ORIGINAL ARTICLE

Role of magnesium sulphate in prevention of imminent eclampsia

Almas Tabassum, Salma Batool Naqvi

Abstract

Objective: To determine the efficacy and safety of magnesium Sulphate on maternal and fetal outcome in patients with imminent eclampsia.

Study design:Case Series Study

Setting: Department of Obstetrics and Gynaecology, Liaquat National Hospital and Medical College, Karachi, Pakistan.

Subject and Methods: All patients admitted with raised blood pressure > 110 mmHg diastolic and > 170 mmHg systolic beyond 20 weeks of gestation diagnosed as having pre-eclampsia were included in the study. Outcome measures included efficacy of magnesium Sulphate and side effects on mother and fetomaternal outcome.

Results: Study was done on 50 in patients with mean age 29 years. The majority were primigravida. Mean blood pressures was159.68/109.90 and mean respiratory rate 20/min. Magnesium Sulphate was used to prevent occurrence of fits in patients with imminent eclampsia. Only one patient had fit after administration of Magnesium Sulphate and one patient had oligourea. 39 patients had babies with APGAR score of more than 5. Adverse neonatal effects monitored were cyanosis 46%, RDS 30%, Jaundice 36%, Hypothermia 26%, Hypoglycemia 8%, Hypocalcaemia 2% and Fits 14%. There were 11 neonatal deaths (20%), 1 IUD (23%) and 1 FSB (2%).

Conclusion: In our study we determined the efficacy and safety of magnesium sulphate in patients with imminent eclampsia and fetomaternal outcome. These results support our hypothesis that there is an effect of magnesium sulphate in the prevention of fits in imminent eclamptic patients and better neonatal outcome.

Keywords: Magnesium Sulphate, Efficacy, Imminent Eclampsia

Department of Obstetrics and Gynaecology
Liaquat National Hospital and Medical College
Karachi – Pakistan
A Tabassum
SB Naqvi

Correspondence:
Dr. Salma Batool Naqvi
Consultant, Department of Obstetrics and Gynaecology, Liaquat National Hospital and Medical College, Karachi – Pakistan
Cell: 0321 2546769

Introduction:

Hypertensive disorders of pregnancy complicate 5-10% of pregnancies. These include "pregnancy-induced hypertension" if not a companied by proteinuria, pre-eclampsia if there is associated proteinuria, and as "eclampsia" if it leads to convulsion and/or coma. The other is chronic hypertension that precedes or coincides with pregnancy and, the combination of the two conditions may occur and is referred as "super imposed pre-eclampsia". These disorders are associated with maternal and fetal complications and have a substantial economic impact. There is a general consensus that anti-hypertensive agents should be given to patients with severe hypertension and this should be in the hospital. The value of antihypertensive drugs in pregnant women with mild hypertension continues to be an area of debate that the evidence is too scanty to securely evaluate the clinical benefits of treating mild hypertension during pregnancy. The choice of the antihypertensive agents depends on individual clinician preference, the specified maternal and foetal benefits and the reproductive complications (teratogenisity, fetotoxicity and neonatal toxicity) of each particular agent. There are unequivocal evidences that Magnesium sulphate is superior to other agents in re-

ducing recurrent eclamptic seizures. There is a strong recent evidence recommended that magnesium sulphate should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia.[1-2]

Imminent eclampsia is defined when diastolic Blood Pressure is more than 110 mm of Hg on two occasions and that with significant proteinuria (1 gram urine protein in 24 hours) with symptoms and signs of severe headache, visual disturbance, epigastric pain, signs of clonus, papilloedema, liver tenderness, platelet count falling to below $100X10^9$/L, Serum Glutamate Pyruvate Transaminase (SGPT) rising to above 50 IU/L.

Eclampsia refers to the occurrence of one or more generalized convulsions and/or coma in the setting of preeclampsia and in the absence of other neurologic conditions. The clinical manifestations appear anytime from the second trimester to the puerperium. Delivery of the fetus and placenta remains the only curative treatment. In the past, eclampsia was thought to be the end result of preeclampsia; however, it is now clear that seizures are only one of several clinical manifestation of severe preeclampsia. It is estimated that eclampsia accounts for 50,000 maternal deaths per year worldwide.

Eclampsia is most common in nonwhite, nulliparous women from lower socioeconomic backgrounds. Peak incidence is in the teenage years and low twenties, but there is also an increased incidence in women over 35 years of age. An eclamptic seizure occurs in 0.5 percent of mildly preeclamptic pregnancies and 2 percent of severe preeclamptics. The incidence of eclampsia is relatively stable at 4 to 5 cases per 10,000 live births in developed countries. In developing countries, however, the incidence varies widely from 6 to 100 per 10,000 live births. Approximately one-half of all cases of eclampsia occur prior to term, with more than one-fifth occurring before 31 weeks of gestation. Just over one-third of cases occur at term, developing intrapartum or within 48 hours of delivery. Late postpartum eclampsia (ie, eclamptic seizures developing greater than 48 hours but less than four weeks postpartum) accounts for the remainder (13 to 16 percent) and represents as many as one-quarter of all postpartum cases.[3-5]

Risk factors include pregestational diabetes, vascular or connective tissue disease, nephropathy, Antiphospholipid antibody syndrome, obesity, positive family history, African American race and socioeconomic status.[6-9]

Eclampsia results from cerebral vasospasm and resulting in ischemia. Pathological deterioration of organs and systems due to vasospasm and ischemia is seen in severe preclamsia and eclampsia.[10]

Magnesium Sulphate has cerebral vasodilator effect thus decreasing the ischemia by decreasing cerebral vasospasm making it a treatment of choice in eclampsia.[11] Magnesium Sulphate is now routinely used in obstetric practice as seizure prophylaxis in women with preeclampsia and is proved to be efficacious in reduction of seizure in women with eclampsia and severe preeclampsia.[2] However despite the years of use and provider familiarity the use of Magnesium Sulphate can occasionally result in accidental overdose and patient harm. Therefore vigilance is required regarding the administration and monitoring of women who require treatment with the drug.[12]

The aim of the study was to determine the role of Magnesium Sulphate in managing hypertensive disorders of pregnancy and to see how helpful this management option would be in reducing maternal morbidity and mortality and neonatal outcome.

Methodology:

Case series study was conducted in gynaecology and obstetrics unit at Liaquat National Hospital Karachi from 17th January 2007 to 17th January 2008. The inclusion criteria for this study was patient with imminent eclampsia diagnosed on the bases of diastolic blood pressure of > 110 mmHg on two occasion or systolic blood pressure > 170 mmHg on two occasion. Patients

with significant proteinuria (1 gram protein in 24 hours) with symptoms & sings of sever headache, visual disturbance, epigestric pain signs of clonus, papilloedema, liver tenderness, platelet count falling to below 100 x 10^9 / L. Serum Glutamate Pyruvate Transaminase (SGPT) rising to above 50 IU/L. Patients with chronic renal disease and cardio-respiratory disorders and known sensitivity to Magnesium Sulphate were excluded.

Magnesium Sulphate used to prevent occurrence of fits in patients with imminent eclampsia.

Study was carried out to determine the efficacy of magnesium Sulphate in prevention of progression of fits in imminent eclampsia, its safety with regards to respiratory depression, oligourea and loss of deep tendon reflexes, fetal outcome for alive or dead, Apgar score in 1 & 5 minutes and birth weight, maternal outcome for general conditions, consciousness, pulse, blood pressure, respiratory rate and recurrent fits.

Dosage used was by Pritchard regimen 4 gm diluted in 12ml of Distilled water infused slowly in 10-15 minutes as a loading dose, followed by a maintenance dose of 1-2 gm/hour at the rate of 60 micro-drops / minute through the infusion pump and continued upto 24 hours after delivery.

The Data was collected from admitted patients having acute rise in diastolic blood pressure > 110 mmHg and systolic blood pressure of 170 > mmHg meeting the other inclusion criteria.

Informed consent was taken for participation in the study. Detailed history & clinical examination was performed on all patients. Complete blood count, coagulation profile, serum uric acid, SGPT, urine detail report 24 hours urine protein were sent to laboratory for analysis. Investigations were repeated according to the situation.

Throughout the treatment patient and fetus was monitored carefully. Patients vitals were monitored hourly, urine autput maintained more than 50 ml/hour and presence of deep tendon reflexes (Patellar) was ensured with tendon hammer. Baby was monitored by Electronic fetal heart monitor during labour & fetal outcome was assessed by noting the Apgar Score at 1 & 5 minutes after delivery.

Data analysis was done on SPSS Version 10. Descriptive statistics like mean + SD frequencies and percentages were calculated.

Results:

There were 50 inpatients included in the study none of the patients left hospital during treatment and followed up till delivery and post partum period. Fetal and maternal outcome was evaluated after analysis of study proforma. The mean age of patients recruited in the study was 29.28 year (SD±4.41). Majority of patients were primigravida. The mean systolic blood pressure was 159.86 mmHg (SD±27.93) and mean diastolic Blood pressure was found to be 109.90 (SD ±14.59). Mean respiratory rate was 20 per minute (SD ±2.2).

In our study 25 patients were booked and 25 were unbooked making a frequency of 25 and 50% of each group. Magnesium sulphate was used to prevent occurrence of fits in patients with imminent eclampsia in all recruited patients. The occurrence of fits is summarized in table I, only 1 patient had fit even after administration of Magnesium sulphate frequency of 1 and percentage of 2 (Summarized in table I).

Magnesium sulphate used in the dose in our study has shown minimum maternal toxicity or complications. No evidence of respiratory depression was observed. Reflexes were normal and remained intact during therapy in all patients. None of the patients had heamaturia or any manifestation of Disseminated Intravascular Coagulation (DIC). However only one patient had oligouria with frequency of 1 and percentage of 2 (Summarized in table I).

Electronic fetal monitoring was done during labour and fetal outcome assessed by noting the APGAR score at 1 and 5 minutes after birth. Majority of the patients 33 and 39 out of 50 had

Table 1: *Maternal side effects of magnesium sulphate (n=50)*

Maternal Side Effects	Present Frequency (%)	Absent Frequency (%)
Fits	1 (2)	49 (98)
oliguria	1 (2)	49 (98)

Table 2: *Complications in baby (n=50)*

Complications in Baby	Present Frequency (%)	Absent Frequency (%)
Cyanosis	23 (46)	27 (54)
Respiratory distress syndrome	15 (30)	35 (70)
Jaundice	18 (36)	32 (64)
Hypothermia	13 (26)	37 (74)
Hypoglycemia	4 (8)	46 (92)
Hypocalcemia	1 (2)	49 (98)
Convulsions	7 (14)	43 (86)

more than 5 APGAR score at one minute and after 5 minutes respectively.

Fetal outcome also assessed by the condition of baby after birth, weight of baby, and the need of admission at Neonatal Intensive Care Unit (NICU) and their condition at discharge from NICU.

Adverse neonatal effects monitored/observed were Cyanosis (46%), Respiratory distress syndrome (30%), Jaundice (36%), Hypothermia (26%), hypoglycemia (8%), hypocalcaemia (2%) and Fits (14%) (Table II).

Among the babies of the recruited patients majority of them were discharged in satisfactory condition i.e. 37 out of 50 with a percentage of 74%.

There were 11 neonatal deaths (22%). There was 1 intrauterine death (2%) and 1 Fresh Still Birth (2%).

These results support our hypothesis that there is an effect of magnesium sulphate in the prevention of fits in imminent eclamptic patients.

Discussion:

The treatment of preeclampsia/ Eclampsia is delivery. As long as the mother remains undelivered, she is at increased risk of complications like seizures, abruption, thrombocytopenia, cerebral hemorrhage, pulmonary edema, liver hemorrhage, and renal failure. The risk of these complications subsides with delivery since preeclampsia is a completely reversible disease process.[1]

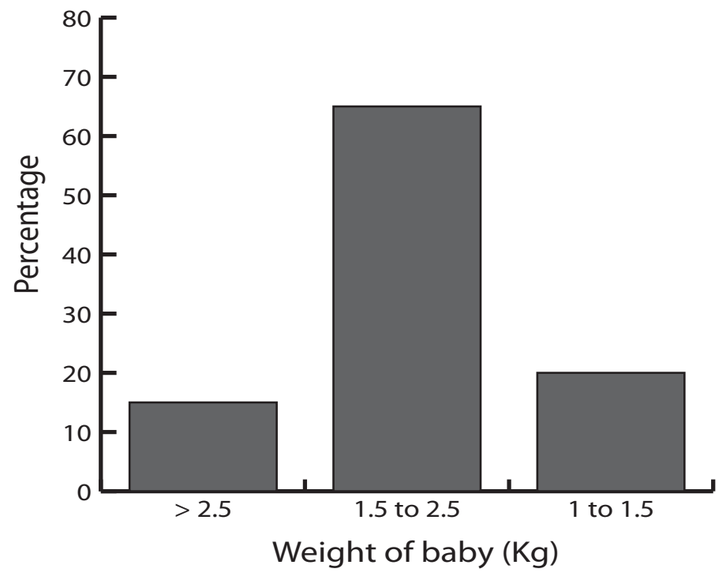

Figure 1: *Weight of baby at birth (n=50)*

Delivery may not be beneficial for the fetus if it is born preterm. Although the fetus is at increased risk of intrauterine growth restriction and stillbirth in the preeclamptic environment, conservative management may be entertained in selected cases to gain fetal maturity.[7]

Pregnancy related hypertension is defined as a systolic blood pressure >140 mm of Hg or diastolic blood pressure > 90 mm of Hg in a woman who was normotensive prior to 20 weeks of gestation. Severe hypertension should be treated to prevent maternal vascular complications. There is no consensus on the exact blood pressure threshold to initiate therapy. In adult women, diastolic blood pressures >105 to 110 mm of Hg or systolic pressures >160 to 180 mmHg have been suggested. The threshold may be lower in adolescents whose baseline diastolic pressure is less than 75 mm of Hg; in such patients, treatment is initiated at diastolic pressures of >100 mmHg.[13]

Preeclamptic women with severe hypertension are treated initially with oral antihypertensive therapy. The choice of the antihypertensive agents depends on individual clinician preference, the specified maternal and foetal benefits and the reproductive complications (teratoge-

nisity, fetotoxicity and neonatal toxicity) of each particular agent. There are unequivocal evidences that Magnesium sulphate is superior to other agents in reducing recurrent eclamptic seizures. There is a strong recent evidence recommended that magnesium sulphate should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia.[1-2]

Researchers in France evaluated indications, mode of administration and safety of magnesium sulphate in severe preeclampsia. They studied a group of 57 preeclamptic women treated by magnesium sulphate (intravenous bolus of 4.5g during 20 minutes followed by a perfusion of 1.5g/h) associated or not with an antihypertensive treatment. Hyperreflexia was the main indication to start magnesium sulphate treatment (75%). About half (47%) of the cases occurred before 33 weeks of gestation No eclampsia occurred in this group. There was one overdosage which regressed when perfusion was stopped. One patient presented minor side effects attributed to magnesium sulphate.This study shown that providing a rigorous protocol; indications of magnesium sulfate therapy in severe preeclampsia are well defined. And this treatment can be easily used without severe complications and major side effects comparable to our study. Magnesium sulphate dosage used in our study has showed minimum maternal toxicity or complications. No evidence of respiratory depression observed. Reflexes were normal and remained intact during therapy in all patients. None of the patients had heamaturia or any manifestation of DIC. However only one patient had oliguria with frequency of 1 and percentage of 2. Unlike this study our study included neonatal outcome.[14]

In Nepal a study was done to see the incidence and impact of changes in the intervention strategy for the management of eclampsia in a maternity hospital on maternal and perinatal outcome. Analysis of case records of all eclampsia cases over two different study periods designated as study period A (April, 1994 to Oct, 1996) and study period B (April, 2000 to April, 2001) were done. Total number of eclampsia cases who received intervention over two different study period (46 in study period A and 47 in study period B) were comparable despite the difference in the duration of study period. During study period A, diazepam was used as anticonvulsant, whereas magnesium sulphate was used to control fits during study period B. Epidemiology and clinical profile of eclamptic patients do not show remarkable change. There was no maternal death in study period B (April, 2000 to April, 2001) whereas there was one maternal death in the study period A (April, 1994 to October, 1996). Marked improvement was noticed in terms of recurrence of fit (19.13% vs 73.91%) with change in the intervention strategy. Perinatal deaths were fewer in study period B (20% vs 33%). Overall, it seems that care of eclamptic patients and use of magnesium sulphate as anticonvulsant has resulted in positive impact on maternal outcome. In our study neonatal deaths are (22%) comparable to the above mentioned study. Our study included magnesium sulphate only.[15]

In another study done in India researchers studied the efficacy of low dose magnesium sulphate regime for control of convulsions in eclampsia and as seizure prophylaxis in imminent eclampsia. 570 cases of eclampsia and 480 cases of imminent eclampsia were treated with low dose magnesium sulphate. Eclamptic convulsions were controlled in 91.93 percent of the cases. Recurrence rate of convulsions was 7.89 percent, which was comparable to that reported in Pritchard regime. Low dose magnesium sulphate regime was 98.75 percent effective as seizure prophylaxis in imminent eclampsia comparable to our study (98 percent). Low dose magnesium sulphate therapy is very effective for controlling convulsions in eclampsia and for preventing convulsions in imminent eclampsia.[16]

In America researchers studied magnesium sulfate's preventive role in disease progression in women with mild preeclampsia. A total of 222 women with mild preeclampsia were randomized to receive intravenous magnesium sulfate (n = 109) or matched placebo (n = 113). The groups were similar with respect to maternal age, ethnicity, gestational age, parity, and maternal

weight at enrollment. Fourteen women (12.8%) in the magnesium group and 19 (16.8%) in the placebo group developed severe preeclampsia after randomization (relative risk = 0.8, 95% confidence interval 0.4, 1.5, P =.41). None in either group developed eclampsia or thrombocytopenia. Women assigned magnesium had similar rates of cesarean delivery (30% versus 25%), chorioamnionitis (3% versus 2.7%), endometritis (5.3% versus 4.3%), and postpartum hemorrhage (1% versus 0.9%), compared to those assigned placebo. Neonates born to women assigned magnesium had similar mean Apgar scores at 1 and 5 minutes as those born to women assigned placebo (7.7 ± 1.5 versus 7.8 ± 1.6 and 8.7 ± 0.7 versus 8.8 ± 0.6, respectively). This study showed that Magnesium sulfate does not have a major impact on disease progression in women with mild preeclampsia. But in our study Magnesium Sulphate was used in imminent eclampsia and it showed 98 percent efficacy in controlling fits.[17]

In another study in Bangladesh researchers assessed the role of injection magnesium sulphate in eclampsia and severe pre-eclampsia patients at community level in a rural set up before referral to the hospital. This study was conducted on 265 cases of eclampsia and severe pre-eclampsia over a period of six months. Among 265 cases, 133 were in intervention group who had received loading dose of injection magnesium sulphate before referral and the rest 132 were in non-intervention group, had not received injection magnesium sulphate before admission in hospital. The numbers (mean ± SD) of convulsion before treatment in intervention and non-intervention groups were 4.7 ± 2.64 & 6.86 ± 2.97 respectively. Recurrence of fits observed more in non-intervention group and the difference was statistically significant (p<.001). Mean (± SD) time taken to regain full consciousness was 12.0±9.6 and 17.4±7.4 hours in the intervention and non-intervention group respectively (p<.05). Control of convulsion by loading dose of 10 gm of injection magnesium sulphate was achieved in 94.0% of the intervention group and 74.0% in non-intervention group. There was only 3(2.3%) maternal death in study group whereas in non-intervention group maternal death was 14(10.4%) and the difference was highly significant (p<.005). Fourteen (13.7%) babies were still born in intervention group and 21(20%) in non-intervention group. The difference was statistically highly significant (p<.001). Remarkable achievements were obtained through use of magnesium sulphate at the community level at rural setting among the eclampsia and severe pre-eclampsia cases comparable to our study.[18]

In our study we determined the efficacy and safety of magnesium sulphate in patients with imminent eclampsia and fetomaternal outcome in patients with imminent eclampsia. These results support our hypothesis that there is an effect of magnesium sulphate in the prevention of fits in imminent eclamptic patients and better neonatal outcome.

Conclusion:

From our study we concluded that magnesium sulphate is effective in reducing Blood Pressure and prevention of fits in imminent eclamptic patients with no significant side effects. There were less fetal side effects as well. Results of our study are comparable to other international studies. Further studies are recommended in our population to establish the effect of magnesium sulphate in severe preeclampsia because of its safer profile.

References:

1. Coppage KH, Sibai BM. Treatment of hypertensive complications in pregnancy. Curr Pharm Des. 2005;11:749-57.
2. Afifi Y, Churchill D. Pharmacological Treatment of Hypertension in Pregnancy. Curr Pharm Des 2003; 9: 1745-53.
3. Sibai BM. Magnesium sulfate prophylaxis in preeclampsia: Lessons learned from recent trials. Am J Obstet Gynecol 2004; 190:1520-6.
4. Sibai BM. Diagnosis, Prevention, and Management of Eclampsia. Obstet Gynecol 2005;105:402-10.
5. Chames MC, Livingston JC, Ivester TS, Barton JR, Sibai BM. Late postpartum eclampsia: A preventable disease? Am J Obstet Gynecol 2002; 186:1174-7.
6. Lombardi DG, Barton JR, O'Brien JM, Istwan NK, Sibai BM. Does an obese prepregnancy body mass index influence outcome in pregnancies complicated by mild gestational hypertension remote from term? Am J Obstet Gynecol 2005 ; 192 :1472-4.
7. Xiong Xu, Fraser William D, Demianczuk, Nestor N. History of abortion, preterm, term birth, and risk of preeclampsia: A population-based study. Am J Obstet Gynecol 2002; 187:1013-8.
8. Akmal N, Raana G. Women with pregnancy induced hypertension; epidemiological differences between normotensive

pregnant women. Professional Med J 2006;13:310-2.

9. Nilsson E, Ros HS, Cnattingius S, Lichtenstein P. The importance of genetic and environmental effects for pre-eclampsia and gestational hypertension: a family study. BJOG 2004; 111:200-6.
10. Lain KY, Roberts JM. Contemporary concepts of the pathogenesis and management of preeclampsia. JAMA 2002; 287:3183-6.
11. Belfort MA, Anthony J, Saade JR, Allen JC. A comparison of MgSO4 and nimodipine for prevention of eclampsia. Eng Med 2003;348:394-11.
12. Simpson KR, Knox GE. Obstetrical accidents involving intravenous magnesium sulphate: Recommendations to promote patient safety. American Journal of maternal Chid Nursing. 2004;29:161-9.
13. Sibai BM. Diagnosis and Management of Gestational Hypertension and Preeclampsia. Obstet Gynecol 2003; 102:181-192.
14. Girard B, Beucher G, Muris C, Simonet T, Dreyfus M. [Magnesium sulphate and severe preeclampsia: its use in current practice].J Gynecol Obstet Biol Reprod 2005; 34:17-22
15. Chaudhary P. Eclampsia : before and after magnesium sulphate. JNMA J Nepal Med Assoc 2005; 44:124-8.
16. Sardesai S, Maira S, Patil A, Patil U. Low dose magnesium sulphate therapy for eclampsia and imminent eclampsia: regime tailored for Indian women. Journal of Obstetrics and Gynaecology of India 2003;53:546-50.
17. Livingston JC, Livingston LW, Ramsey R, Mabie BC, Sibai BM. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. Obstet Gynecol 2003;101:217-20.
18. Shamsuddin L, Nahar K, Nasrin B, Nahar S, Tamanna S, Kabir RM et al. Use of parenteral magnesium sulphate in eclampsia and severe pre-eclampsia cases in a rural set up of Bangladesh. Bangladesh Med Res Counc Bull 2005; 31:75-82.
19.