Magnesium Sulfate for Control of Eclampsia: Do Indian Women Need Lower Doses?

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ABSTRACT

Background: Pritchard regime is considered the benchmark for control of convulsions in patients with eclampsia. Indian patients with smaller body mass may require smaller doses of Magnesium sulfate.

Aims: To compare the efficacy of low dose magnesium sulfate (MgSO₄) regimen in eclampsia with standard Pritchard’s regimen.

Materials and methods: A total of 60 patients presenting with eclampsia were recruited and randomly divided into two groups: Group A: 30 patients who received standard Pritchard’s regime and Group B: 30 patients who were given low dose MgSO₄. The outcome was measured in terms of effectiveness in control of convulsions and magnesium related toxicity.

Results: Overall success rate was 100% with a low dose regimen as compared to 93.3% with Pritchard’s regime. Failure to control convulsions was noted in two patients on Pritchard’s regime group as compared to none on a low dose regimen (p <0.01). No difference was observed among study groups with respect to the type of delivery (p <0.59). Maternal complications were higher in cases receiving Pritchard’s regimen: loss of knee jerk (30% vs. 16.7%), oliguria (16.7% vs. 10%) and postpartum hemorrhage (PPH) (23.3% vs. 16.7%). However, the difference was not statistically significant.

Conclusion: A lower dose of magnesium sulfate is equally efficient with fewer complications as compared to the standard dose regimen in the management of eclampsia.

Keywords: Eclampsia, Low dose MgSO₄ for Indian women, MgSO₄ toxicity, Pritchard’s regimen for eclampsia.

INTRODUCTION

Eclampsia is a serious complication of pregnancy that affects the safety of the mother as well as the fetus. Until recently the treatment of eclampsia was diverse throughout the world. Various drugs and regimens have been advocated for the management of eclampsia. In 1950, Menon introduced the famous ‘lytic cocktail’ in India.¹ The lytic cocktail was a combination of drugs like pethidine, promethazine, and chlorpromazine. This lytic cocktail was only partially effective. Dr Prichard in 1984 used MgSO₄ for control of convulsions in eclamptic patients. This regimen was found to be very effective and became standard treatment for eclampsia. Indian women have lower body mass as compared to their western counterparts. Therefore, appropriate doses of magnesium sulfate and the therapeutic serum magnesium levels among the Indian patients have been a matter of debate.² This study was carried out to find out whether lower doses of MgSO₄ are as effective as standard doses for treatment of eclampsia in Indian patients.

AIM AND OBJECTIVES

To compare the effectiveness of low dose magnesium sulfate regimen in eclampsia and severe preeclampsia with standard Pritchard’s regimen in terms of:

- Effectiveness in control of convulsions,
- Maternal outcome
- Magnesium related toxicity

MATERIALS AND METHODS

Study Area

Department of Obstetrics and Gynecology at the MGM Hospital, Kalamboli, Mumbai, Maharashtra, India.

Study Population

Pregnant patients above 20 weeks presenting with eclampsia at our hospital.

Study Design

A randomized comparative study

Sample Size Calculation

A total of 60 cases presenting with eclampsia at our hospital were randomly divided into two groups (30 each) using computer-generated random numbers:

Group A: Standard Pritchard’s regime.
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Group B: Low dose MgSO₄ regime.
Study Duration: July 2016–Feb 2018

Inclusion Criteria

- Pregnant patients presenting after the 20th week of pregnancy with BP>140/90 mm Hg and history of convulsions with or without proteinuria.
- Patients who have not received any anticonvulsant treatment before admission.

Exclusion Criteria

- Cases presenting with serious complications of eclampsia, namely:
  - Renal failure
  - Cerebrovascular accident
  - HELLP syndrome
- Patients not consenting to participate in the study.

Methodology

Informed consent was taken from all the patients or their relatives (in case the patient was not in a condition to give consent). A detailed history was taken with special emphasis on the history of epilepsy or renal failure. Clinical assessment was carried out. Prepregnancy BMI was obtained from her old records. Following investigations were carried out: blood group, complete blood count (CBC), platelet count, serum creatinine, liver function tests, prothrombin time and urine analysis. Additional investigations were performed on the case to case basis.

Drug (MgSO₄) Regimen for Group A

- 4 g MgSO₄ 20% IV stat.
- 3 g IM in each buttock stat.
- 2 g IM on alternate buttock four hourly for 24 hours after delivery or last convulsion whichever was later.

Drug (MgSO₄) Regimen for Group B

- 4 g MgSO₄ 20% IV stat.
- 5 g on each buttock.
- 5 g IM 4 hourly on the alternate buttock. Medication was continued for 24 hours after the delivery or last seizure.

Respiratory rate, patellar reflexes and urinary output were monitored hourly for impending magnesium toxicity. Next scheduled dose of MgSO₄ was not given if there was any sign of magnesium toxicity (absence of patellar reflex, urinary output less than 30 mL/hour or respiratory rate less than 16/min). If convulsions recurred after the initial dose, the patient was given additional of 2 g of MgSO₄ by IV route. This additional dose of MgSO₄ was given to the patients in both groups. In case the patient had convulsions even after an additional dose of MgSO₄, IV diazepam was given. Intravenous Labetalol in incremental doses of 20–80 mg was used if BP was more than 160/110. Lower segment cesserian section (LSCS)/ induction of labor was done to terminate the pregnancy within 48 hours of an initial dose of MgSO₄.

Statistical Analysis

The quantitative data are represented as their mean ± SD. Categorical and nominal data is expressed in percentage. The t-test is used for analyzing quantitative data, or else nonparametric data are analyzed by Mann–Whitney test and categorical data are analyzed by using Chi-square test. The significance threshold of \( p \) value is set at < 0.05. All analyses were carried out by using Statistical Package for Social Sciences (SPSS) software version 21.

RESULTS

Mean age of patients in the study was 27.3 years with the majority of them (73.3%) between 21–30 years of age. No difference was observed among study groups with respect to age distribution (\( p = 1.0 \)). Out of the total 60 cases, 58.3% were primipara while the remaining 41.7% were multipara. No difference was observed among study groups with respect to parity (\( p = 1.0 \)). No difference was observed among study groups with respect to mean BMI and gestation age (\( p > 0.05 \)), (Table 1).

Out of the total 60 cases, 25% had more than five episodes of convulsions. No difference was observed among the number of convulsion episodes (\( p = 1.0 \)). Overall success rate observed was 100% with a low dose regimen as compared to 93.3% with Pritchard’s regimen. Additional doses were required in 2 cases of each group. Failure to control convulsions was

<table>
<thead>
<tr>
<th>Age group</th>
<th>Low dose</th>
<th>Pritchard’s</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>21–25</td>
<td>16</td>
<td>15</td>
<td>31</td>
</tr>
<tr>
<td>26–30</td>
<td>12</td>
<td>11</td>
<td>23</td>
</tr>
<tr>
<td>&gt;0</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parity</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primi</td>
<td>17</td>
<td>18</td>
<td>35</td>
</tr>
<tr>
<td>Multi</td>
<td>13</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 1: Baseline distribution of patients in two groups
Table 2: Comparison of no. of convulsions in both the groups and the outcome related to the control of convulsions in both the groups

<table>
<thead>
<tr>
<th>Number of convulsions</th>
<th>Regimen low dose</th>
<th>Regimen Pritchard's</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1=5</td>
<td>22</td>
<td>23</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>73.3%</td>
<td>76.7%</td>
<td>75.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>7</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Convolusions controlled</td>
<td>30</td>
<td>28</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Additional dose required</td>
<td>6.7%</td>
<td>6.7%</td>
<td>6.7%</td>
<td>1.0</td>
</tr>
<tr>
<td>Failure rate</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0%</td>
<td>6.7%</td>
<td>3.3%</td>
<td>0.49</td>
</tr>
</tbody>
</table>

noted in 2 cases of Pritchard’s regimen group and none in the low dose regimen group (Table 2).

The higher mean dose of MgSO₄ was associated with Pritchard’s regimen (33.8 g) as compared to the low dose regimen (21.7 g) (p <0.01) (Table 3).

Higher prevalence of cesarean section was observed in both groups (overall 61.7%). No difference was observed among study groups with respect to the type of delivery (p 0.59). Complications associated with magnesium, i.e., loss of knee jerk (30% vs. 6.7%) and oliguria (16.7% vs. 10%) were higher in cases with Pritchard’s regimen (Table 4).

DISCUSSION

Eclampsia is a major cause of maternal and fetal morbidity and mortality around the world, especially so in a developing country like India. Magnesium sulfate is the drug of choice for the treatment of eclampsia. The effectiveness of magnesium sulfate has been proven in a variety of randomized controlled trials. There has been a constant debate concerning the dose of magnesium sulfate. Pritchard’s regimen has been tailored at different hospitals offering different regimes. Low-dose MgSO₄ regimen has been standardized. Pritchard himself in 1984 suggested that the dose of magnesium sulfate should be limited in women who appear to be small built. The present study was thus planned to compare the effectiveness of low dose magnesium sulfate regimen with Pritchard’s regimen in controlling convulsions during eclampsia in Indian women.

Baseline Characteristics

Mean age of the females in the study was 27.2 years and 27.4 years in a low dose regimen group and Pritchard’s regimen group respectively (p 0.93). Mean BMI was 21.34 and 20.96 kg/m² in low doses and Pritchard’s regimen group respectively (p 0.71). Parity, gestation age and a number of convulsions (Table 1) were also comparable in this study.

The similar demographic pattern was also observed in other studies. Ranjana et al. reported that the mean age of the patients was 25.8 ± 3.43 years with low dose regimen and 25.7 ± 3.53 years with Pritchard’s regimen. Most women were of small built with a body mass index of 20.31 ± 1.34 kg/m² and 19.99 ± 2.15 kg/m² in groups A and group B, respectively. Nautiyal et al. in their study observed the mean age of the patients of eclampsia/preeclampsia as 25.5 years while Sharma et al. recorded a mean age of 25.9 years in their study. Kumar et al. reported a mean age of 25.07 (range 19–40) years in their study of 123 cases. The majority were in the age group of 21–25 years (51.21%), followed by 26–30 years (35.78%). Jana et al. reported that measured most women were of small stature, with a mean body mass index of 19.3 ± 2.1. Bangal et al. observed that 70% of women had a body weight less than 50 kilograms at the time of admission.

Eclampsia occurs mostly in primigravida as seen in the study (59%). Others have observed similar incidence: Ranjana et al. reported 70%, Bangal et al. 15 75% and Sardesai et al. 79%.

CONTROL OF CONVULSIONS

A number of seizures occurring after the initial dose of MgSO₄ was the parameter used to measure the effectiveness of the drug. Recurrence of convulsions occurred in two patients in each group after the initial dose. These patients were given an additional dose of MgSO₄. In group A, both the patients responded while in group B, in spite of giving 2 g i.v. dose of MgSO₄, further convulsions occurred in both the patients. The failure rate was 6.7% in Pritchard’s regimen as compared to 0% in the low dose regimen (Table 2).

Table 3: Comparison of mean dose of MgSO₄ used in both group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO₄ dose (G)</td>
<td>Low dose</td>
<td>30</td>
<td>21.70</td>
<td>2.27</td>
<td></td>
</tr>
<tr>
<td>Pritchard’s</td>
<td>30</td>
<td>33.80</td>
<td>7.64</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Comparison of study groups based on mode of delivery and maternal complications

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Low dose regimen</th>
<th>Pritchard’s regimen</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSCS</td>
<td>17</td>
<td>20</td>
<td>37</td>
<td>0.59</td>
</tr>
<tr>
<td>Vaginal</td>
<td>13</td>
<td>10</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>30</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Maternal complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of knee jerks</td>
<td>5</td>
<td>9</td>
<td>14</td>
<td>0.36</td>
</tr>
<tr>
<td>Oliguria</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.0%</td>
<td>16.7%</td>
<td>13.3%</td>
<td>0.70</td>
</tr>
</tbody>
</table>
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Magnesium Sulfate for Control of Eclampsia: Do Indian Women Need Lower Doses?

Pritchard et al.\(^2\) the pioneer of MgSO\(_4\) regimen reported a 12.1% recurrence rate in 83 patients. By using the Pritchard regimen in his patients, Sibai et al.\(^4\) reported 14.2% recurrence with Pritchard’s regime. Jana et al.\(^14\) reported a 5.7% recurrence rate with the same regimen. Recurrence rate with Pritchard’s regime as noted by Ranjana et al.\(^10\) Sharma et al.\(^15\) and Mohanapu et al.\(^17\) was 2.5%, 6.7%, and 4%, respectively. The recurrence rate of 7.89% by Sardesai et al.\(^16\) and 1.5% by Begum et al.\(^18\) was reported. Ranjana et al.\(^10\) Kumar et al.,\(^13\) Nautiyal et al.\(^11\) and Mohanapu et al.\(^17\) reported recurrence rate of 5%, 0.81%, 6.6%, and 10%, respectively with low dose regimen. All these results indicate that a low dose regime is as effective as the standard regime in controlling eclamptic seizures in Indian patients are in conformity to our study also.

Higher prevalence of cesarean section was observed in both groups (overall 61.7%). No difference was observed among study groups with respect to the type of delivery (p 0.59). Most cesarean sections were carried out for fetal distress and nonprogress of labor (Table 4). Cesarean section rate noted by Ranjana et al.\(^10\) was 57.5% in Low Dose regimen and 67.5% in Pritchard’s regimen. Nautiyal et al.\(^11\) reported a cesarean section rate of 63% and Ali et al.\(^19\) 57.5%. The high rate of LSCS in eclamptic mothers as seen in most studies shows that obstetricians prefer elective LSCS to avoid complications likely to occur in mother and fetus while awaiting delivery. Institutional policies and protocols also have an influence on decision-making, whether to go for LSCS or vaginal delivery in patients with eclampsia.

MATERNAL COMPLICATIONS

A higher dose of MgSO\(_4\) was used in Pritchard’s regimen (mean 33.8 g) as compared to the low dose regimen (mean 21.7 g) (Table 3). Higher doses used in Pritchard regimen may be responsible for higher complication rates due to magnesium toxicity in this group, namely, loss of knee jerk (30% vs. 16.7%) and oliguria (16.7% vs. 10%) (Table 4).

Ranjana et al.\(^10\) reported a loss of deep tendon reflexes in 25% of patients receiving Pritchard’s regimen and 15% patients of low dose regimen. Oliguria occurred in 15% of patients of the Pritchard regimen group and 10% of patients receiving Dhaka regime. Shilva et al.\(^20\) reported absent deep tendon reflexes (DTR) in low dose group as 8% while 32% of patients in the standard group had loss of DTR (p = 0.03). Similarly in the study by Nautiyal et al.\(^11\) 4 (13%) patients in group B (Pritchard’s) compared to three patients (10%) in group A (low dose) experienced loss of deep tendon reflexes. Six (20%) patients developed oliguria in standard dose group compared to two (6.6%) patients on a low dose regimen of MgSO\(_4\).

Maternal mortality in cases of eclampsia ranges from 0.4% to 14%. Greater the organ damage and longer the delay in seeking treatment, higher is the mortality. In the present study, no mortality was observed because patients with serious complications of eclampsia were excluded.

A study conducted by Ranjana et al.,\(^10\) one mortality was reported in a low dose group and two in Pritchard’s regimen (combined mortality rate of 3.75%). Sardesai et al.\(^16\) reported a maternal mortality of 2.63%. The maternal mortality was 3% with a Pritchard regime group in the Collaborative eclampsia trial.\(^2\) and study by Nautiyal et al.\(^11\) reported a maternal mortality rate of 3.3%.

CONCLUSION

With this study, we came to a conclusion that a lower dose of magnesium sulfate is effective in controlling convulsions in eclampsia and has lesser complications compared to standard Pritchard’s regimen in Indian patients, probably because of their less body mass. Further studies need to be conducted to re-evaluate the correct dosage of magnesium sulfate for the treatment of Indian patients with eclampsia. After all, why should we use higher doses of drugs if lesser doses are as effective and less toxic?

REFERENCES


