | 31 | 62.0 |
| 0 | 2 | 4.0 |
| Total | 50 | 100.0 |

1. No progress in labor, failed Induction of labor 40%.

### *Neonatal intensive care unit admission*

12 out of 50 patients, that is, 24% of babies required to be referred to the neonatal intensive care unit while 35 out of 50, that is, 70% babies were with their mothers. Two patients had stillbirth (4%).

| NICU | Frequency | Percent |
|---|---|---|
| No | 28 | 56.0 |
| Yes | 19 | 38.0 |
| Total | 47 | 94.0 |

NICU: Neonatal intensive care unit

There was not a single case of maternal mortality in this study in eclampsia patients treated with low-dose magnesium sulfate. There was no recurrence of convulsion in all the 50 treated patients of eclampsia.

Thus making this protocol is 100% effective in preventing the recurrence of convulsions in eclampsia patients.

### *Tendon reflex*

During clinical monitoring, none of the fifty patients had a loss of knee jerk, one of the signs of magnesium sulfate toxicity.

### *Urine output*

The urine output of all the studied patients was in the normal range throughout the treatment protocol, another sign to assess toxicity.

### *Recurrence of convulsions*

There was no recurrence noted in the study subjects during the study period.

### *Comparison of serum magnesium levels*

| SRMG | *n* | Mean | Standard Deviation | *P*-value | Significance |
|---|---|---|---|---|---|
| SMg0 | 50 | 2.084 | 0.3899 | ------- | ------- |
| SMg4 | 50 | 2.728 | 0.4233 | <0.001 | Significant |
| SMg12 | 50 | 3.062 | 0.4998 | <0.001 | Significant |
| SMg20 | 50 | 3.576 | 0.6859 | <0.001 | Significant |

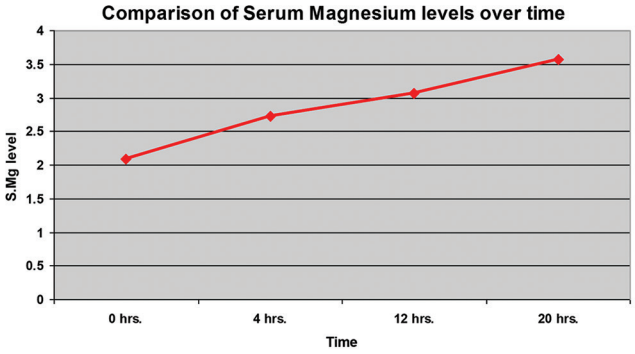
Repeated measures ANOVA test, Serum Mg level at 0 hour, 4 hour, 12 hour of loading dose

Serum magnesium level monitoring was done at four different times, that is, at 0 h, 4 h, 8 h, and 12 h of loading dosage.

The therapeutic range for serum magnesium level is from 2.0–3.5 mmol/L.

No patient in the study group had serum magnesium levels above the therapeutic range.

### *Comparison of serum magnesium levels over time*




## DISCUSSION

The latest report by UNICEF on maternal health in India is that every five minutes an Indian woman dies from complications related to pregnancy and childbirth, adding up to approximately 1, 30,000 women deaths per year. Eclampsia accounts for about 12% of maternal deaths in the world and 8% of maternal deaths in India.

Eclamptic convulsions are life-threatening emergencies and require proper treatment to decrease maternal morbidity and mortality. Incidence of eclampsia varies widely from country to country, and even between different zones of the same country. While in developed countries its prevalence is low, in developing countries, particularly in rural areas, it is still highly prevalent and contributes significantly to maternal mortality. Incidence of eclampsia in India varies from 0.5% to 1.8%. Globally, overall maternal mortality associated with eclampsia is 2%. Most of these deaths occur in developing countries. The maternal mortality rate or the rate of deaths among women during or after pregnancy, in India has declined to 212/100,000 live births in 2007–2009 as against 254 in 2004–2006, according to data released by the Registrar General of India. Although there is a decline of 17% during the period, the country needs to achieve a target of 109 deaths by 2015 to achieve the United Nations-mandated Millennium Development Goals – a feat already achieved by Kerala, Maharashtra, and Tamil Nadu. Four other states–Andhra Pradesh, West Bengal, Gujarat, and Haryana–are close to the MDG target.

Note: in Maharashtra MMR IS 104/100000 live births.

Magnesium sulfate has been used for the treatment of eclampsia since 1906 and has been popular for over 70 years

in the USA. It has not been widely used in many countries, however, including India. In Eastern India, magnesium sulfate was introduced in the treatment of eclampsia in the late 1990s following the publication of the multi-centric Collaborative Eclampsia Trial in 1995.

## CONCLUSION

Serum magnesium levels in these were within the therapeutic range, therefore routine estimation of these cations is not necessary. The low-dose regime appears to control and prevent convulsions effectively in Indian women.

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