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Original Research Article

Comparison of low dose Dhaka regimen of magnesium sulphate with standard pritchard regimen in eclampsia

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ABSTRACT

Background: The purpose of this study was to determine the effects of altitude on severe preeclampsia and eclampsia and subsequent perinatal outcome.
Methods: This prospective study was carried out during 1st March 2011 to 29th February 2012 in Department of Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla situated at a height of 2200m from sea level. All the subjects with severe preeclampsia or eclampsia were included in the study and their perinatal outcome was noted.
Results: There were a total of 5897 deliveries. There were 423 cases of PIH making an incidence of severe preeclampsia and eclampsia 15.4% and 7.3% among PIH, respectively. Majority of cases (60.4%) belonged to age group 18-25 year with mean systolic blood pressure in eclampsia was 184.3±18.6 mm of Hg and in severe preeclampsia was 171.5±13.9 mm of Hg. Mean diastolic blood pressure was 125.8±12.6 mm of Hg in eclampsia and 118.6±4.3 mm of Hg in severe preeclampsia. Various other complications in eclampsia and severe preeclampsia cases included IUGR (35.1%) cases, abruptio placentae (15.9%), HELLP syndrome (9.6%) cases, spontaneous preterm labour (21.3%) and intrauterine death (6.4%). Live births were 85.1%; fresh still births were 8.5%. Mean birth weight was 2192.5±572grams. Respiratory distress syndrome was seen in 21.3% neonates, Hyperbilirubinemia was seen in 26.2% neonates intracranial bleeding was seen in 7.5% neonates. Perinatal mortality was 27.7% which constitute14.9% still birth neonatal deaths.
Conclusions: Efficacy of MgSO4 in prevention and treatment of eclamptic convulsions is time tested and supported with a variety of studies. Since its narrow therapeutic and toxicity is major concern, the use of low dose MgSO4 protocols is a viable alternative to standard dose therapy. However, because of small study design further studies on the larger scale are required to support routine clinical use of low dose protocols.

Keywords: Eclampsia, Magnesium sulphate, Preeclampsia

INTRODUCTION

Hypertensive disorders are considered as one of the important cause of maternal and fetal morbidity and mortality. It is estimated that every year eclampsia is associated with 50,000 deaths worldwide.[1] Management of pre-eclampsia and eclampsia continues to pose a challenge. The only definitive cure is termination of pregnancy. Standard practice is to use anticonvulsants to control immediate fits and prevent further seizures, but choice of anticonvulsants is controversial. Magnesium sulphate has become more popular after collaborative

eclampsia trial which provided a strong evidence of significantly lower recurrence rate of seizures and reduced maternal and perinatal mortality compared to diazepam and phenytoin.[2] Efficacy of magnesium sulphate in severe preeclampsia and eclampsia is time tested and supported with variety of studies. However, its narrow therapeutic index, toxicity and side effects are major concern in clinical use. Magnesium sulphate toxicity is extremely rare with correct preparation of the infused magnesium solution and diligent clinical monitoring. Study conducted by various authors (Seth S et al[3], Chaudhary JR et al[4] and Bhattacharya N et al[5]) had shown prolonged labour, increased caesarean rate and increased postpartum hemorrhage.

Various efforts have made to determine the effectiveness of low dose regimens in controlling seizures along with maternal and fetal outcome. Efficacy of Ultra short regimen (4 grams magnesium sulphate intravenously and 10 grams intramuscularly as the sole anticonvulsant agent) was used in a study conducted by Ekele BA et al and was effective in controlling fits in 92.6% of cases in the study group.[6] Another study conducted by JR Chaudhary et al showed no significant difference in recurrence of convulsion, maternal mortality, serious maternal morbidity, perinatal morbidity or mortality between the low dose i.v regimen of magnesium sulphate infusion (0.6 gm/h) and standard pritchard regimen.[4] Using low dose regimens will not only decrease the risk of maternal toxicity and fetal side effects but also decrease the cost of therapy and increase its safety for rural low resources setting where magnesium sulphate level monitoring is not readily available.[6]

A low dose magnesium sulphate may be more appropriate in cases of mild renal impairment which is usually present in these patients. A study conducted by MR begum et al had explained that the low BMI of the women in Dhaka explains the efficacy of low dose regimen in controlling fits.[7] In view of the benefits of low dose of magnesium sulphate, a study was proposed in Kamla Nehru State Hospital for Mother and Child, Indira Gandhi medical college, Shimla in which low dose Dhaka regimen was compared with standard Pritchard regimen for eclampsia.

METHODS

This prospective interventional study was carried out in Department of Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla during 1st March 2011 to 29th February 2012. All subjects with eclampsia were included in the study. Subjects who had been given any other anticonvulsant like diazepam or phenytoin or conditions where magnesium sulphate therapy like renal failure (severe oliguria or anuria), disseminated intravascular coagulation or shock, were excluded. Eclampsia is defined as the development of convulsions and/or unexplained coma during pregnancy or postpartum in subjects with signs and symptoms of pre-eclampsia.[9]

Subjects with eclampsia were admitted in the labour room and initial supportive treatment was given. Once the subject was stabilized, a thorough but quick general physical, abdominal and vaginal examination was made. Investigations were carried out as per standard protocol. Anti-hypertensive was given if systolic blood pressure was >160 mm Hg or diastolic blood pressure ≥110mm of Hg. Magnesium sulphate was given as an anticonvulsant. Either of the following two regimens of magnesium sulphate was followed.

Pritchard regimen

It includes loading dose of 4 grams intravenous (in 20% solution) in 10-15 minutes slow infusion with 5 grams intramuscular (in 50% solution) in each buttock and maintenance dose of 5 grams intramuscular in alternate buttock 4 hourly for 24 hours after last fit or delivery, whichever is later. In case of repeat fits, 2 grams intravenous as 20% solution is given as i.v bolus.

Dhaka regimen

It comprises a loading dose of 4 grams intravenous slow infusion with 3 grams intramuscular in each buttock along with maintenance dose of 2.5 grams intramuscular in alternate buttock every 4 hours for 24 hours after last fit or delivery, whichever is later. In case of repeat fits, 2 grams intravenous as 20% solution is given. Subjects were divided in two groups. Computer generated random number table was used to allocate regimen to the subjects. Informed consent was taken. Patients consent was taken from the relatives accompanying the patient.

Magnesium sulphate toxicity was defined by the clinical signs which include urine output <100mL in 4 hours, absent patellar reflexes, respiratory depression.

Subjects were observed for recurrence of fits and monitored for magnesium sulphate toxicity. Subjects were monitored every 30 minutes for pulse, blood pressure, respiratory rate and deep tendon reflexes. Urinary output was noted hourly. In case of absence of deep tendon reflex or respiratory rate < 16/min or urinary output <100ml in previous four hours, magnesium sulphate therapy was discontinued. After stabilization of subjects, labour was induced or augmented and managed partographically. Mode of delivery was noted. Maternal and fetal outcome was recorded.

RESULTS

There were 31 cases of eclampsia. Two subjects died immediately after reporting to the hospital before any treatment could be given and hence were not included in the studies. During study period there were a total of

5897 deliveries. Incidence of eclampsia was 0.53% of total deliveries.

Table 1: Demographic parameters.

Parameter	%
Age (year)	
<18	9.7%
18-25	64.5%
26-30	19.4%
>30	6.4%
Booked	17.2%
Unbooked	82.8%
Parity	
Primigravidae	71%
Multipara	29%
Socioeconomic status	
I-II	16.1%
III-V	83.9%
Past history HTN	
YES	29%
NO	71%
Family HTN	
Yes	90.3%
No	09.7%
Type of eclampsia	
Antepartum	61.3%
Intrapartum	35.5%
Postpartum	03.2%
BP recording	
Systolic	
<160	31.0
160-180	20.7
>180-200	44.8
>200	03.5
Diastolic	
<90	0
90-110	10.3
>/110	89.7
Complications	
IUGR	35.5%
Abruptio placenta	29%
IUD	12.8%
HELLP	22.6%

There were 423 cases of PIH (gestational hypertension, preeclampsia and eclampsia) making an incidence of eclampsia 7.3% among PIH. The demographic profile of the women is summarised in Table 1. Most of the women belonged to 18-25 years, unbooked, primigravidae, with low socioeconomic status and had antepartum eclampsia.

There was no magnesium sulphate toxicity in 76.1% cases on Pritchard regimen and 93.7% cases on Dhaka regimen. The difference was statistically significant (p=0.05).

Deep tendon reflexes were found to be absent in 17.4% cases on Pritchard regimen and 6.3% cases on Dhaka regimen. The difference was statistically significant (p=0.01). Oliguria was present only in 3 (6.7%) cases with Pritchard regimen. None of the cases with Dhaka regimen developed oliguria. However, the statistical significance could not be determined as the sample size was very small. None of the cases of eclampsia developed respiratory depression with either of the regimen. Recurrence of fits was significantly more with Dhaka regimen. However, atonic postpartum haemorrhage was higher with Pritchard regimen. There was no difference in duration of labour with either of regimen.

Table 2: Maternal outcome.

Parameters	Pritchard regimen (%)	Dhaka regimen (%)	P-value
No toxicity	76.1	93.7	0.05
Absent DTRS	17.4	6.3	0.01
Oliguria*	6.7	0	
Respiratory depression**	0	0	
Recurrence of fit	6.7	21.4	<0.0001
Mode of delivery			
Normal	71.1	58.3	0.04
Instrumental	17.4	12.5	0.31
LSCS	10.9	29.2	0.001
Duration of labour (>12 h)***	58.7	62.5	0.56
Atonic PPH****	13	6.2	0.04

DTRS= Deep Tendon Reflexes, LSCS= Lower Segment Caesarean Section; * Urine output >100ml/ 4hours which was refractory to fluid challenge; **Respiratory rate <12/min; *** From onset of labour pains till delivery; **** Blood loss >500ml in normal delivery and >1000 ml in caesarean section.

Table 3: Fetal outcome.

Parameters	Pritchard regimen (%)	Dhaka regimen (%)	P-value
Live births	80.5	89.6	0.04
Fresh still births	15.2	2.1	<0.0001
Early neonates death	13	12.5	>0.9
Perinatal mortality	32.6	22.9	0.83
Apgar <7 at 1 min	27	16.3	0.04
Apgar <7 at 5 min	29.7	16.3	0.01
Complication in neonates			
No complication	54.1	55.8	0.88
Severe birth asphyxia	13.5	13.9	0.9
Respiratory distress syndrome	8.1	6.9	0.78

Intracranial bleed	10.8	4.6	0.11
Sepsis	5.4	6.9	0.66
Hyperbilirubinemia	24.3	27.9	0.15

Fresh still birth was significantly higher and Apgar at 1 and 5 minutes was significantly lower with Pritchard regimen. Early neonatal death and perinatal mortality was also higher with Pritchard regimen compared to Dhaka regimen but the difference was not statistically significant. Neonatal complications were comparable in both the groups.

In the present study, 2 out of 31 eclampsia cases died immediately after admission before any anticonvulsant could be given. However, there was no mortality among either of treatment group.

DISCUSSION

Hypertensive disorders are important cause of maternal and fetal morbidity and mortality. It is the most common medical complication of pregnancy and can occur at any time during the second half of pregnancy or the first few weeks after delivery. Unlike preeclampsia, eclampsia can be considered as a preventable condition. Magnesium sulfate (MgSO4) is the first choice for the prevention and the treatment of eclampsia. Despite its efficacy, narrow therapeutic index is a concern related with its toxicity. Recently, low dose MgSO4 regimens were reported to decrease the side effects without significant decrease in therapeutic benefit.

In the present study as well as in the study conducted by Begum R et al and Seth S et al absent deep tendon reflexes were more among those on Pritchard regimen as compared to Dhaka regimen.[3,9] The study conducted by Chaudhary JR et al showed that loss of deep tendon reflexes and oliguria was seen in only 3.2% with the standard regimen which was less as compared to the present study.[4] In all the above mentioned studies as well as in the present study none of cases developed respiratory depression suggesting that magnesium sulphate toxicity was not severe with either of the regimens. Atonic PPH was significantly more with Pritchard regimen as compared to Dhaka regime in the present study Due to its induction of vasodilation and effects on the blood like red cell deformity, platelet activity inhibition and a prolonged bleeding time, there is a correlation between magnesium sulphate therapy and PPH is suspected.[10] Similar results were obtained in the study conducted by Seth S et al and Bhattacharjee N.[3,5]

In the present study, recurrence of fits was significantly less with Pritchard regimen (6.7%) as compared to Dhaka regimen (21.4%). However, in none of the cases recurrence of fits observed for more than once. Mean duration of recurrence of fit was 6.5 hours. The overall rate of recurrence was less in the study conducted by Begum R et al and Begum MR et al.[7,9] This may be because of the fact that both these studies were done in Bangladesh and women in Bangladesh are lean as a result of which serum therapeutic concentration of magnesium sulphate is achieved with low dose in majority of cases. In the present study, significantly more patients on Dhaka regimen (29.2%) underwent caesarean section as compared to Pritchard regimen (10.9%) which was comparable to the study conducted by Shikha Seth et al.[3]

Various studies have shown that magnesium sulphate prolongs the duration of labour. However, in our study the difference was not significant between the two regimens in the present study.

The increased association of higher blood levels of magnesium with increased still birth, early neonatal death, birth asphyxia, bradycardia, hypotonia, gastrointestinal hypomotility is a major concern. In present study, fresh still birth was significantly higher with Pritchard regimen compared to those on Dhaka regimen. Early neonatal death and perinatal mortality was higher with Pritchard regimen however, difference was not significant. The results are in collaboration with study conducted by Seth S et al, Chaudhary JR et al and Bhattacharjee N.[3-5] Apgar was significantly less at 1 and 5 minutes with Prichard regimen as compared to those who were given Dhaka regimen. Similar results were observed in the study conducted by Seth S et al, 88.9% of those on standard regimen and 53.3% of those on low dose regimen had Apgar less than 5 in 1 minute.[3] The number of cases with low Apgar at 1 and 5 minutes is higher in above mentioned studies as compared to present study. This may be due to better fetal monitoring during intrapartum period, expedite delivery and better neonatal resuscitation in the tertiary care institute of the state. Alternatively, effects of magnesium sulfate on control of eclamptic convulsions may be wholly or partially, through its role as a blocker of N-methyl-D-aspartate (NMDA) receptors in the brain. These NMDA receptors are activated in response to asphyxia, leading to calcium influx in the neurons, which causes cell injury.[11] Similar results were obtained in the study conducted by Das M et al who used Bankura regimen (low dose regimen with 3g i.v and 2.5g in each buttock and 2.5g in alternate buttock every 4 hourly) and observed lower incidence of low Apgar scores, hypotonia, intubation in the delivery room, admission to NICU along with decreased perinatal mortality.

In the study conducted by Begum MR et al, Seth S et al and Chaudhary JR et al mortality with standard regimen was higher (5.02%, 7.7% and 5% respectively) than those on low dose regimen (0%,4.45% and 3.3%, respectively).[3-5] However, In our study, there was no mortality among those cases that were treated with either of the regimen.

CONCLUSION

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. The concept of low dose in the form of Dhaka regimen was adopted principally in the Bangladesh. Because of the small size of Bangladeshi women and concerns about toxicity in circumstances in which measuring serum levels of magnesium would be difficult. From the results of the present study and the foregoing review, there is compelling evidence of the safety and effectiveness of low dose regimen of magnesium sulphate as compared to standard Pritchard regimen. The low-dose regimen was based on the concept that the average women of Himachal Pradesh also have a low BMI, as compared with women in several other parts of the country and the world. Associated with similar efficacy in controlling convulsions and potentially more favorable toxicity and complication rates and better perinatal outcome the use of low dose MgSO4 protocols is a viable alternative to standard dose therapy. However, because of small study design further studies on the larger scale are required to support routine clinical use of low dose protocols.

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