Maternal outcomes after 12 hours and 24 hours of magnesium sulfate therapy for eclampsia

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Objective: To assess the effectiveness of a reduced duration (12 hours) of magnesium sulfate (MgSO4) administration for eclampsia. Methods: In a prospective randomized study, women with eclampsia (prepartum, intrapartum, or postpartum) attending Jawaharlal Nehru Medical College, Aligarh, India, between January 2012 and September 2013 were enrolled. The inclusion criteria were blood pressure of at least 140/90 mm Hg after 20 weeks, proteinuria (dipstick value ≥ 1), and seizures not attributed to other causes. Participants were assigned to control and study groups according to the time of enrollment (6-month blocks). All patients received a MgSO4 loading dose (4 g, intravenously), followed by maintenance doses (1 g/hour) for 12 hours (study group) and 24 hours (control group). The primary outcome was recurrent convulsions after completion of MgSO4 therapy. Patients with treatment failure were excluded from analyses. Results: Analyses included 132 patients in the study group and 72 patients in the control group. No convulsions recurred in either group after the completion of treatment. Conclusion: For women with eclampsia, 12 hours of magnesium sulfate could effectively prevent recurrent convulsions.

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1. Introduction

Eclampsia is an important cause of maternal morbidity and mortality, especially in low-resource countries. Together, pre-eclampsia and eclampsia account for 40,000 maternal deaths worldwide every year [1]. In India, these conditions account for 5% of all maternal deaths [1].

The accepted therapeutic management includes: prevention of seizures; adequate control of blood pressure; stabilization of cardiovascular, renal, and electrolyte status; and prompt delivery. Administration of magnesium sulfate (MgSO4) for 24 hours after the last fit or delivery (whichever is later) is considered best empirical practice, but it has not been properly subjected to scientific scrutiny [2]. Decreasing the duration of MgSO4 infusion would benefit both the patient and healthcare systems. One randomized controlled trial [3] showed that seizures can be effectively controlled in cases of eclampsia by giving only a loading dose of MgSO4; the recurrent convulsion rate was found to be almost the same among patients who received the loading dose (3.96%) and among those who received the standard regimen (3.51%; P > 0.05).

The aim of the present study was therefore to determine whether decreasing the duration of the intravenous MgSO4 regimen to 12 hours instead of 24 hours after the last fit or delivery is effective in improving maternal outcome in eclampsia.

2. Materials and methods

In the present prospective randomized study, women with eclampsia attending the Department of Obstetrics and Gynecology at Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, India, were enrolled between January 1, 2012, and September 30, 2013. The inclusion criteria were: prepartum, intrapartum, or postpartum eclampsia with a blood pressure of 140/90 mm Hg or higher after 20 weeks of pregnancy; proteinuria with a dipstick value of +1 or higher; and seizures not attributed to other causes among women with pre-eclampsia. The exclusion criteria were eclampsia with complications [e.g. acute renal failure, HELLP syndrome [hemolysis, elevated liver enzymes, and low platelet count], or pulmonary edema] or associated maternal disease, contraindication to MgSO4 (e.g. drug hypersensitivity, myasthenia gravis, anuria, or oliguria), prior intake of any other anticonvulsant, and a history of epilepsy. The study was approved by the Ethical Committee of the institution, and patients provided informed consent before the administration of MgSO4.

Patients with eclampsia who were admitted during the study period were randomly assigned to either the study group (12 h MgSO4) or the control group (24 h MgSO4) as follows: patients admitted in the first 6 months were enrolled into the control group, and those admitted in the next 6 months were enrolled into the study group. This alternating pattern of enrollment was followed for the duration of study.
Participants were not told which group they had been assigned to, but because the groups received treatments for different lengths of time, full masking was not possible. Investigators and data analysts were not masked to group assignment.

All women were examined at the time of admission and a detailed history was taken. Complete blood counts, coagulograms, liver and renal function tests, and urine protein measurements were performed. Women in the study group were given a loading dose of 4 g of intravenous MgSO4, followed by a maintenance dose of 1 g per hour for 12 hours after the last fit or delivery (whichever was later). Those in the control group were given a loading dose of 4 g of intravenous MgSO4 followed by a maintenance dose of 1 g per hour for 24 hours after the last fit or delivery.

All women were monitored for the entire duration of MgSO4 infusion by trained obstetricians and gynecologists for blood pressure, patellar reflexes, respiratory rate, urine output, and reoccurrence of convulsions. In the case of MgSO4 toxic effects, the plan of management was the reported by relatives for most women (data not shown).

2 (1.0%) had a history of prenatal care, 146 (70.2%) came from a rural setting, 39 (18.8%) of postpartum eclampsia. Among the study participants, 132 were assigned to the study group and received the conventional 24-hour regime of MgSO4.

However, 10 patients in the control group had repeat convulsions during the first 2 hours of therapy. Six of these patients responded to a repeat loading dose of 2 g of MgSO4 and then underwent 24 hours of MgSO4; the remaining four patients were switched to phenytoin therapy. These four cases were categorized as treatment failures and excluded from the study analysis. Thus, the failure rate of MgSO4 therapy was 1.9%.

Among the patients included in analyses, those in each of the two groups were similar in terms of age, number of previous pregnancies, and length of pregnancy (Table 1). In addition, systolic blood pressure, diastolic blood pressure, and albuminuria on admission and at discharge were similar in the two groups.

Regarding the primary outcome, no convulsions recurred in either group after the completion of MgSO4 for 12 hours or 24 hours. Regarding the secondary outcomes, significantly higher total amounts of MgSO4 duration of Foley catheterization, and duration of monitoring were noted in the control group when compared with the study group ($P < 0.001$ for all) (Table 2). No patients developed complications attributed to eclampsia after admission.

Among a total of 169 deliveries after eclampsia onset, 79 (46.7%) occurred vaginally and 90 (53.3%) by cesarean. Overall, 113 (66.9%) had live births, 31 (18.3%) had intrauterine death, and 25 (14.8%) had neonatal death. Apgar scores and admission to the neonatal intensive care unit were not recorded.

Among patients with vaginal delivery, the mean duration of hospital stay was 5.3 ± 0.8 days in the study group as compared with 7.5 ± 1.5 days in the control group ($P < 0.001$). A similar difference in the mean duration of hospital stay was seen among patients who delivered by cesarean (7.7 ± 0.9 vs 10.5 ± 1.5 days; $P < 0.001$).

No toxic effects of MgSO4 were noted in either group.

4. Discussion

In the present study, no convulsions were recorded after either MgSO4 infusion for 12 hours or 24 hours after delivery or the last seizure (whichever occurred later) among women with eclampsia. This finding could represent a breakthrough in the management of patients with eclampsia in low-resource nations where the incidence of this disorder is high and puts an increased burden on health care.

The incidence of eclampsia was 3.9% in the present study, which is higher than previously reported values of 0.7%, 0.87%, and 3.2% [4–6]. The incidence of eclampsia in the present study might be higher because the study was conducted in a referral center for a large rural population where patients are often admitted at a complicated stage of labor, which might also be responsible for the high case fatality rate (6.7%). Notably, 99% of the study participants were unbooked or unregistered. It was noted as far back as 1952 that eclampsia would be a clinical rarity if effective prenatal care were made available [7].

Previous studies have assessed the minimum amount and duration of MgSO4 for preventing recurrent convulsions in cases of eclampsia. For example, in a large study on low-dose MgSO4, Sardesai et al. [8] reported that convulsions were controlled in 94% of cases of eclampsia. Similarly, Begum et al. [3] reported that eclamptic convulsions were controlled in 98% of women treated with a modified (Dhaka) regime of MgSO4.

In the present study, 10 patients had repeat convulsions during the first 2 hours of therapy. Six of them responded to a repeat loading dose of 2 g of MgSO4, but four were switched to phenytoin in accordance with the protocol of the hospital. After completion of therapy, no recurrent convulsions occurred in either group. To our knowledge, there are no previous data on the recurrence of convulsions after the completion of 24 hours of therapy. In the present study, patients who had repeat convulsions in the first 2 hours of therapy were routinely given 24 hours of MgSO4. Further studies are needed to determine the effects of decreasing the dose and duration of MgSO4 in complicated eclampsia cases.
In the present study, the mean duration of monitoring was 19.3 ± 4.9 hours in the 12-hour group as compared with 31.8 ± 4.7 hours in the 24-hour group. This reduction will be beneficial at the level of tertiary-care centers, district hospitals, and primary healthcare centers in many low-resource countries. It will reduce the burden on the healthcare staff and allow appropriate mother–child bonding. The mean amount of MgSO₄ administered was 23.2 ± 2.8 g in the 12-hour group as compared with 34.9 ± 3.2 g in the 24-hour group. In the Collaborative Eclampsia Trial [9], the mean dose of MgSO₄ was 38 ± 9.7 g, which is similar to that seen in the 24-hour group in the present study. The lower dose of MgSO₄ administered in the 12-hour group would safeguard patients against MgSO₄ toxic effects.

Early Foley catheter removal has substantial advantages for the early mobilization of a patient, and indicates better bladder function. The mean duration of Foley catheterization in the present study was 19.6 hours in the 12-hour group as compared with 31.5 hours in the 24-hour group.

Among patients with vaginal delivery, the mean duration of hospital stay was 5.3 days in the study group as compared with 7.5 days in the control group. A similar reduction in hospital stay was seen among patients who had cesarean delivery (7.7 days vs 10.7 days). A shortened hospital stay is beneficial for both patients and healthcare centers because it decreases the overall cost of treatment, reduces unnecessary exposure to nosocomial infections, and allows better utilization of available health resources.

Some limitations of the present study should be noted. There were no prespecified criteria for the assessment of the advantages of early mobilization. Additionally, a Foley tip culture could have been analyzed to quantitatively assess the reduction in the risk of urinary tract infection as a result of early removal of the Foley catheter.

### Table 1
Baseline characteristics.a

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>12 h MgSO₄ (n = 132)</th>
<th>24 h MgSO₄ (n = 76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, y</td>
<td>23.8 ± 3.4</td>
<td>24.5 ± 3.6</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>94 (71.2)</td>
<td>60 (78.9)</td>
</tr>
<tr>
<td>2–4</td>
<td>30 (22.7)</td>
<td>14 (18.4)</td>
</tr>
<tr>
<td>≥5</td>
<td>8 (6.1)</td>
<td>2 (2.6)</td>
</tr>
<tr>
<td>Length of pregnancy, wk</td>
<td>35.6 ± 1.2</td>
<td>36.5 ± 1.6</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>166.7 ± 18.8</td>
<td>161.6 ± 21.5</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>102.2 ± 8.7</td>
<td>99.7 ± 9.7</td>
</tr>
<tr>
<td>Proteinuria, dipstick value</td>
<td>2.97 ± 0.4</td>
<td>2.77 ± 0.7</td>
</tr>
<tr>
<td>On discharge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean systolic blood pressure, mm Hg</td>
<td>126.6 ± 7.6</td>
<td>125.4 ± 8.0</td>
</tr>
<tr>
<td>Mean diastolic blood pressure, mm Hg</td>
<td>86.4 ± 3.5</td>
<td>84.8 ± 5.0</td>
</tr>
</tbody>
</table>

Abbreviation: MgSO₄, magnesium sulfate.

### Table 2
Secondary outcomes.a

<table>
<thead>
<tr>
<th>Outcome</th>
<th>12 h MgSO₄ (n = 132)</th>
<th>24 h MgSO₄ (n = 72)</th>
<th>t value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total amount of MgSO₄, g</td>
<td>23.2 ± 2.8</td>
<td>34.9 ± 3.2</td>
<td>24.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of Foley catheterization, h</td>
<td>19.6 ± 2.5</td>
<td>31.5 ± 2.4</td>
<td>27.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of monitoring, h</td>
<td>19.3 ± 4.9</td>
<td>31.8 ± 4.7</td>
<td>16.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital stay</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery, d</td>
<td>5.3 ± 0.8</td>
<td>7.5 ± 1.5</td>
<td>8.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Cesarean delivery, d</td>
<td>7.7 ± 0.9</td>
<td>10.5 ± 1.9</td>
<td>9.0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Abbreviation: MgSO₄, magnesium sulfate.

a Values are given as mean ± SD or number (percentage).
In summary, 12 hours of MgSO₄ therapy was found to be effective in preventing recurrent convulsions among women with eclampsia. The lower dose led to shorter durations of monitoring and catheterization, and shorter hospital stays, which are important considerations in the provision of health care in low-resource countries.

Conflict of interest

The authors have no conflicts of interest.

References