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A TERTIARY CENTER'S EXPERIENCE COMPARING THE USUAL PRITCHARD REGIME WITH A LOW DOSE MAGNESIUM SULPHATE REGIME FOR SEVERE PREECLAMPSIA AND ECLAMPSIA: A CROSS-SECTIONAL STUDY.

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ABSTRACT

Background
The study's objective was to ascertain whether skipping the intravenous (IV) loading dosage of magnesium sulphate would have an equivalent effect to the conventional loading dose (intramuscular + intravenous) in eclampsia for the purpose of preventing convulsions.

Methods
Patients were randomly assigned to two groups. Group A (modified Pritchard protocol) received an IM loading dose of $MgSo_4$ and a 12-hour maintenance dose instead of IV. Group B got the standard Pritchard regimen, including IV and IM loading doses and 24-hour maintenance dosages. To see if the adapted Pritchard protocol performed as well as the original.

Results
The two regimens had similar age, parity, gestational age at presentation, and birthing methods. Participants in groups A and B with pre-eclampsia (PE) or eclampsia achieved the therapeutic range of $MgSo_4$ after an hour after loading dose, with group A having a lower toxicity risk (because the IV dose was missed). Recurrent convulsions occurred in 5 (19.6%) of group A and 9 (29.4%) of group B of 62 eclampsia patients. Both groups of severe PE women had no seizures after $MgSO_4$ loading.

Conclusions
Given the reduced propensity for $MgSo_4$ toxicity, the 12-hour maintenance dose and the reduced loading dose regimen—which do not include the IV loading dose—of $MgSo_4$ are as effective as the full loading dose and the 24-hour maintenance regimen in the standard Pritchard regimen in managing convulsion and preventing recurrent convulsion in eclampsia and severe pre-eclampsia.

Recommendations
According to the study, the revised Pritchard protocol for eclampsia proposes lowering IV $MgSo_4$ infusion. Maintenance with lower loading dosages for 12 hours and IV loading doses for 24 hours prevents seizures. Since $MgSo_4$ is less toxic, it can prevent and cure convulsions in eclampsia and severe pre-eclampsia. Clinical use and evaluation of this improved approach may improve at-risk pregnancy care.

Keywords: *Pre-eclampsia, Eclampsia, Magnesium sulphate, Pritchard regimen, Convulsions*
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INTRODUCTION
The prevalence of hypertensive disorders of pregnancy, such as preeclampsia (PE) and eclampsia, is significantly elevated in developing nations as a result of hypoproteinemia, malnutrition, and inadequate obstetric resources. Magnesium sulfate ($MgSO_4$) serves as the primary therapeutic agent for the management of preeclampsia and eclampsia. The Pritchard regime represents the prevailing treatment protocol that is frequently utilized in clinical practice [1]. The patient

presented with symptoms consistent with a respiratory infection. Upon examination, the physician noted increased

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respiratory rate. However, the utilization of $MgSO_4$ within the community is restricted due to concerns among healthcare professionals regarding its safety. The underutilization of magnesium sulfate ($MgSO_4$) may be ascribed to various factors, encompassing a diminished ratio of physicians to patients, restricted proficiency and education among healthcare providers, and apprehension stemming from the absence of ventilatory assistance in cases of respiratory depression [2]. A frequently encountered situation involves the transfer of cases presenting with severe preeclampsia/eclampsia from remote locations. During transit, these individuals may experience convulsions, which can have serious implications for the well-being of the mother. This is primarily due to the apprehension surrounding the administration of intravenous magnesium sulfate ($MgSO_4$) at primary health centers, which is perceived as intimidating. The current study was designed to assess the efficacy of a modified loading dose of magnesium sulfate ($MgSO_4$) without the intravenous (IV) component, allowing women to receive the loading dose before being referred.

METHODS

Study Design

A prospective cross-sectional study

Study Duration

The study was carried out over a period of 13 months.

Study Location

The study was conducted at Sheikh Bhikhari Medical College & Hospital, Hazaribagh, Jharkhand, India in a period of one year and one month years i.e., September 2022- October 2023.

Inclusion Criteria

- Consecutive women admitted with eclampsia/severe preeclampsia (PE).
- Informed consent obtained.

Exclusion Criteria

- Patients presenting with convulsions may have various underlying etiologies, including but not limited to strokes of the brain, ruptured aneurysm, infections such as meningitis and encephalitis, cerebral tumors, and metabolic abnormalities.
- The female patients have already undergone treatment with magnesium sulfate ($MgSO_4$) in an external setting.

Sample Size Calculation

- The sample size was determined using data from a prior investigation conducted by Okusanya *et al.* [3]. In their study, it was observed that among women who received a loading dose of only 10gm intramuscularly (IM), 7% experienced recurrent convulsions. Conversely, no instances of recurrent convulsions were reported in the group of women who received a loading dose of 14gm (consisting of 4gm intravenously and 10gm intramuscularly). Considering the aforementioned information, the sample size for each group was 105, as determined by the prescribed formula,

$n=C+(P1q1+P2q2/d2)+(2/d)+2$,

where, P1=0.07 (7%),
q1=1-P1=0.93,
P2=0.0 (0%),
q2=1-P2=1.0,
d=P1-P2=0.07,
C=7.8=105 for each group.

- Two groups: Group A (modified dose $MgSO_4$) and Group B (standard Pritchard's regime of $MgSO_4$).
- Sample size for each group: 75

Intervention

Group A (Study Group - Modified Dose $MgSO_4$):
- Loading dose: 10 gm IM $MgSO_4$ (5 gm in each buttock).
- The recommended maintenance dosage entails the administration of 5 grams intramuscularly, alternating between the buttocks, at intervals of 4 hours. This regimen shuld be continued for a duration of 12 hours following delivery or the occurrence of the most recent convulsion, depending on which event transpires later.

Group B (Control Group - Standard Pritchard's Regime of $MgSO_4$):
- Loading dose: 4 gm IV and 10 gm IM $MgSO_4$ (5 gm in each buttock).
- Maintenance dose: 5 gm IM in alternate buttock every 4 hours for 24 hours after delivery/last convulsion, whichever is later.
- Additional 2 gm IV $MgSO_4$ allowed if convulsion occurred after the loading dose, up to a maximum of 2 times.

Randomization

Computer-generated random number allocation in blocks of 4.

Allocation Concealment

Sequentially numbered opaque sealed envelopes (SNOSE).

Blinding

The study participants were administered intravenous normal saline solution at a volume of 20 ml, with the intention of blinding them to the intervention. The assessment of potential magnesium toxicity involves the vigilant observation of various clinical indicators. These include the evaluation of respiratory rate, assessment of

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knee jerk reflex, and estimation of urinary output on an hourly basis.

Outcome Measures

The incidence of convulsions in cases of severe pre-eclampsia (PE) is being discussed. The phenomenon of convulsions reoccurring in cases of eclampsia is a matter of concern and clinical significance. Serum magnesium levels were assessed prior to the administration of magnesium sulfate ($MgSO_4$), as well as at 15 minutes and 1 hour following the administration of $MgSO_4$. Recurrent eclampsia is characterized by the manifestation of seizures subsequent to the administration of the loading dose.

- Patients in both groups (Group A and Group B) were randomly assigned to ensure baseline comparability. The key baseline characteristics were assessed, including age, parity, gestational age at presentation, and birthing methods, and found no significant differences between the two groups, indicating baseline similarity.
- To minimize bias, the healthcare providers administering the treatment were blinded to the treatment assignments. All patients received intravenous normal saline solution (20 ml) to maintain blinding, ensuring that the treatment providers were unaware of the specific magnesium sulfate protocol.
- The assessors responsible for evaluating outcomes, such as the occurrence of convulsions, were also blinded to the treatment assignments. This blinding was maintained throughout the study to prevent any potential bias in outcome assessment.
- Apart from the magnesium sulfate intervention, all other aspects of care, including monitoring, supportive measures, and follow-up, were standardized and identical for both groups. This approach aimed to ensure that the treatment groups received equivalent care, minimizing potential confounding factors.
- The study achieved a high level of follow-up completeness for both groups. Any differences in follow-up rates were minimal and did not introduce significant bias into the results. Missing data were handled appropriately during the analysis.

Statistical analysis

SPSS (statistical package for social sciences) version 21.0 statistical analysis software was used for the statistical analysis. The expression for continuous variables was Mean±SD. The terms frequency and percentage were used to express categorical variables. Chi square analysis was also performed.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULTS

Distribution of Cases by Parameters

Following the administration of the initial dose, it was observed that group B exhibited notably elevated serum magnesium levels at both the 15-minute and 1-hour time points. Patients diagnosed with eclampsia demonstrated the attainment of therapeutic levels of magnesium within a span of 15 minutes. However, it is noteworthy that patients diagnosed with severe preeclampsia (PE) did not exhibit the same prompt response, potentially attributable to heightened fluid loss observed in cases of severe PE. Prior to the administration of the initial dose, the serum magnesium levels exhibited no significant disparity between the two groups of patients diagnosed with antepartum eclampsia. The serum magnesium levels in Group B were found to be significantly elevated at both the 15-minute and 1-hour time points following administration of the initial dose.

Recurrence of Convulsions

In a cohort of 62 patients diagnosed with antepartum eclampsia, it was observed that recurrent convulsions manifested in 19.6% of individuals in group A, while in group B, this occurrence was noted in 29.4% of patients. The study group received a maintenance dose for a duration of 12 hours, while the control group received a maintenance dose for a duration of 24 hours. While lacking statistical significance, the study findings indicate that the omission of the initial intravenous (IV) dose does not appear to elevate the likelihood of recurrent convulsions.

Time of Recurrence of Convulsions

The temporal occurrence of recurrent convulsions did not yield any statistically significant findings among the cohort of 16 patients who presented with such episodes. There were no instances observed among the 62 patients wherein low platelet counts were identified as a contraindication for the administration of $MgSO_4$. No instances of severe local site pain or gluteal abscess were documented in any patients who received intramuscular magnesium sulfate ($MgSO_4$) treatment.

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Table 1: Distribution of cases according to various parameters.

Parameters		Group A (n= 71) %	Group B (n= 79) %	Total (n= 150) %	χ^2
Severe PE or antepartum eclampsia	Severe PE	69.78	65.35	68.08	0.633
	Eclampsia	27.16	32.65	29.92	
Age group (in years)	20-30	4.83	3.81	4.31	0.356
	>30	76.67	18.23	75.81	
Number of antenatal care visits	≤4 visits (unbooked)	75.70	74.96	75.33	0.015
	>4 visits (booked)	22.30	23.04	22.67	
Parity	0	57.25	52.85	55.04	0.308
	1	21.33	20.15	20.74	
	2	11.62	13.42	12.53	
	≥3	5.80	9.58	7.70	
History of hypertension/PE/eclampsia	Yes	4.83	2.85	3.83	0.341
	No	93.17	95.15	94.17	
Mode of delivery	Vaginal	41.72	36.50	39.10	2.328
	LSCS	56.28	59.58	57.94	
	Not delivered	0.00	0.92	0.87	
Perinatal outcomes	Live	69.87	71.55	70.71	0.061
	Stillborn	28.13	26.45	27.29	
Maternal outcomes	Improved	97.06	96.12	96.58	0.185
	Expired	0.94	1.88	1.42	

DISCUSSION

The present study compared a modified low-dose $MgSO_4$ regimen (only 10gm IM loading dose, omitting IV dose, and continuing maintenance dose for 12 hours) to the standard Pritchard regime (4gm IV + 10gm IM of $MgSO_4$ loading dose) in terms of convulsion occurrence in severe PE, convulsion recurrence in eclampsia, and serum magnesium levels.

Hypertensive disorders manifesting during the gestational period, encompassing preeclampsia (PE) and eclampsia, are prevalent in approximately 5-10% of pregnancies on a global scale [4]. These conditions, along with hemorrhage and infection, contribute to maternal health problems and deaths. The incidence is higher in developing countries due to factors like malnutrition and limited access to medical care. Approximately 10-15% of maternal mortalities can be attributed directly to the occurrence of preeclampsia (PE) and eclampsia [5]. A comprehensive examination of the available literature in 1995 established magnesium sulfate ($MgSO_4$) as the optimal therapeutic intervention for the management of eclampsia, surpassing alternative pharmaceutical agents such as diazepam or phenytoin. $MgSO_4$ significantly reduced maternal deaths and recurrence of convulsions [6].

There has been ongoing debate about the appropriate dosage and therapeutic magnesium levels for $MgSO_4$, with some suggesting variations based on a woman's weight or body mass index [7].

It is crucial to monitor patients receiving $MgSO_4$ to prevent side effects. Frequent monitoring was recommended, but it could be challenging in high patient-to-staff ratio settings. This study found that both groups achieved therapeutic serum magnesium levels within an hour after the initial dose. Recurrence of convulsions in eclampsia was higher than expected group A, possibly due to delayed healthcare seeking by Indian women. High numbers of seizures before admission might have lowered the seizure threshold and caused hypoxic brain injury, leading to recurrent seizures. $MgSO_4$ effectively prevented convulsions in severe PE cases in both groups. In the present investigation, Samoriski *et al.* [8] conducted an examination wherein they made the observation that generalized clonic seizures were associated with a gradual reduction in the threshold for generalized seizures. Furthermore, these seizures were found to induce hypoxic brain injury. It has been hypothesized that the heightened incidence of seizures prior to hospitalization has resulted in a diminished seizure threshold and hypoxic brain injury, thereby elucidating the augmented occurrence of recurring seizures subsequent to the administration of a loading dose of magnesium sulfate in both cohorts.

Maternal outcomes were generally positive, with most women being discharged in good health. Maternal deaths

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were similar in both groups and occurred in a small percentage of cases. The causes of death included pulmonary edema, pulmonary embolism, and DIC with pulmonary embolism. These maternal mortality rates were lower than reported in some other studies, which could be due to variations in patient conditions and hospital facilities.

Generalizability

The findings of this study comparing a modified low-dose $MgSO_4$ regimen to the standard Pritchard regime for managing hypertensive disorders of pregnancy, including severe preeclampsia (PE) and eclampsia, have important implications for global maternal health. These conditions are a significant concern, particularly in developing countries with limited access to medical care. Approximately 10-15% of maternal deaths can be attributed to PE and eclampsia. While the study emphasizes the importance of monitoring patients receiving $MgSO_4$ to prevent side effects, it also highlights the challenge of frequent monitoring in high patient-to-staff ratio settings. Despite differences in convulsion recurrence rates, both groups achieved therapeutic serum magnesium levels rapidly after the initial dose, supporting the efficacy of $MgSO_4$. Maternal outcomes were generally positive, with low maternal mortality rates, suggesting that appropriate $MgSO_4$ administration can contribute to improved maternal health outcomes in these high-risk conditions. However, further research may be needed to explore variations in patient conditions and healthcare facilities that could affect these outcomes.

CONCLUSION

According to this study, the usual Pritchard protocol is not as efficient as a lower loading dosage of $MgSO_4$ (10 gm IM) and a shorter duration of maintenance dose (12 hours after delivery or convulsion) for managing and avoiding convulsions in Indian women with eclampsia. It also saves money and eliminates the need for uncomfortable intramuscular injections. By using this strategy in primary care settings, eclampsia could be effectively treated at the initial point of contact, potentially saving many lives. Despite the fact that the study's high rate of severe maternal and perinatal outcomes can probably be attributed to subpar prenatal care, it suggests that low-dose $MgSO_4$ therapy for eclampsia be taken into consideration, as it is just as effective as the conventional regimen. Patients can be transported without the risk of convulsions during transit by using the IM regime in nations such as India, which have transportation issues and a high patient-to-staff ratio. The suggested dosage is modest and simple to use. To determine the viability and efficacy of treating eclampsia and severe preeclampsia with merely intravenous magnesium SO_4 loading dose, more investigation ideally a randomized control trial is advised.

Limitations

The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendations

Based on the study's findings, it is recommended that healthcare providers consider the adapted Pritchard protocol, which involves skipping the intravenous (IV) loading dose of magnesium sulfate ($MgSo_4$) in the management of eclampsia. This modified regimen, with a 12-hour maintenance dose and reduced loading dose, has been shown to be as effective as the standard 24-hour maintenance regimen with IV loading doses in preventing convulsions. Importantly, it offers the advantage of lower toxicity risk associated with $MgSo_4$ administration, making it a viable alternative for preventing and managing convulsions in eclampsia and severe pre-eclampsia. Further clinical implementation and evaluation of this adapted protocol may be beneficial in optimizing care for pregnant women at risk.

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List of abbreviations

$MgSo_4$- magnesium sulphate
PE- pre-eclampsia
IV- intravenous
IM- intramuscularly
SNOSE- Sequentially numbered opaque sealed envelopes
SD- Standard deviation

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Conflict of interest

The authors have no competing interests to declare.

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