Original Article

Magnesium Sulphate Therapy in Pre-Eclampsia and Eclampsia: One Year Experience

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ABSTRACT

Objective: To study the efficacy of Magnesium Sulphate Therapy for prevention and control of fits in patients with preeclampsia and eclampsia

Study Design: Interventional Study.

Place and Duration of Study: This Study was conducted at the Department of Obstetric and Gynecology Unit II, Mother and Child Health Centre, Pakistan Institute of Medical Sciences, Islamabad from April 2002 to March 2003.

Materials and Methods: Total 50 women with preeclampsia / imminent eclampsia and eclampsia fulfilling the study criteria were admitted in HDA, adjacent to labour ward. Magnesium Sulphate therapy started after complete evaluation of the patients according to the study protocol.Patients monitored carefully for any side effects of magnesium therapy and occurrence of convulsions. Primary outcome measures were development of eclampsia or recurrent seizures in patients with eclampsia, neonatal morbidity and mortality. **Secondary outcome measures** were serious maternal morbidity, magnesium toxicity and other side effects of $MgSO_4$ and complications of labour and delivery.

Results: Total 50 women were entered into the study over a period of one year. Out of these 12 (24%) women presented with eclampsia, 5 (10%) had imminent eclampsia and 33 (66%) were diagnosed as pre-eclampsia. Of the 12 women with eclampsia, none had recurrent seizures. Out of 38 women with pre-eclampsia and imminent eclampsia, only one (2%) woman developed eclampsia.There was no case of magnesium toxicity. Overall 12 (24%) of the babies were delivered with poor Apgar score. Two babies were expired within five minutes of delivery while 5 babies expired in NICU. There were 6 intrauterine deaths and 4 intrapartum deaths.

Conclusion: Magnesium sulphate is an effective anticonvulsant for the treatment and prevention of eclampsia when used judiciously. In the dosage used it does not have any substantive harmful effects on women and their babies.

Key Words: Eclampsia, Magnesium Sulphate, Convulsions.

INTRODUCTION

Pre-eclampsia/eclampsia is an unpredictable multiorgan disorder unique to human pregnancy. The international society for the study of hypertension in pregnancy (ISSHP) currently defines PE as the occurrence of hypertension in combination with proteinuria, developing after 20 weeks gestation in a previously normotensive, non-proteinuric patient.[1] PE is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. It complicates around 2-8% of pregnancies.[2-4] Although outcome is often good PE is a major cause of maternal and fetal morbidity and mortality worldwide[5] and it accounts for around 16% of maternal deaths in UK (mortality rate 0.9/100,000 maternities).[6] Mortality from hypertensive disorders is much higher in developing countries reaching rates of 70-120/100,000 maternities.[6] The risk of eclampsia in women with severe PE appears to be 1-2%.[6]

Currently eclampsia is defined as "the occurrence of generalized convulsion(s) associated with signs of PE during pregnancy, labor, or within 7 days of delivery and not caused by epilepsy or other convulsive disorders." Of seizures 44% occur postnatally, the remainder being antepartum (38%) or intrapartum (18%).[6] Almost without exception, PE precedes the onset of eclamptic convulsions.

In developed countries eclampsia is rare, affecting around 1 in 2000 deliveries,[7] while in developing countries estimates vary from 1 in 100 to 1 in 1700.[8-11] In Pakistan, an analysis of 644 maternal deaths in hospital of four provinces showed hypertensive disease, mostly eclampsia, to be the second most common cause (18.6%) preceded only by hemorrhage (21%).[12] Worldwide cerebral infarction and haemorrhage is the principal cause of death[13,14] although in the UK pulmonary complications have now superseded cerebral causes.[6]

Although hypertension is a requisite to diagnosing PE it may not be central to the pathogenesis of PE. Thus eclampsia is not prevented simply by adequate BP control.[15] The main objectives[1] in the management of PE are prevention of convulsions, complications such as pulmonary edema, renal failure, cardiovascular accidents and abruptio placentae and delivery of a healthy neonate with minimal maternal morbidity. So Anticonvulsants are important in the management of PE and eclampsia in addition to antihypertensive therapy.

For well over half a century, magnesium sulfate ($MgSO_4$) has been advocated for seizure prophylaxis in PE and eclampsia, yet its use remained controversial.[16]

Although MgSO4 is being used effectively worldwide, it is not being used in most of the obstetric units of our country for eclampsia and pre eclampsia. The burden of this disease, however, occurs in poor countries and majority of significant morbidity and mortality associated with the disease also occur in these countries. It is therefore more important for developing countries like ours' to establish whether the benefits of administering MgSO4 to all women with PE and eclampsia outweigh the risk. The purpose of this study is to know the safety and efficacy of MgSO4 in reducing the risk of eclampsia or to arrest the recurrent seizures in eclampsia.

MATERIALS AND METHODS

This single centre based interventional study was conducted over a period of one year from April 2002 to March 2003, at department of Obstetric and Gynecology Unit II, Mother and Child Health Centre, Pakistan Institute of Medical Sciences, Islamabad, a postgraduate teaching institution that provides tertiary level care. Fifty women with severe pre-eclampsia and eclampsia who received $MgSO_4$ Therapy fulfilling the study inclusion criteria were studied.

Women with severe pre-eclampsia where decision for delivery had been made, Imminent eclampsia (e.g. aura, headache, nausea, vomiting, epigastric pain, visual disturbances) and women with eclampsia were included in the study. The criteria for severe pre-eclampsia included:

- Diastolic BP $\geq$ 110 mm Hg on two occasions at least 6 hours apart
- Significant protienuria (> ++)

Women with mild hypertension, and other neurological disorders causing convulsions were excluded from the study. All women with severe pre-eclampsia and eclampsia were admitted in high dependency area (HDA) adjoining the labour ward. Before starting magnesium sulphate therapy, it was confirmed that the knee jerk or other tendon reflexes were present, the respiratory rate was normal (> 16 resp/min), and urine output was 100ml or more during last 4 hours, or greater than 30ml/h. Magnesium sulphate therapy then started.

Loading dose: 4gm of $MgSO_4$ (8ml of 50% solution) given i.v slowly over 10-15 minutes followed immediately by 6gm i.m given as 3gm (6ml of 50% solution) in the upper and outer quadrant of each buttock.

Maintenance therapy: 2.5gm (5ml of 50% solution) given deep intramuscular every 4 hours in the alternate buttocks.

Clinical monitoring of the women continued throughout the treatment with particular attention to BP levels, urine output and development of symptoms. Once stabilized, women not in labour either had their labour induced or were delivered by caesarean section where indicated. $MgSO_4$ therapy was continued until 24hours after delivery or last convulsion whichever was later. Therapy stopped early if there were any side effects or urine output dropped below 30 ml/hour because of the risk of toxicity.

Primary outcome measures were development of eclampsia or recurrent seizures in patients with eclampsia, neonatal morbidity (poor apgar score, intubation at place of delivery, and admission to neonatal intensive care unit (NICU) and neonatal mortality.

Secondary outcome measures were serious maternal morbidity (respiratory depression, respiratory arrest, cardiac arrest, coagulopathy, renal failure, liver failure, pulmonary oedema, and cerebral haemorrhage), magnesium toxicity (need for calcium gluconate, stopped or reduced treatment due to side effects or toxicity), and other side effects of $MgSO_4$ (nausea, vomiting, flushing of skin, drowsiness, abscess), and complications of labour and delivery (caesarean section, retained placenta, blood loss and transfusion).

Women were retained in HDA until the completion of $MgSO_4$ therapy and then shifted to postnatal ward. Follow up of women and their babies was until discharge from hospital. The data of all women was recorded on a predesigned Performa which was filled at the time of discharge. Data was entered and analyzed on SPSS. As this was a descriptive study, data are expressed as frequencies, mean with standard deviation and median with range.

RESULTS

Total 50 women were entered into the study over a period of one year. Out of these 12 (24%) women presented with eclampsia, 5 (10%) had imminent eclampsia and 33 (66%) were diagnosed as pre-eclampsia. 40% of these patients were booked and 60% were non-booked.

Table No.1:Maternal Demographic Indicators(n=50)

Variable	Mean	Range	S.D
Age (years)	26.3	18-40	4.3
Gestation (weeks)	34.1	26.6-41	3.8
Hospital stay (days)	6.8	2-15	3.2

Table No.2: Maternal Complications

Complication	Number	Percentage
Eclampsia	1	2%
HELLP Syndrome	2	4%
Low platelet count	2	4%
Impaired renal function	2	4%
PPH	2	6%
Need for transfusion	4	8%
Hypotension	1	2%

The characteristics of the study population are shown in Table 1. The maternal demographics show that mean age was 26.3 years (SD=4.3 years). The mean

gestational age at admission was 34 weeks and 1 day (range 26.6-41 weeks). The mean number of days spent by the women in the hospital were 6.8 days (SD of 3.2 days). Primigravidae comprised the bulk of the group (54%) followed by multigravidae (34%) and grandmultigravidae (12%)

Table No.3: Side Effects of Magnesium Sulphate Therapy (n=6)

Side effect	Number
Respiratory depression	1
Absent tendon reflexes	3
Pain at injection site	2

Table No.4: Neonatal Outcomes (n=50)

	Number	Percentage
Live born	**40**	**80%**
a) NICU admission	**13**	**26%**
- prematurity	6	
- prematurity+IUGR	2	
- IUGR	2	
- Neonatal sepsis	3	
b) Neonatal mortality	**7**	**14%**
- prematurity	5	
- prematurity+IUGR	2	
Still born	**10**	**20%**
a) IUD	**6**	**12%**
b) Intrapartum deaths	**4**	**8%**
- prematurity	2	
- prematurity+IUGR	2	

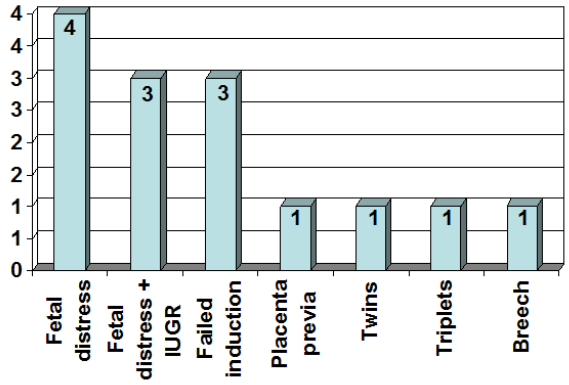

Figure No.1: Indications For LSCS (n=14)
EL=3 EM=11

The major maternal complications that occurred in women receiving magnesium sulphate are shown in Table 2. Of the 12 women with eclampsia who received magnesium sulphate therapy none had recurrent seizures. Out of 38 women with pre-eclampsia and imminent eclampsia, only one (2%) woman developed eclampsia after receiving magnesium sulphate therapy. At admission 2 women were diagnosed to have HELLP syndrome. Low platelet count and impaired renal functions were present in 2 women each. 72% of the patients delivered vaginally and 28% women had caesarean section. The various indications for caesarean section are shown in Figure 1.

Mean duration of magnesium sulphate therapy was 29.2 hours (SD 12.3 hours). Side effects of magnesium were observed in 6 (12%) of the patients (Table 3). There was no case of magnesium toxicity. In 2 women the magnesium sulphate was discontinued due to prolonged therapy and oliguria.

9 (18%) of the women were diagnosed to have IUGR. The mean birth weight was 1700 g (SD 700g). The mean Apgar score at 1 and 5 minutes was 4.7 and 6.6 respectively. Overall 12 (24%) of the babies were delivered with poor Apgar score and needed intubation at the place of delivery. Neonatal outcomes are shown in table 4. 13 (26%) of the babies were admitted to NICU. The main reasons for admission were prematurity and IUGR. Two babies were expired within five minutes of delivery while 5 babies expired in NICU with severe hyaline membrane disease and sepsis related complications being the most common problems. In all of these neonatal deaths the fetal birth weight was less than 1500 grams. There were 6 intrauterine deaths and 4 intrapartum deaths. All of these deaths occurred between birth weight of 900 and 1200 grams and no operative interventions were done on fetal grounds due to extremely high mortality in infants weighing less than 1500 grams in our nursery.

DISCUSSION

Every minute, a woman dies in pregnancy or child birth, and 99 out of every 100 of these women live in developing countries.[17] Among deaths from causes other than abortion which are directly attributable to the complications of pregnancy, about quarter are associated with pre-eclampsia / eclampsia. As the aetiology of the syndrome has remained obscure, many different approaches have been used to prevent and manage it. One of these—magnesium sulphate as an anticonvulsant—was introduced to obstetric practice in the USA almost a century ago. However, the drug was mainly used in USA until recently. One reason that magnesium sulphate did not initially gain universal acceptance was the lack of reliable empirical evidence of its effects from controlled trials. While another reason was that some critics maintained that no theory existed to explain how magnesium sulphate could be helpful in eclampsia.

The women in this study represented a high risk group. They presented at early gestational age (mean 34 weeks) with high blood pressure values, often suffering from headache. Most of these pregnancies were terminated for maternal reasons or due to intrauterine deaths. This study shows that magnesium sulphate in the dosage used is effective in treatment of eclamptic convulsions and it considerably reduces the risk of

eclampsia in women with severe pre-eclampsia. However the routine use of magnesium sulphate in all cases of pre-eclampsia is not justified as the incidence of eclampsia is likely to be lower in milder cases than those with a severe disease.[18]

The most significant randomized clinical trial on the subject of anticonvulsants in eclampsia was the Collaborative Eclampsia Trial.[19] The study concluded that there was compelling evidence in favour of magnesium sulphate rather than phenytoin or diazepam for the treatment of eclampsia. Chein et al[20] carried out an over view of the evidence from randomized trials of magnesium sulphate in the treatment of eclampsia and pre-eclampsia and concluded that there was strong support for the use of magnesium sulphate in preventing recurrent seizures in eclampsia. Duley and Johanson[21] also agreed with this view.

Lucas et al[22] conducted a prospective study comparing magnesium sulphate to phenytoin in the prevention of eclampsia. In their study no woman receiving magnesium sulphate developed eclampsia, while 10 women randomized to the phenytoin group had convulsions. A systematic review[23] of evidence from controlled trials involving women with pre-eclampsia showed that magnesium sulphate was the most promising among the alternative anticonvulsants studied. The Magpie Trial[24], which involved 10141 women with pre-eclampsia and their carers in 175 hospitals in 33 countries, shows that magnesium sulphate reduces the risks of eclampsia among women with pre-eclampsia.

In patients with HELLP syndrome or deranged renal profile at admission no deterioration in renal functions or coagulation profile was found on subsequent investigations during magnesium sulphate therapy. Similar results were observed in The Magpie Trial.[24] Roberts[25] suggested that there are other beneficial effects of magnesium sulphate in addition to prevention of convulsions in pre-eclampsia.

The mean duration of magnesium sulphate therapy in this study was 29.2 hours. One of the concerns about magnesium sulphate has been the risk of respiratory depression. In our study only one patient had respiratory depression while there was no case of magnesium toxicity or respiratory arrest. However problems at injection site were observed in 2 women. In one woman the i.m regimen was then stopped and maintenance i.v infusion of magnesium sulphate started at 1gm/hour. Absent tendon reflexes were observed in 3 women. These side effects were not life threatening and observed in few patients. It is of note that there were no adverse effects attributable to the use of magnesium sulphate in the Collaborative Eclampsia Trial.[19]

14 (28%) of the women had caesarean section. In Magpie Trial[24] there was 5% increase in the relative risk of caesarean section but this increase was related to other factors. One of the beliefs supporting the unevaluated use of magnesium sulphate over many decades has been that it improves the outcome for the child. Recent support for this belief has come from case control studies, suggesting that in-utero exposure to magnesium sulphate might reduce the risk of cerebral palsy for low birth weight (<1500grams) babies.[26,27] In our study out of 40 live born babies 16 had a birth weight less than 1500grams. Of these 16 babies only 7 expired later while 9 babies survived. There was no neonatal death in birth weight > 1500 grams. These findings indicate relatively good neonatal outcome in women with eclampsia and pre-eclampsia who received magnesium sulphate.

CONCLUSION

Magnesium sulphate is an effective anticonvulsant for the treatment and prevention of eclampsia when used judiciously. In the dosage used it does not have any substantive harmful effects on women and their babies. As it is an inexpensive drug, it is especially suitable for use in low income countries. Serum monitoring is not necessary. So consideration should be given to the administration of magnesium sulphate to all women with severe pre-eclampsia and eclampsia, together with adequate antihypertensive therapy and early delivery.

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