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Original Research Article

Serum Magnesium Levels between Low Dose $MgSO_4$ and Pritchard Regimen in Treatment of Eclampsia: A Comparative study

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Abstract

Introduction: Eclampsia is an extremely severe form of preeclampsia characterized by sudden onset of generalized tonic-clonic seizures responsible for 17–30% maternal mortality and 22% perinatal mortality. Since then, MgSO4 has been proven to more than halve the risk of occurrence of eclampsia in women with preeclampsia and of recurrence in women with eclampsia. ***Material and Methods:*** This is a Prospective study conducted in the Department of Obstetrics and Gynaecology at Shadan Institute of Medical Sciences, Teaching Hospital & Research Centre, Hyderabad over a period of 1 year. Eclamptic patients who got admitted in department of obstetrics and gynecology. Standard principles of management of eclampsia will be followed. Patients are divided into two groups as cases & control alternatively. Groups are chosen based on inclusion & exclusion criteria. Group I Control will follow Pritchard standard regimen. Group II Cases will receive low dose magnesium sulphate regimen. ***Result:*** Among low dose and standard regime groups about 11.4% & 17.1% each had previous history of PIH. Among low dose group, 15% were intra uterine deaths, 20% needed NICU admissions, 10% were early neonatal deaths and none were perinatal deaths. Among standard regime group, 20% were intra uterine death, 30% were NICU admissions, 25% were early neonatal deaths &10% were perinatal deaths. The average birth weight among low dose and standard group was 2.18kgs and 2.02kgs respectively. The mean APGAR score at 5 minutes was 7.21 among low dose and 6.4 among standard regimen. There is no major correlation in both groups with respect to fetal outcome. ***Conclusion:*** The occurrence of eclampsia in two groups was more common in the age range of 20 to 26 years among the primigravida and with previous history of PIH. There is no major difference in the outcome of maternal and fetal in both groups. Nonetheless the magnesium levels among low dose group are significantly lower in comparison with standard regimen group. In cases and controls the magnesium levels are maintained in normal therapeutic range. Low dose regimen is better alternative to control seizures in eclamptic patients.

Keywords: Eclampsia, Serum Magnesium, Primigravid.

INTRODUCTION

Eclampsia is an extremely severe form of preeclampsia characterized by sudden onset of generalized tonic-clonic seizures responsible for 17–30% maternal mortality and 22% perinatal mortality. [1] The incidence of eclampsia in developed countries is around 1.610 cases per 10,000 deliveries while it is 6–157 per 10,000 deliveries in developing world. [2] The mortality rates also vary widely 5–15%. The incidence of eclampsia in India as per Eclampsia Registry is 41/10,000 deliveries, and mortality is around 1% cases of eclampsia. Eclamptic convulsions are life-threatening emergencies and carry a risk of high morbidity and mortality if not managed timely and appropriately. Amongst the principles of management of eclampsia, the first and foremost is the control of convulsions. [3]

In 1925, magnesium sulphate was introduced into clinical practice to treat eclampsia.8 Since then, MgSO4 has been proven to more than halve the risk of occurrence of eclampsia in women with preeclampsia and of recurrence in women with eclampsia. [4] A Cochrane review of alternative MgSO4 dosing regimens included four randomized controlled trials from LMICs, three from India, and one from South Africa. [5] MgSO4 is recognized by the World Health

Organization and the United Nations as both a priority medicine and a life-saving commodity for the treatment of severe preeclampsia and/or eclampsia. [6] MgSO4 is generally administered parenterally in a loading dose (IV with or without additional IM dosing) followed by maintenance dosing (by continuous IV infusion or intermittent IM injections). The two most commonly used regimens are the Zuspan regimen (a loading dose of 4 g IV, and maintenance dosing of 1 g/hr IV) and the Pritchard regimen (loading doses of 4 g IV and 10 g IM, and maintenance dosing of 5 g IM/4hr). [7]

MgSO4 for treatment of severe preeclampsia and eclampsia was listed on only 50% of 89 countries' Essential Medicines Lists in a recent review.18 Another major challenge to the effective use of MgSO4 is the lack of prenatal care received by women in LMICs, which leads to late (if any) presentation to the tertiary health care facilities where MgSO4 is most commonly available. All of these barriers may result in suboptimal use of MgSO4. [8] The global health community has recognized the barriers to use of MgSO4 for eclampsia prevention and treatment as a key issue. Consequently, the United Nations Population Fund is addressing the issues of variability in formulation and the potential for mixing errors by mapping MgSO4 manufacturers and moving towards a standardized formulation and presentation of MgSO4.

MATERIALS AND METHODS

This is a Prospective study conducted in the Department of Obstetrics and Gynaecology at Shadan Institute of Medical Sciences, Teaching Hospital & Research Centre, Hyderabad over a period of 1 year. A total 70 cases in present study. Eclamptic patients who got admitted in department of obstetrics and gynaecology.

Inclusion Criteria: Eclamptic patients.

Exclusion Criteria: History of epilepsy**,** Stroke patients**,** Space occupying lesions in brain Patients with previous history of hypertension**,** Renal failure history**,** Magnesium therapy contraindications.

Methodology: Among 70 study group, patients were grouped into two groups i.e controls (Pritchard regimen) and cases (low dose regimen). Patients were divided into groups based on randomization.

CONTROLS: 14gm of MgS04 (5gm IM+5gm IM+4g iv in 100ml NS) as Loading Dose and 5gm IM every 4 hourly in alternate buttocks till delivery or convulsions whichever is later for 24 hours as Maintenance Dose.

CASES: 4gm MgSO4 iv in 100ml NS as Loading Dose and 2gm IV bolus every 3hourly till delivery or convulsions whichever is later for 24 hours as Maintenance Dose.

Measurement of serum magnesium levels was done before 2nd dose, before delivery, before last dose in both groups. Magnesium toxicity levels in both groups were compared by measuring deep tendon reflexes, urine output, respiratory rate. If convulsions are not controlled by low dose regimen Pritchard regimen will be used as rescue therapy.

Statistical Analysis:

The data was collected, compiled and analysed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantative variables were both categorised and expressed in terms of percentages or in terms of mean and standard deviations. Difference between two proportions was analysed using chi square or fisher exact test. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS

About 17.2% were between 18 to 20 years, 60.0% are in the age of 21 to 25 years and 22.8% were in age group of 25 - 30 years among low dose group. Among the standard group, 8.5% were 18 to 20, 54.2% are in age group of 21 to 25 and 37.1% were between 25 to 30 years. There is no significant difference between the age groups among the groups.

Table 1: Distribution of the study subjects based on the age groups among the groups

Age group	Low dose		Standard dose		P value
	Number	%	Number	%	
18 to 20	6	17.2	3	8.5	0.435
21 to 25	21	60.0	19	54.2	
25 to 30	8	22.8	13	37.1	
Total	35	100	35	100	

Table 2: Distribution of the study subjects based on the past history of PIH among the groups

Past history of PIH	Low dose		Standard dose		P value
	Number	%	Number	%	
Yes	4	11.4	6	17.1	0.364
No	31	88.5	29	82.8	
Total	35	100	35	100	

Among low dose and standard regime groups about 11.4% & 17.1% each had previous history of PIH.

Table 3: Distribution of the study subjects based on the foetal outcome among the groups

Outcome of baby	Low dose		Standard dose		P value
	Number	%	Number	%	
IUD'S and neonatal deaths	4	11.4	9	25.71	0.054
NICU admissions	5	14.2	6	17.14	0.325
Mean APGAR at 5 minutes	7.14	2.1	6.54	2.3	0.526
Mean birth weight	2.34	0.54	2.54	0.52	0.9123
Intra uterine death	1	2.8	2	5.7	0.535
Early neonatal death	1	2.8	3	8.5	0.453
Perinatal death	0	0	1	2.8	-

Among low dose group, 15% were intra uterine deaths, 20% needed NICU admissions, 10% were early neonatal deaths and none were perinatal deaths. Among standard regime group, 20% were intra uterine death, 30% were NICU admissions, 25% were early neonatal deaths &10% were perinatal deaths. The average birth weight among low dose and standard group was 2.18kgs and 2.02kgs respectively. The mean APGAR score at 5 minutes was 7.21 among low dose and 6.4 among standard regimen. There is no major correlation in both groups with respect to fetal outcome.

Table 4: Distribution of Intrauterine Deaths based on the onset of convulsions

Intrauterine deaths	Low dose		Standard dose		P value
	Number	%	Number	%	
Before onset of convulsions	1	2.8	2	5.7	0.535
After onset of convulsions	1	2.8	3	8.5	0.453
Total	2	100.00	5	100.00	

Table 5: Distribution of the study subjects based on blood pressure among the groups

Blood pressures	Low dose		Standard dose		P value
	Mean	SD	Mean	SD	
Systolic blood pressure	142.34	12.45	153.63	13.54	0.064
Diastolic blood pressure	101.24	7.38	107.64	7.34	0.245

The average SBP was 142.34 mmHg in low dose and 153.63 mmHg in standard group. The average DBP was 101.24 among low dose and 107.64 among the standard group.

Table 6: Distribution of the study subjects based on magnesium levels among the groups

Magnesium levels	Low dose		Standard dose		P value
	Mean	SD	Mean	SD	
Before delivery	2.65	0.56	2.91	0.26	0.354
Before second dose	3.25	0.54	4.91	0.63	<0.001
Before last dose	3.05	0.62	5.01	0.36	<0.001

Before delivery the magnesium levels among low dose and standard dose group were 2.65 and 2.73 respectively. Before the second dose, the average Mg+2 levels are 3.25 in low dose and 4.91 among standard group and this difference is statistically significant. Before the last dose, average Mg+2 levels are 3.05 in cases and 5.01 in standard group and this shows difference which is significant.

DISCUSSION

Eclampsia is a life-threatening emergency that continues to be a major cause of serious maternal morbidity and mortality. Eclampsia affects 0.2% to 0.5% of all deliveries. In our hospital, the incidence of eclampsia is 1.8-2%. Noor et al showed an incidence of 3.9% in his study. [9] The incidence of eclampsia does not appear to have really come down. The majority of cases, of course, came from villages and mostly these patients did not have antenatal check-ups. The efficacy of magnesium sulfate in the prevention and control of eclamptic convulsions has been validated in randomized controlled trials performed worldwide. Since the introduction of Pritchard regime there has been a constant discussion in literature regarding the dose of magnesium sulfate and therapeutic serum magnesium levels. [10]

In India pritchard's regime has been modified at many places. Different hospitals are having different regimes. A long term statistical data has not been reported and the protocol has not been standardized. Pritchard himself in 1984 suggested that the dose of magnesium sulfate should be limited in women who appear to be small. [11] This study was planned to compare the efficacy of low dose magnesium sulfate regime with pritchard's regime in controlling convulsions in eclampsia in Indian women. In the present study, the average weight of the patients in both groups and all the other parameters were comparable.

In this study convulsions were controlled in 90% of cases with loading dose of 4gm only, instead of 14 gm as prescribed in pritchard's regime, and the recurrence rate of convulsion with low dose magnesiumsulfate therapy was 10%. With pritchard's regime in 96% of cases convulsions were controlled and the recurrence rate is 4%. Recurrence rate reported in various studies with Pritchard's regime is 9.7%. Pritchard and Sibai both had reported a recurrence rate of 10-12% cases. Several studies showed a recurrence rate of 4-6% with low dose magnesium sulphate therapy. [12] The recurrence rate with standard protocol reported in collaborative eclamptic trial, the largest multicentre randomized controlled trial ranged between 5.7% and 13.2%. The two Asian studies one by Suman P et al and another by R. Begum of Dhaka have concluded that the low dose magnesium sulfate therapy is as effective as standard Pritchard's regime in the Asian Group. [13]

In this study with low dose magnesium sulfate therapy, the recurrence rate was 10% which is comparable with a study by Sardesai SP et al, where the recurrence rate was 8%. Bangal V et al have clearly demonstrated in their studies that 94% cases of eclampsia can be controlled with low dose magnesium sulphate therapy. [14] Ekele et al in his study demonstrated that limiting the dosage of magnesium sulphate to 14 grams loading dose (4 grams intravenous and 10 grams intramuscular) was effective in controlling fits in 92.6% of cases. [15] With Pritchard's regime, 3 (6%) patients had absent knee jerks, but no such drug toxicity was seen with low dose magnesium sulphate therapy. This is in accordance with Dasgupta who showed that magnesium toxicity was less with low dose therapy than with standard regimen. [16]

There is ample evidence that the dose regime needs to be modified according to patient's weight. Phuapradit W et al from Bangkok - state that "it seems appropriate to take in to account body weight when considering the dosage of drug and the regime used is appropriate for Asian women with body weight usually less than 70kg". Witlin A in her review article on eclampsia in Clinical Obs. and Gyn. commented that "one may also speculate that magnesium sulfate dosing should vary according to the patients' weights or body mass index." [17]

Administering pritchard regime might prove to be hazardous in these low weight women and there is every possibility of respiratory failure. The risk of respiratory failure greatly exceeds the risk imposed by administering small doses with slight possibility of one more convulsion. More over switching over to standard regime from the low dose protocol is simple in the event of such a need. The low dose protocol suffices to meet the requirements in small built eclamptic women with a recurrence rate of 10%, as shown in this study. In the magnesium sulfate metabolism, 50% of the infused dose is excreted in the urine when the concentration of serum Mg exceeds 2 mg/dl. Thus even, if we give Pritchard's regime the excess of Mg is excreted by the kidneys. This is a strong justification for giving low dose regime.

Therefore there is a need to start treatment at primary care level itself. The low dose magnesium sulfate therapy can be given safely by the medical officers and ANMs working at primary care level where facilities for specialized treatment for eclampsia is not available and can be administered to tide over the crisis without fear of precipitating respiratory failure before transferring the patient to a higher centre.

CONCLUSION

To conclude, the occurrence of eclampsia in two groups was more common in the age range of 20 to 26 years among the primigravida and with previous history of PIH. There is no major difference in the outcome of maternal and fetal in both groups. Nonetheless the magnesium levels among low dose group are significantly lower in comparison with standard regimen group. In cases and controls the magnesium levels are maintained in normal therapeutic range. Low dose regimen is better alternative to control seizures in eclamptic patients.

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