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CLINICAL ARTICLE

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

Shaheen Anjum *, Namarata Goel, Rajyashri Sharma, Zehra Mohsin, Nidhi Garg

Department of Obstetrics and Gynecology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India

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ABSTRACT

Objective: To assess the effectiveness of a reduced duration (12 hours) of magnesium sulfate ($MgSO_4$) 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 $MgSO_4$ 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 $MgSO_4$ 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.

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 ($MgSO_4$) 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 $MgSO_4$ infusion would beneficial to 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 $MgSO_4$: 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 $MgSO_4$ 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 $MgSO_4$ (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 $MgSO_4$.

Patients with eclampsia who were admitted during the study period were randomly assigned to either the study group (12 h $MgSO_4$) or the control group (24 h $MgSO_4$) 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.

* Corresponding author at: Department of Obstetrics and Gynecology, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002, India. Tel.: +91 9319861442; fax: +91 01123844992.
E-mail address: shahanjum73@gmail.com (S. Anjum).

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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 $MgSO_4$, 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 $MgSO_4$, 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 $MgSO_4$ infusion by trained obstetricians and gynecologists for blood pressure, patellar reflexes, respiratory rate, urine output, and reoccurrence of convulsions. In the case of $MgSO_4$ toxic effects, the plan of management was to stop further infusions of $MgSO_4$, to inject 1 g of calcium gluconate (10 mL of 10% solution) intravenously, and to switch the therapy to another anticonvulsant. These patients were considered to have treatment failure. After completion of the $MgSO_4$ infusion, patients were monitored every 4 hours until normalization of blood pressure, and then every 12 hours until discharge.

Labetalol was used as an antihypertensive drug as per the management protocol of the study institute. The participants were induced, allowed to undergo spontaneous labor, or underwent cesarean delivery depending on the obstetric indication and the patient's general condition.

The primary outcome was recurrent convulsions once the $MgSO_4$ therapy was completed. If a repeat convulsion occurred before completion of therapy, the patient was infused with a 2 g loading dose of $MgSO_4$, and women in the study group were switched to a maintenance dose of $MgSO_4$ for 24 hours. If a second convulsion was observed during the therapy, the treatment was switched from $MgSO_4$ to phenytoin and considered as an $MgSO_4$ failure.

Secondary outcomes were related to patient recovery, which was analyzed in terms of total dose of $MgSO_4$ given, duration of hospital stay, and duration of Foley catheterization. The patients were followed up until discharge from hospital.

The study data were analyzed by SPSS version 21 (IBM, Armonk, NY, USA). The study and control groups were compared by *t* test and χ^2 test as appropriate. Patients with treatment failures were excluded from analysis. $P < 0.001$ was considered significant.

3. Results

During the study period, there were 5705 deliveries, among which eclampsia was recorded in 223 (3.9%). All women with eclampsia were monitored in the high dependency unit and transferred to the intensive care unit if their general condition deteriorated. In a few cases, the systolic blood pressure of the patients ranged from 130 to 140 mm Hg, but there were no cases of eclampsia without proteinuria. There were 15 maternal deaths due to eclampsia, giving a case fatality rate of 6.7%.

After the exclusion of 15 cases of complicated eclampsia, 208 patients were included in the study (Fig. 1). There were 162 (77.9%) cases of prepartum eclampsia, 7 (3.4%) of intrapartum eclampsia, and 39 (18.8%) of postpartum eclampsia. Among the study participants, 2 (1.0%) had a history of prenatal care, 146 (70.2%) came from a rural background, 8 (3.8%) were literate, and 206 (99.0%) were unbooked. Several of the patients who were referred to the study hospital had episodes of convulsions that were not witnessed by any member of the family, although two to three episodes of convulsions before admission had been the reported by relatives for most women (data not shown).

Among the study participants, 132 were assigned to the study group and received the 12-hour regime of $MgSO_4$, and 76 were assigned to the control group and received the conventional 24-hour regime of $MgSO_4$. 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 $MgSO_4$ and then underwent 24 hours of $MgSO_4$; 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 $MgSO_4$ 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 $MgSO_4$ for 12 hours or 24 hours. Regarding the secondary outcomes, significantly higher total amounts of $MgSO_4$, 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 $MgSO_4$ were noted in either group.

4. Discussion

In the present study, no convulsions were recorded after either $MgSO_4$ 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 $MgSO_4$ for preventing recurrent convulsions in cases of eclampsia. For example, in a large study on low-dose $MgSO_4$, 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 $MgSO_4$.

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 $MgSO_4$, 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 $MgSO_4$. Further studies are needed to determine the effects of decreasing the dose and duration of $MgSO_4$ in complicated eclampsia cases.