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RESEARCH ARTICLE

COMPARATIVE STUDY OF LOW DOSE V/S STANDARD DOSE REGIME OF MAGNESIUM SULPHATE
(MgSO₄) IN MANAGEMENT OF ECLAMPSIA

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ABSTRACT

This study is to compare the low dose with standard Pritchard's regime for controlling convulsion in patients of eclampsia. In this hospital based prospective study, cases presenting with classical features of eclampsia (beyond 20 weeks of pregnancy and upto 7 days postpartum) and meeting inclusion criteria's were included as per confounding of both the groups i.e. Group-A and Group-B. 25 cases were given low dose Magnesium Sulphate (Study Group; Group-A) and 25 cases were given standard dose regimen (Control Group; Group-B) after informed and written consent. In our study after statistical analysis we concluded that Magnesium Sulphate is required for controlling the convulsions of eclampsia but low dose regime is very simple to administer and easy to monitor and is as effective as Pritchard's regime with minimal possible side effects and better perinatal outcome.

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INTRODUCTION

"Eclampsia" is defined as the occurrence of generalized convulsions associated with signs of pre-eclampsia (William's Obstetrics, 2010). Which is defined as hypertension developing after 20 weeks of gestation, during labour or during puerperium associated with proteinuria (i.e. urinary excretion of proteins, 300 mg/L or more in a 24 hrs urine collection or $\geq +1$ by qualitative estimation using albustix reagent in a sample of urine) in a previously normotensive non-proteinuric woman. It is classified as antepartum, intrapartum and postpartum (Ian Donald's and Renu Mishra, 2012; Dutta and Hiralal Konar, 2001). If the convulsions occur after 7 days postpartum, in the absence of high blood pressure, the condition is referred to as "atypical eclampsia" (Dutta and Hiralal Konar, 2001) and when convulsions occur in quick succession it is called as status eclampticus (Paruk and Moodley, 2000). Eclampsia usually manifests after 20 weeks of pregnancy and is more frequent as term approaches (Ian Donald's and Renu Mishra, 2012). It is primarily a disease of primigravid as compared to multigravida. Eclampsia is a multisystem disorder of unknown etiology, (Maharaj and Moodley, 2000) however abnormal placentation, immunological factors, inflammatory factors and oxidative stress have all been implicated.

Management of eclampsia is basically at three fronts

- Control of convulsion - By anticonvulsant drugs
- Control of hypertension - By antihypertensive drugs (Labetalol being the first line medication)
- Expedite delivery and intensive postpartum care

To control convulsion, presently Magnesium Sulphate is accepted world wide as the anti-convulsant of choice. It has ability to block neuromuscular transmission by decreasing release of acetylcholine in response to nerve action potential. It also acts as a vasodilator. Respiratory depression, pulmonary odema, oliguria, cardiac arrest are some of the known side effects of Magnesium Sulphate. In neonates it causes respiratory depression and hyporeflexia.

Dr. J.A. Pritchard from USA gets the credit of popularizing Magnesium Sulphate therapy for eclampsia in modern obstetrics. This dose regime is popularly known as "Pritchard's Regime" or "Standard dose regime".⁶ Pritchard commented that "if a woman, known to be or appears to be small, the dose of Magnesium Sulphate should probably be limited". These comments initiated to modify and to formulate low dose Magnesium Sulphate regime. It seems appropriate to take into account the body weight, when considering the drug dosage and the regime used.

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Expedite delivery after haemodynamic stabilization of the patient is the treatment of eclampsia. The mode of delivery is based on obstetric indications. Vaginal delivery is allowed when the cervix is favourable. Intensive postpartum care for first 24-48 hrs is important as blood pressure may fluctuate and patient is still at risk of developing complications. Magnesium Sulphate is continued for a minimum of 24 hrs following delivery or convulsion whichever occurs later.

MATERIALS AND METHODS

This hospital based prospective study was conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur (Rajasthan). After taking informed and written consent, cases presenting with classical features of eclampsia (beyond 20 weeks of pregnancy and upto 7 days postpartum), attending the OPD and meeting our inclusion criteria were recruited with simple random sampling for our study as per confounding of both the groups i.e. Group-A and Group-B. 25 cases were given low dose MgSO₄ (Study Group; Group-A) and 25 cases were given standard dose regime (Control Group; Group-B).

In each case detailed history was taken either from attendant or from the patient, if she was conscious. General and obstetrical examination was done. Routine laboratory investigations and special investigations were done as required. Convulsions were managed accordingly after dividing them in respective groups.

Group-A (study group)	Group-B (control group)
Low dose MgSO ₄ regime ⁷	Standard dose MgSO ₄ regime ⁸
Loading dose	Loading dose
4 gm IV (20% solution)	4 gm. IV (20% solution) + 10 gm IM (50% solution)
{8 ml (4 gm) of 50% of MgSO ₄ diluted with 12 ml of sterile water given at a rate of 1 gm/minute over a period of three minutes}	{8 ml (4 gm) of 50% of MgSO ₄ diluted with 12 ml of sterile water given at a rate of 1 gm/ minute followed immediately by 20 ml (10gm) of 50% MgSO ₄ solution given half in each buttock}
Maintenance dose	Maintenance dose
2 gm. IM (50% solution) three hourly in alternate buttock, continued till 24 hours after delivery or last fit, whichever occurs later.	5 gm. IM (50% solution) four hourly in alternate buttock, continued till 24 hours after delivery or last fit, whichever occurs later.

Toxicity of MgSO₄ was monitored clinically by (Agarwal, 2010)

- Presence of knee jerk (Deep tendon reflex) {Patellar reflex}
- Urine output - should be at least 30 ml/hr or \geq 100 ml in previous 4 hours.
- Respiratory rate - should be \geq 14/min.

If any of the above parameters were deranged than next dose of MgSO₄ was withheld until it returned back to normal. 10 ml of 10% Calcium Gluconate (antidote) was kept standby. If diastolic blood pressure was \geq 110 mmHg than antihypertensive was given as required.

All cases of antepartum eclampsia were terminated. The method of termination depends on Bishop's score. Intensive postpartum surveillance was maintained, as patient was still at risk of developing complications. Neonatal assessment done. Mother was discharged only when BP and urine albumin returned back to normal. Patient showing residual hypertension was referred to physician.

RESULTS

Majority of the patients were young primiparas in late third trimester with unsupervised pregnancies, as is prevalent in low socio-economic status (Table-1). In our study 92% of cases in low dose group and 96% of cases in standard dose group had no convulsions after initiating the treatment and the convulsions were controlled by loading dose itself. The fit recurrence rate was 8% in low dose group and 4% in standard dose group which was statistically non-significant with p-value 0.20 (Table-2). Absent patellar reflex is the first and most important adverse effect of MgSO₄ toxicity which can be detected clinically earliest and which is not altered by disease process.

The rest two parameters i.e. decreased urine output and respiratory depression can be due to magnesium intoxication as well as disease process. Our study reveals that 4% cases had absent knee jerk, 4% had decreased urine output and none had respiratory depression in study group. In control group 28% had absent knee jerk, 12% had decreased urine output and 4% had respiratory depression (Table-3). After studying 50 cases of eclampsia, there was only one maternal death. The death was in the standard dose group. It was not a complication of the regime used but instead it was due to pulmonary embolism giving rise to cardiopulmonary arrest due to severity of the disease, showing reduction in complication by using low dose regime (Table-4).

In study group (low dose group) out of 21 live born babies, 10 had no complications, 1 expired immediately after birth and 10 were admitted in NICU. Out of which 4 expired in NICU. In control group, out of 23 live born babies 12 had no complications, whereas 11 were admitted in NICU and 7 expired in NICU. In standard dose group number of admissions to NICU and neonatal death was more. This may be a reflexion of respiratory depressant effect of the high dose of magnesium on the baby (Table-5).

DISCUSSION

The word "Eclampsia" is derived from Greek word "eclampusum" which means "like a flash of lightning". Eclampsia is a disease of first pregnancy of young female affected by quality of antenatal care, nutritional status, socio-economic status and age. Guidance accumulated till date indicates that abnormal placentation is one of the initial events in pathogenesis of eclampsia (Agarwal, 2010). Ominous features of prognosis in eclampsia are interval between onset of convulsions and commencement of treatment, long delivery interval from commencement of convulsions, no. of fits >10, coma in between fits, hyperpyrexia (temp over 102°F), blood

Table 1. Distribution of Cases According to their Demographic Profile

	Low Dose Group / Study Group (Group-A) (N = 25)	Standard Dose Group / Control Group (Group-B) (N = 25)	
Age (in years)			$\chi^2 = 0.136$;
≤ 25	20 (80%)	21 (84%)	d.f. = 1; p > 0.10
> 25	5 (20%)	4 (16%)	(non-significant)
Parity			$\chi^2 = 0.5$;
Primi	21 (84%)	19 (76%)	d.f. = 1; p > 0.10
Multi	4 (16%)	6 (24%)	(non-significant)
Gestational Age (in weeks)			$\chi^2 = 0.01$;
≤ 28 (20-28)	2 (9.09%)	2 (10%)	d.f. = 1; p > 0.10
> 28	20 (90.90%)	18 (90%)	(non-significant)
Socio-economic Status			

Table 2. Distribution of Cases According to Number of Convulsion After Initiation of Treatment (Regime)

No. of Convulsions	Low Dose Group / Study Group (Group-A) (N = 25)	Standard Dose Group / Control Group (Group-B) (N = 25)
Nil	23 (92%)	24 (96%)
1 - 2	2 (8%)	1 (4%)
≥ 3	-	-

t = p = 0.20 (non-significant)

Table 3. Distribution of Cases According to Adverse Effects of the Two Regimes

Adverse Effects	Low Dose Group / Study Group (Group-A) (N = 25)	Standard Dose Group / Control Group (Group-B) (N = 25)
Absent patellar reflex (knee jerk)	1 (4%)	7 (28%)
Decreased urine output	1 (4%)	3 (12%)
Respiratory depression	Nil	1 (4%)

Table 4. Distribution of Cases According to Case of Maternal Mortality

Maternal Mortality	Low Dose Group / Study Group (Group-A) (N = 25)	Standard Dose Group / Control Group (Group-B) (N = 25)
Cerebral Haemorrhage	-	-
Pulmonary Oedema	-	-
Pulmonary Embolism	-	1 (4%)
HELLP Syndrome	-	-
PPH / DIC	-	-
Acute Renal Failure	-	-
Acute Hepatic Failure	-	-
Number of Maternal Deaths	Nil	1 (4%)

Table 5. Distribution According to Neonatal Outcome

Neonatal Outcome	Low Dose Group / Study Group (Group-A) (N = 21)	Standard Dose Group / Control Group (Group-B) (N = 23)
Expired immediately	1	0
Developed no complications	10	12
Admitted to NICU	10	11
Expired in NICU	4	7
Stay in NICU		
≤ 7 days	9	8
> 7 days	1	3

pressure over 200 mmHG systolic, oliguria (<400 ml/24 hrs) and proteinuria (>5 mg/24 hrs). Prompt control of convulsions and blood pressure along with steps to initiate delivery and termination of pregnancy form the foundation stones of treatment of eclampsia. The popular and universal regime of MgSO₄ which is being used in cases of pre-eclampsia and eclampsia was developed by the efforts of Pritchard and Zuspan (William's Obstetrics, 2010).

Various studies conducted so far reached to the final conclusion that MgSO₄ is the most suitable drug available for control of convulsions with least recurrence rate and with minimal maternal mortality and perinatal mortality. Pritchard commented on the respiratory depression caused by MgSO₄ and advised to limit the dose of MgSO₄ according to the weight of the patient.

Our study concluded that only loading dose of MgSO₄ can control convulsions in eclampsia and low dose regime is as effective as standard dose while the total dose of MgSO₄ injected to the patient is very much reduced.

Conclusion

All data suggest that low dose Magnesium Sulphate regime is as effective as the standard dose regime in controlling the convulsions in eclampsia and in preventing their recurrence with minimal possible side effects, especially in women from rural areas of low socio-economic strata having smaller body weight.

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