



ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

THE STUDY OF EFFICACY OF SINGLE LOADING DOSE OF MAGNESIUM SULPHATE TO PREVENT SEIZURE ON SEVERE PREECLAMPSIA AND ECLAMPSIA

KEY WORDS: Preeclampsia, Eclampsia, Magnesium sulphate.

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ABSTRACT

AIMS & OBJECTIVE: To evaluate and compare the efficacy of loading dose (reduced dose) magnesium sulphate with standard Pritchard's regime in severe Preeclampsia & Eclampsia patients for analysis of maternal and fetal outcome with MgSO₄ toxicity and side effects in both the regimes irrespective of state of pregnancy and period of gestation.
MATERIALS & METHODS: A prospective observational study conducted in the Department of Obstetrics and Gynaecology, Calcutta National Medical College, Kolkata, during the period MARCH 2018 to FEBRUARY 2019. A total number of 100 patients were taken for the study, out of which 50 were severe preeclamptic\ eclamptic patients cases and equal number of controls (In Antepartum eclampsia patients to whom standard Pritchard's regime given.)
RESULTS: In the present study maximum number of patients belong to teenage group. Incidence of Eclampsia is high in this age group. Loading dose of Magsulf is as effective as standard regime in controlling seizures in eclampsia and preventing the seizures in severe preeclampsia. The recurrent seizures rate were almost the same in both the group.
CONCLUSION: Single loading dose (reduced dose) magnesium sulphate is efficacious in preventing recurrence of convulsions and Perinatal & Maternal outcome is better and toxicity of MgSO₄ is less in our study.

INTRODUCTION

Preeclampsia , considered as a syndrome that can affect every organ system is seen in 5-8% of all pregnancies. Convulsion in the Preeclampsia that cannot be attributed to any other factor defined as eclampsia. Hypertensive disorder are important cause of maternal & perinatal morbidity and mortality. Incidence of eclamptic convulsions were reported around 1\2000 in developed countries . In developing countries incidence varies from 1\500 - 1\5000.

Eclampsia is a multi system disorder with complex pathogenesis which is not completely understood. Cerebral involvement causing convulsions can kill the mother and the fetus unless expertly managed. Among many anticonvulsants, magnesium sulphate topped the list for the treatment of convulsion. Magnesium sulphate is widely used now a days for prophylaxis in severe Preeclampsia as well as treatment of seizures in eclampsia. There are principally two main regimes available for administration of MgSO₄.

In the Pritchard's regime loading bolus of 4 gm of MgSO₄ is given slowly intravenously over 5-10 mins and followed by 10gm given intramuscularly (5 gm in each buttock) subsequently 5 gm is given intramuscularly into alternate buttock every 4 hrs(8). In the Zuspan's regime loading dose consist of initial intravenously dose of 4 gm slowly over 5-10 mins followed by maintenance dose of 2 gm every hour by infusion pumps. Despite its efficacy , narrow therapeutic index is a concern related with its toxicity.

The choice of which regime to use depends on number of factors , such as availability of staff to monitor the drugs as well as the expertise of the staff. Some workers have reported modifications in the above mentioned regimes. It has recently been suggested that an initial loading dose of magsulf is sufficient to arrest convulsion. We also observed that most of the patient didn't receive maintenance therapy due to suspicion of toxicity and they didn't convulse further.

In this study we aimed to determine the effectiveness of single loading dose magsulf regime for prevention and control of convulsion in patients with severe Preeclampsia and eclampsia respectively.

AIMS AND OBJECTIVES

The study was done in Department of Obstetrics &

Gynaecology, Calcutta National Medical college and Hospital, Kolkata with a total number of 100 patients.

The aims and objectives of this study were to evaluate the following:

- To compare whether the reduced dose(Loading dose) of Magsulf suitable for our mostly underweight patient , has the same efficacy and results as full recommended dose so that the toxicity and side effects can be avoided.
- To formulate a legitimate management protocol for Eclampsia in our hospital.
- Present study was carried out to evaluate and compare the efficacy of loading dose magnesium sulphate with standard Pritchard,s regime in severe Preeclampsia & Eclampsia patients and also to analyze maternal and fetal outcome in both the regimes irrespective of state of pregnancy and period of gestation.
- To evaluate the effect of single loading dose magsulf to achieve a therapeutic level of serum Mg for prevention of convulsion.

MATERIALS & METHODS

The present study was conducted on patients attending to either the emergency or OPD of department of Obstetrics and Gynaecology of Calcutta National Medical College & Hospital, Kolkata.

STUDY PERIOD : One Year (March 2018 to Feb 2019)

SAMPLE SIZE: A total number of 100 patients were taken for the study, out of which 50 were severe preeclamptic\ eclamptic patients cases and equal number of controls (In Antepartum eclampsia patients to whom standard Pritchard's regime of Magsulf given.)

STUDY DESIGN: Institution based Prospective study.

INCLUSION CRITERA:

All the pregnant women having severe preeclampsia (diagnostic criteria : BP > 160/110 mm of Hg with features of Proteinuria > 2+ or MAP > 110 mm of Hg along with features of thrombocytopenia / headache / HELLP Syndrome / Epigastric pain) and Eclampsia (antepartum eclampsia only)

EXCLUSION CRITERIA:

1. All pregnant women having mild preeclampsia
2. Gestational HTN
3. Chronic HTN

PARAMETERS STUDIED:

History of the patient: Age, Gravida, Parity, LMP, EDD, Gestational Age, past obstetrics history of preeclampsia or eclampsia and family history of and complicating factors(headache thrombocytopenia, HELLP syndrome etc.)

Examination : BP, urine output, respiratory rate , DTR and obs.Examination - fundal height , fetal ultrasound.

Lab Prameters: Urine dipstick testing , full blood count, LFT, RFT, monitoring and charting of fluid balance, serum Mg level

Study Technique: On admission, a quick survey was done and treatment was initiated with following:

1. General management of severe preeclampsia & eclampsia
2. Obs. Exmanation was done after stabilising the pt. with anticonvulsant regime. These regimes were main stay of therapy. As conventional standard dose as proposed by Pritchard et al. and loading dose as proposed by different workers suitable for Indian women.
3. Doses scheduled were described below

Dose Schedule for Conventional Standard dose:

As propseed by Pritchard consists of both loading and maintenance doses.

1. Loading Dose: Soon after admission 20 ml of 20% magsulf (4 gm) slowly IV over atleast 5mins followed by 10 ml of 50% magsulf (5 gm) deep IM in upper and outer quadrant of each buttock using a 3 inch long 20 gauge needle.
2. Maintanance Dose : Every 4 hrs after the loading dose 10 ml 50% magsulf(5 gm) in upper and outer quadrant of alternate buttocks injected deep IM after ensuring that
 - a. Patellar reflex was present
 - b. U/O > 100 ml during the preceding 4 hrs
 - c. The RR > 14/min

Dose Schedule for Loading Dose Regime:

1. 20 ml of 20% magsulf (4 gm) slowly IV over atleast 5 mins followed by 10 ml of 50% magsulf (5 gm) deep IM in upper and outer qudarent of each buttock using a 3 inch long 20 gauge needle , in cases where convulsions recurs, these considered as failure cases.

- Control of blood pressure if the diastolic blood pressure was >110mmHg, an injection of labetalol 20mg intravenously was given.

Blood pressure was monitored at 15min intervals and stopped when diastolic blood pressure dropped to 90mmHg. Methyl dopa and Nifedipine were used in variable doses depending upon the level of blood pressure.

Labour management: Labour was induced by an artificial rupture of membrane and oxytocin drip in cases where the cervix was unfavorable for giving birth. Labour was induced by prostaglandin gel or Indications for caesarean section were failed progress after induction, prolonged labour, malpresentations, fetal distress, previous caesarean section, Intrauterine Growth Restriction (IUGR), Bishop score <6 and obstructed labour.

The efficacy of both regimes was assessed by measuring the rate of recurrent convulsion. Comparisons between groups were made.

Statistical Analysis:

All the data were recorded in the proforma which is attached herewith statistical analysis of the data were carried out where

possible using Chi square test (X²)&standard t test. The level of significance was set at 5%.

RESULTS

Total time period of study : 1 year (March 2018 to February 2019) Total number of severe preeclampsia and eclampsia cases were 50 out of which severe preeclampsia (n=35) and eclampsia(n=15) were taken and equal number of controls(n=50).They were studied for age, parity, SES, Gestational age, number of antenatal visits, maternal and perinatal outcome, mean serum Mg level and recurrence of convulsions. The age of patients in the study population ranged from 15 years to more than 25 years of age. Though the maximum number of patients in both the groups belonging to less then 25 years of age i.e. more than 80% of the patients less than 25 years of age. According to the B G Prasad Classification more than 80% women in study and control group were belong to poor SES group while there were no cases from upper class of society. Most of the patients were nulliparous. More than 2/3rd of the women were illiterate. More than 80% cases in both the groups had no antenatal visits i.e. Unbooked. Only 14% cases were booked cases. Majority of patients were presented in last trimester. 51% of severe preeclampsia between 33-36 of age & 43 % were in more than 37 age where 67% of eclampsia between 33-36 age. in Control group 62% between 33-3 of age. 90-95% of cases of both the group received treatment within 12 hrs of first convulsion. 80% of cases of study group and 56% cases of controlled group delivered within 12 hrs of first fit and no cases of study group delivered in more than 18 hrs. 54% cases of preeclampsia and 60% cases eclampsia delivered vaginally in study group & 70% in control group. Incidence of LUCS was 40-45% in study group and 30% in control group. Incidence of live births were more in study group compared to controlled group (80% vs. 68%). Perinatal mortality were almost same (32% in eclampsia & control group), lower in severe preeclampsia group (24%). Mean serum Mg level in study group and control group just before the loading dose were almost same, there was no significant between the two. The P value (0.084) was > 0.05. After 12 hrs of Magsulf regimen Mean Serum Mg level in study group 4.4 mEq/ltr. & in control group 5.2 mEq/ltr. By applying student 't' test , p value < 0.05 (significant difference between serum Magnesium level). With statistical analysis(Applying Chi-Square Test on data), there is no significant difference between these two groups on rate of recurrence of convulsion (With p value set 5%)

TABLE:- 1 Distribution of study population according to Age Group of Patients:

Age (yrs)	Group A (study Group) (n=50)		Group B (Control Group) (n=50)
	Severe Preeclampsia (n=35)	Eclampsia (n=15)	
15-20	14(40%)	4(27%)	16(32%)
21-25	15(43%)	8(53%)	26(52%)
>25	6(17%)	3(20%)	8(16%)

TABLE:- 2 Distribution of study population according to Gestational Age:

Gestational Age	Group A (study Group) (n=50)		Group B (Control Group) (n=50)
	Severe Preeclampsia (n=35)	Eclampsia (n=15)	
28-32wk	2(6%)	2(13%)	4(8%)
33-36wk	18(51%)	10(67%)	31(62%)
>37wk	15(43%)	3(20%)	15(30%)

Table:- 3 Mean Serum Mg (meq/ltr) Level In Study And Control Group

Time of Measurement	Group A (Study Group) (n=50)	Group B (Control Group) (n=50)
Before Loading Dose	1.5 ± 0.20	1.4 ± 0.36
12 hrs after Loading Dose	4.4 ± 0.22	5.2 ± 0.22

TABLE:- 4 Efficacy of Loading Dose and Standard Regime: Severe Preeclampsia and Eclampsia

	Convulsion Controlled	Recurrence of Convulsions
Group A (Study Group) Severe Preeclampsia (n=35)	33	2
Group A (Study Group) Eclampsia (n=15)	12	3
Group B (Control Group) (n=50)	46	4

TABLE:- 5 Distribution of cases according to Maternal Mortality and Morbidity

Maternal Complications	Group A (Study Group) (n=50)		Group B (Control Group) (n=50)
	Severe Preeclampsia (n=35)	Eclampsia (n=15)	
Mortality	Nil	1 (7%)	2 (4%)
No Complications	32 (92%)	11 (73%)	39 (78%)
Morbidity			
Pulmonary oedema	Nil	1 (7%)	2 (4%)
PostPartum Psychosis	Nil	Nil	1 (2%)
Renal Failure	Nil	Nil	1 (2%)
Aspiration Pneumonia	Nil	Nil	1 (2%)
PPH	3 (8%)	2 (13%)	4 (8%)

DISCUSSION

Eclampsia is still a common obstetric emergency in the developing world. Although, it cannot always be prevented, but the morbidity and mortality associated with it, can be reduced by early recognition of hypertension during antenatal visits.

In the present study, about 44% of cases were below 20 years of age. Maternal age of less than 20 years is the strongest risk factor for eclampsia [5]. This high incidence in teenagers may be related to subnormal development of uterine vasculature.

In the present study, 65% of cases were primigravida and remaining multigravida. Eclampsia is a disease of primigravida. Pritchard et al, Biswas, Sardesai in these studies observed that, 75%, 88%, 80%, and 79% of eclampsia cases primigravidas respectively [1][6][13]. According to Hellman incidence of eclampsia in primigravida and multigravida was in the proportion of 3:1 [7].

In the present study 85% of cases were unbooked. Similar studies by Sardesai et al and Chowdhury et al revealed that 76.6% and 75.8% of cases were unbooked respectively [13][4].

Efficacy of MgSO4 in prevention and treatment of eclamptic convulsions is time tested and supported with a variety of studies. However protocols and dose of MgSO4 are not evidence based and narrow therapeutic index and toxicity is still a major concern in clinical use.

Pritchard also suggested a dose reduction in women with small body size [1]. Witlin recommended the dose adjustment according to patients' weight or body mass index [8]. A variety of modified dose regimes have been proposed. Begum et al. described "Dhaka Regime" as 10 gm loading followed by 2.5gm intramuscularly 4 hourly for 24 hours [9]. Our regimen, almost one third of standard magnesium dosage, is quite safe for rural low resource setting where magnesium level monitoring is not readily available.

The incidence of eclampsia in our hospital is high that reflect the illiteracy, lack of awareness, limited health care facilities of the region. Of course this high incidence can only be decreased by proper antenatal care, increasing health awareness, early diagnosis and proper management of preeclampsia cases with training of medical personnel. The

reported maternal mortality ranges from 0.4% to 14% depending on the condition of women on admission and hospital facilities. Pritchard et al. reported only one maternal death (0.4% maternal mortality) among 245 women with eclampsia. Begum et al. had reported maternal mortality of 4.5% and 5.0% in loading and Pritchard regimens, respectively. They reported similar rates of recurrent convulsions 3.9% and 3.5% in both groups, ir.

Magnesium sulfate is the most commonly used medication in the USA for the treatment or prevention of seizure activity in patients with preeclampsia and eclampsia. It is superior to all other anticonvulsants in terms of controlling and preventing convulsions.

The two most widely used regimens are the continuous intravenous infusion, as recommended by Zuspan and the combined intramuscular and intravenous regimen, described by Pritchard et al [2]. Because of the pain associated with intramuscular injections of magnesium, several investigators feel that use of MgSO4 should be limited solely to the intravenous route. However, Sibai et al. claimed that although the intramuscular regimen is more painful, it seems to achieve therapeutic concentrations more rapidly. As both intramuscular and intravenous methods have been used successfully, there is little difference in success rates to distinguish between these routes [3]. In our study we used the combined intravenous and intramuscular route.

The relevance of our study lies in the fact that MgSO4 is not an innocuous drug. It is necessary to monitor the patients who are receiving the medication to prevent serious side-effects. It is recommended that frequent monitoring (every 5-10 min) should be undertaken during the first 2hrs of therapy when the intravenous regimen is being used. Whether the number of patients are high in relation to attending doctors, frequent monitoring is sometimes difficult. Considering this, Intramuscular maintenance therapy appears to be most suitable.

Although MgSO4 is a potent anticonvulsant, in many occasions convulsion recurs. The result of the Collaborative Eclampsia Trial shows recurrent convulsion rate 13.2% (60/453) and 5.7% (22/388) in two controlled trials. Our experience shows that the recurrent convulsion is not much higher in our population.

Puapradit et al. found that mean serum magnesium levels were significantly lower in women having a weight >70 kg than the level observed in patients with a body weight <70 kg [10]. After a loading dose, the drug is distributed throughout the body especially in skeletal tissue and only a small amount is left in the extracellular fluid. Since lighter patients have a lower total body volume the drug concentration is accordingly higher in serum during treatment with a maintenance regime. Indian women are lighter with the mean body weight of pre pregnant women being 39-41kg and that of pregnant women is only 53 kg. This may explain the low rates of recurrent convulsion during MgSO4 therapy. Pritchard and co-workers described repeated recurrent convulsions in two women having prepregnancy weights of 130 and 180 kg, respectively.

Sibai and Ramanthan found that about 10% of eclamptics experience a further convulsion after receiving a loading dose of MgSO4 [11]. In present study the recurrent convulsion rates were Only 6% & 8% in the study (Preeclampsia) and control group. In Eclampsia group it was 20% & 8% respectively. After the statistical analysis (Applying Chi-Square Test), there is no significant difference in the rate of recurrence of convulsions in between these two groups. However recurrence rate does not vary whether the maintenance regimen is continued or not, then omission of further painful intramuscular injections will reduce the risks associated with magnesium administration and will increase

patients' compliance.

In our series, maternal mortality was 7% in study group (eclampsia) and 4% in control group. The Eclampsia Trial Collaborative Group showed a reduction in the risk of recurrent seizures of 52% and 62% with MgSO₄ compared with diazepam and phenytoin. But the reduction of seizure rates did not affect maternal mortality rates. Magnesium sulfate was associated with a significant reduction in the number of seizures without any effect on maternal mortality or morbidity. As eclampsia is a multiorgan disorder, mortality depends on the severity of the organ damage. In this series mortality was a bit higher in the control group. So loading or maintenance schedule probably had no effect on mortality.

Desai et al. has reported perinatal mortality of 33.8% with Pritchard regimen [12]. In our study we found highest perinatal mortality (32%) in Pritchard regimen followed by in loading dose (25%) in severe preeclampsia and 30% in eclampsia. Sardesai reported similar (25%) perinatal mortality in both Pritchard and low dose regimen [13]. Therefore, MgSO₄ can greatly reduce maternal morbidity and mortality due to eclampsia but close monitoring is required during labor and postpartum period to prevent complications.

Mean serum Mg level were studied and it was observed that Serum Mg level before giving Magsulf (mean 1.5 mEq/ltr) were well below the therapeutic level of Mg required for control of convulsion. The mean serum Mg level remain in the range of 4.1 to 4.7 mEq/ltr during loading dose Magsulf regime (after 12 hrs). These levels were well below the level required to produce Mg toxicity thus loading dose was found to be safe regarding the risk of hypermagnesemia.

CONCLUSION

The present study was conducted in department of Obst. & Gynae.

Calcutta National Medical College & Hospital from March 2018 to Feb 2019. A total number of 100 patients were taken in the study, out of which 50 were cases of severe preeclampsia and eclampsia and 50 were of control group.

In Study group loading dose Magsulf (14 gm) given by IV & IM route and in control group full loading and maintenance dose (IV & IM both) continued for 24 hrs.

We followed up the patients for recurrence of convulsions. Summary of the study given below-

- Maximum number of patients belong to less than 25 yrs of age (around 80%) and belonging to low SES (monthly family income < 2500/month).
- Maximum number of patients were primigravida and unbooked (i.e. no antenatal visits previously)
- Most of the patients present with BP > 160/110 mm of Hg with proteinuria > 2+ with certain features of severity, like headache/ low platelet count/ Hellp syndrome/ episodes of convulsions with gestational age of 33-36 weeks (around 80%)
- Maximum number of patients received the treatment after ther,,
- onset of first fit within 12 hrs (90-95%) with termination of pregnancy with 12-18 hrs (90%).
- Most of the patients delivered vaginally both by aided and unaided methods.
- Perinatal & Maternal outcome is better in study group as compared to control group as there was one maternal mortality in study groups.
- After the statistical analysis (Applying Chi-Square Test), there is no significant difference in the rate of recurrence of convulsions in between the two groups.
- Mean serum Mg level in the study group were well below the therapeutic level (mean value 4.4 mEq/ltr) after giving

loading dose of Magsulf.

- Our study suggested that loading dose of Magsulf is as effective as standard regime in controlling seizures in eclampsia and preventing the seizures in severe preeclampsia. The recurrent seizures rate were almost the same in both the group.
- Loading dose of Magsulf can lessen the cost of measuring the laboratory value of Serum Mg level (as Mg level has narrow therapeutic range) & also the painful IM injections making it quite a suitable drug for management of eclampsia and severe preeclampsia.

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