J Ayub Med Coll Abbottabad;16(2)

MAGNESIUM SULPHATE IN THE PROPHYLAXIS AND TREATMENT OF ECLAMPSIA

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Background: Magnesium Sulphate is considered to be the agent of choice for the control of eclamptic seizures in pregnant women. Our objectives were to determine frequency of eclampsia and pre-eclampsia in our unit and to determine the effect of initial loading dose of magnesium sulphate on maternal and fetal outcome. **Methods:** This study was carried out in Department of Gynaecology at Lady Reading Hospital, Peshawar. In the year 2000 only 133 patients received magnesium sulphate out of 228 cases of eclampsia and pre eclampsia due to the problems with the continuous supply of the drug. This included 53 cases of eclampsia and 80 cases of pre-eclampsia. Information regarding the dosage of magnesium sulphate labor out come, maternal and fetal outcome, side effects and complications of therapy were evaluated from hospital case records. The magnesium sulphate regimen consisted of 4 gm loading dose as 20% solution intravenously over 10-15 minutes followed immediately by 5 gm into each buttock. Dose of 5gm intramuscularly was repeated only if the patient developed convulsions. **Results:** Eclampsia and pre-eclampsia occurred in 1 in 25.5 and 1 in 34.4 deliveries respectively. Majority of patients received the initial loading dose of magnesium sulphate, but in 2 patients dose had to be repeated. In two patients of pregnancy induced hypertension convulsions occurred soon after delivery unheralded by any signs and symptoms of impending eclampsia. Perinatal mortality was 19 (35.8%) and 16 (20%) in eclampsia and pre-eclampsia respectively. High perinatal mortality was attributed to prematurity as only 16.98% of eclampsia and 57.5% of Pre eclampsia were more than 37 weeks. One patient of sever pre-eclampsia developed postpartum hemorrhage and acute renal failure, but she recovered while another one developed sudden postpartum collapse immediately after delivery and died due to cerebrovascular accident. 8 patients of eclampsia died despite intensive management. All of them were referred from periphery with history of multiple fits and were brought in a serious state. **Conclusion:** Frequency of eclampsia and pre-eclampsia is high in this region with high perinatal and maternal morbidity and mortality. Magnesium sulphate is an effective drug to prevent and control seizures. It is easy to administer and subsequent nursing is easy. Seizures usually terminate after the initial loading dose of magnesium sulphate.

INTRODUCTION

Eclampsia and pre-eclampsia are important causes of morbidity and mortality during pregnancy childbirth and puerperium.[1] The prevention of seizure activity in pre-eclampsia and recurrent seizures in eclampsia is an essential aspect of management.[2] A number of different anticonvulsants are used to control eclamptic fits and to prevent future seizures.[3] In North America, parenteral magnesium sulphate is the drug of choice for the prevention and treatment of eclamptic convulsions.[4] Magnesium sulphate appears to act as a cerebral vasodilator (particularly on the small diameter vessels) in patients with pre eclampsia. With its potential to relieve cerebral ischemia this vasodilatation may help explain why magnesium sulphate has anti seizure activity in pre-eclampsia.[5] Its dosing schedules and effectiveness however is empiric, because no randomized trials have demonstrated whether it works and what is the therapeutic level that might prevent seizure.[6] After the report of collaborative eclampsia trial role of magnesium sulphate for the control of seizures in eclampsia has been firmly established. In lancet it was reported six years ago that since magnesium sulphate is cheap and easy to produce its ready availability should be a priority for all those concerned with maternal health and the essential drug list of World Health Organization, and other bodies need to be amended accordingly".[7] But still women in developing countries are being treated with diazepam and phenytoin, main problem being the continuous supply of drug. The question whether magnesium sulphate reduces the risk of eclampsia in women with pre-eclampsia and its benefits was at last answered by MAGPIE TRIAL conducted by Royal college of Gynaecology, which concludes that Magnesium sulphate reduces the risk of eclampsia,

and it is likely that it also reduces the risk of maternal death.[8] Magnesium sulphate is not a benign drug it is associated with complications and although most studies have shown that it does not increase the duration of labour ,maternal blood loss or caesarean delivery rate, it does change intrapartum and postpartum care and does affect many maternal and fetal parameter.[9] The aim of this study was to determine the frequency of eclampsia and pre-eclampsia and to evaluate the maternal and fetal outcome of patients with pre-eclampsia and eclampsia treated with initial loading dose of magnesium sulphate.

MATERIAL AND METHODS

Hospital history sheets of all those patients who received magnesium Sulphate from January 2000 to December 2000 were reviewed and scrutinized. Descriptive statistics were obtained after chart analysis and review of all notes. Patient who did not receive Magnesium sulphate were excluded. Frequency of eclampsia was calculated out of total number of deliveries in one year in that unit.

Magnesium sulphate was given by intramuscular regimen as described by Pritchard[10] and colleagues i.e. loading dose of 4 gm intravenously as 20% solution over 10-15 minutes followed by 5gm into each buttock intramuscularly. As the main problem with magnesium sulphate was its availability, therefore the dose of magnesium sulphate was modified. Only loading dose was given, and 5 gm intramuscular was repeated only if either signs of impending eclampsia developed or convulsions occurred. Patient was monitored clinically with respiratory rate (>16/ minutes), urine output (>25ml/hour) and patellar reflex. Hypertension was controlled with methyldopa and nifedipine. Induction was started in all cases of eclampsia and severe pre-eclampsia provided they were not already in labour, irrespective of gestational age. Maternal outcome was measured regarding recurrence of convulsions, mode of delivery, any complications during labor , delivery and puerperium who were admitted before delivery of baby, development of complications such as pulmonary edema, cardiac arrest, respiratory depression, pneumonia, renal failure, disseminated intravascular coagulation, cerebrovascular accident, liver failure and maternal death.

Fetal outcome was measured in terms of perinatal morbidity (Apgar score <7 at 5 minutes interval, intubations at the time of delivery, nursery admissions) and mortality.

RESULTS

There were 6693 obstetric admission from January to December 2000. Total deliveries were 3342. This included 307(4.58%) cases of hypertension associated with pregnancy, the distribution of whom is given in table-1.

Total patients treated with Magnesium sulphate were 133 that included 53 (39.8%) cases of eclampsia and 80 (60.15%) cases of pre-eclampsia.

Eclampsia and pre-eclampsia was found to be common in the reproductive age rather than at the extremes of age as shown in table 2. Eclampsia was common in first pregnancy i.e. (54.7%) but pre-eclampsia was found to be frequent among grand multigravidae (40%) and multigravidae (35%) as shown in table 2.

40 patients with eclampsia were admitted as antenatal cases and 13 as postnatal eclampsia, while 76 cases of pre-eclampsia were antenatal, and 4 were postnatal. Only 9(16.98%) patients of eclampsia were of more than 37 weeks gestation while 46 (57.5%) patients of pre-eclampsia were of more than 37 weeks gestation. Majority of patients were admitted with sever hypertension as shown in table 3(A).

6 patients of eclampsia had no protienuria. Two patients who were labeled as cases of pregnancy induced hypertension with mild hypertension of 160/100mmHg respectively and no protienuria, developed fits in the hospital. One during labour and another soon after delivery. Both were administered diazepam during the acute attack and then loading dose of magnesium sulphate.

24 (45.20%) patients of eclampsia were induced with prostaglandin vaginal pessary while 40(50%) of patients of pre-eclampsia were already in labour, and labour was only augmented. 11(13.75%) patients of pre-eclampsia underwent caesarean section. These were performed purely for obstetrical reasons., 5 patients had failure to progress, 4 for obstructed labour and 1 each for neglected transverse lie and brow presentation. All these case were referred from periphery in advanced labour. 24 (45.2%) of eclampsia and 52(65%) of pre eclampsia had normal vaginal deliveries while 20 (15%) had instrumental deliveries as shown in table 4(b).

6 patients with pre eclampsia and gestational age less than 34 weeks ,who were administered loading dose of magnesium sulphate and anti hypertensive drugs were discharged on conservative treatment after their all clinical and laboratory parameters were improved. One patient with sever preeclampsia left against medical advise.

Table-1: Frequency out of 6693 obstetric admissions

	No.	**%** **(n=6693)**	**Ratio (n=3342)**
Eclampsia	131	1.95%	1 in 25.5 deliveries
Pre-Eclapsia	97	1.44%	1 in 34.5 deliveries
Pregnancy Induced Hypertension	52	0.77%	1 in 64.2 deliveries
Essential Hypertension	27	0.4%	1 in 123.77 deliveries
Total	307	4.5%	3342 deliveries

Table-2: Patient Characteristics

	Eclampsia	**Preeclampsia**
A) Age		
Teenage	04(7.5%)	01(1.25%)
20 – 30	34(64%)	43(53.75%)
31 – 40	15(28.3%)	34(42.5%)
Above	NIL	02(2.5%)
B)Parity		
Primegravida	29(54.7%)	20(25%)
Multigravida	12(22.6%)	28(35%)
Grandmulti-gravida	12(22.6%)	32(40%)
Total	53	80
C) Gestational Age		
<30	08	07
30 -34	08	08
34-37	15	15
<37	31(58.49%)	30(37.50%)

>37	09(16.98%)	46(57.50%)
Postnatal	13(24.50%)	04(5%)

Table-3: Level of Blood Pressure and Albuminuria at Admission

	Eclampsia	Preeclampsia
A)Hypertension		
Mild	18(33.90%)	14(17.5%)
Severe	35(66%)	66(82.5%)
B)Protienuria		
0	06	NIL
+1	13	17
+2	09	28
+3	12	24
+4	13	11
TOTAL	53	80

Table-4: Pregnancy & Labour Outcome

	Eclampsia	Preeclampsia	Total
A) Induction			
Prostaglandin	24(45.20)	15(18.75%)	39
ARM+Oxytocin	05(9.40%)	09(11.25%)	14
Augm-ented	11(20.75%)	40(50%)	51
Conservative Treatment=6(Went Home)			
Lama =1			
B)Mode Of Delivery			
NVD	24(45.20%)	52(65%)	76
Forceps	09(16.98%)	03(3.75%)	2O
Vacuum	05(9.40)	03(3.75%)	
Cesarean	NIL	11(13.75%)	

In 22(41.5%) and 57(71.2%) cases of eclampsia and preeclampsia. babies were born alive, while 2(3.77%) babies of eclampsia and 8(10%) babies of pre-eclampsia needed nursery admissions. Perinatal mortality was 19(35.8%) in eclampsia and 16(20%) in pre-eclampsia.

Table-5: Perinatal outcome

	Eclampsia	Preeclampsia
Alive	24(41.50%)	57(71.20%)
Fresh Stillbith	15(28.30%)	10(12.50%)
Macerated Stillbirth	01(1.80%)	02(2.50%)
Neonatal Death	03(5.60%)	04(05%)
Perinatal Mortality Rate	19(35.80%) 358/1000	16(20%)200/1000
Nursery Admission	02(3.77%)	08(10%)

Total 9 patients died. 8 were of eclampsia and 1 was of pre-eclampsia.One patient of pre-eclampsia who was admitted with twin pregnancy of 30 weeks gestation and APH developed postpartum hemorrhage and acute

renal failure. She was transfused fresh frozen plasma and haemodialysed twice. She recovered completely. Another patient of pre –eclampsia developed pulmonary edema soon after delivery. She was treated and recovered.

One patient of preeclampsia who had normal vaginal delivery became unconscious after delivery. She did not have any kind of fits. She was shifted to I.C.U put on ventilator but expired after 11 hours of delivery probably due to C.V.A.

Total 8 patients of eclampsia died. 3 were admitted as postnatal eclampsia (2 were four days postnatal while one was one day postnatal) All had history of multiple fits and were deeply unconscious. 3patients who were antenatal were induced. One was admitted with a full blown HELLP syndrome while 2 were admitted with sever pulmonary edema. Although all possible emergency measures were taken but died despite intensive care. 2 patients of eclampsia died undelivered. All these patients were admitted with history of multiple fits in a very serious condition and were referred from periphery.

DISCUSSION

This study was a descriptive study to find about the maternal and fetal outcomes that were treated with magnesium sulphate. Eclampsia and pre-eclampsia are important causes of morbidity and mortality during childbirth, and puerperium.[1] Eclampsia accounts for approximately 50,000 maternal deaths worldwide annually.[11] In Europe and other developed countries eclampsia complicates about 1 in 2000 deliveries while in developing countries estimates vary widely from 1 in 100 to 1 in 1700.3 Thus eclampsia is now largely regarded as disease of developing countries. And it is one of the leading causes of maternal mortality after hemorrhage and sepsis. In our study frequency was 1 in 34.4 deliveries of pre-eclampsia and 1 in 25.5 deliveries of eclampsia. Only two patients of pre-eclampsia were booked. The high frequency of these conditions reflects the lack of antenatal care and lack of functioning health care system at primary and secondary levels. It is also because ours is the only easily accessible main referral centre for whole of the province. Two patients with pregnancy induced hypertension without protienuria developed convulsions in the hospital. Thus on one hand lack of antenatal care may be one of the predisposing factor for such a high frequency of eclampsia but on the other hand it may not be easy to predict seizures in cases of pregnancy induced hypertension. Study by Katz et al questions the traditions that eclampsia evolves in a fairly linear manner from mild preeclampsia to sever preeclampsia to seizures. It also question the assumption that seizures are predictable.[9] Mattar and Sibai conclude that women with mild hypertension or mild preeclampsia either before labour or intrapartum continuous evaluation of maternal symptoms and educations of patients and nurses regarding reporting of these symptoms and the need for immediate medical response to any of these symptoms are extremely important.[12] Most patients with pregnancy induced hypertension do not progress to seizures.[13]

In this study six patients of eclampsia had no protienuria, thus hypertension and protienuria are neither the only nor necessarily the most important signs of pre-eclampsia. Douglas and Redman had noted that protienuria was the only premonitory sign in 10% of cases and that one third of women had only mild hypertension before the onset of convulsion.[14] Renal function tests, thrombocytopenia, and abnormal plasma concentration of liver enzymes gives important information about the extent to which the maternal system is affected.[14] Because of lack of hospital resources and trained laboratory staff in evening and night these biochemical markers were often not available in the evening and night time for patients admitted as emergency cases. According to Douglas et al confirmatory signs should be sought assiduously in the first 48 hours after a fit even if there are no features of preeclampsia previously. Thus convulsions may be unheralded by warning sign and symptoms.

A major problem for preventing and treating eclampsia is that the pathogenesis of this condition is not known.[7] As pre-eclampsia had no preventive strategy, its management relies on early detection, control of its manifestation, such as hypertension and ultimately on the delivery of the fetus and placenta.[15]

In this study vaginal delivery was the preferred mode of delivery. Caesarean sections which were performed in case of pre-eclampsia were mainly done for obstetrical indications. Thus this study also showed that magnesium sulphate does not increase the duration of labour, maternal blood loss or caesarean delivery rate. Perinatal mortality was very high in eclampsia i.e19 (35.8%) as compared to pre eclampsia i.e. 16(20%). Main cause of this high perinatal mortality was prematurity and antepartum hemorrhage. Comparatively perinatal mortality was low, considering the gestational ages. This may be attributed to the affect of magnesium sulphate on very low birth weight babies. Schendel et al reported that a reduced risk for cerebral palsy and possibly mental retardation, among very low birth weight children is associated with prenatal magnesium sulphate exposure.[16] Nelson and Grether also revealed an 80% reduction in the risk for cerebral palsy associated with intrapartum magnesium sulphate exposure that appeared to be independent of a variety of perinatal conditions including pre-eclampsia and number of known risk factors for cerebral palsy.[17]

Anticonvulsants are given to women with severe pre-eclampsia with the aim of preventing the first fit although whether this does more good than harm is unclear.[7] Anticonvulsants are used to prevent recurrence of seizures in patients with eclampsia as well as in fulminating pre-eclampsia for prophylaxis against seizures.[1] There is now compelling evidence in favor of magnesium sulphate, rather than diazepam or phenytoin for the treatment of eclampsia.[7] Results from the MAGPIE[8] trial demonstrate clearly that magnesium sulphate is effective in considerably reducing the risk of eclampsia for women with preeclampsia. But still in developing countries such as ours, diazepam is being used as an anticonvulsant. The main problem is the free availability of the drug. In our study patient did not develop convulsions after only the loading dose was given. In only 2 patients who developed fits dose had to be repeated. Thus the dose of magnesium sulphate and duration of therapy should be further evaluated according to the individual and geographical differences, as it is quite plausible that higher dose will increase the hazards (such as respiratory arrest without any increase in the benefits associated with the use of magnesium sulphate.[18] Sibai had reported that approximately 10% to 15% of women with eclampsia will have a second convulsion after receiving the loading dose of magnesium sulphate. Pritchard et al reported that 12% who had eclampsia treated before delivery again suffered convulsions shortly after an initial injection of the loading dose.[10]

8 patients of eclampsia and 1 patient of pre eclampsia died, who developed sudden unconciouness. All patients of eclampsia had multiple fits and were brought to the hospital in very late stage. studies from Turkey, Columbia, Mexico city and Nigeria have all noted an unacceptably high morbidity and mortality rate among patients with eclampsia primarily among patients who have seizures outside the hospital and almost all among patients without any prenatal care.[9]

Our study raises question regarding the routine prophylaxis of magnesium sulphate in pre-eclampsia and dosage and duration of magnesium sulphate in eclampsia.

CONCLUSION AND RECOMMENDATIONS

Magnesium sulphate is the drug of choice in eclampsia. Initial loading dose of magnesium sulphate is effective in prevention and treatment of Eclampsia. As it is cheaper and easy to administer, and subsequent nursing is easier, it may be appropriate for use at primary health level so as to reduce maternal morbidity and mortality. As eclampsia is considered to be a disease of developing countries, prospective studies are needed regarding dosage and duration of magnesium sulphate therapy.

REFERENCES

1. Chien PF, Khan KS, Arnott N. Magnesium sulphate in the treatment of eclampsia and pre eclampsia: an overview of the of the evidence from randomized trials. Br J Obs gynecol 1996; 103:1085-91.

2. Anthony J, Johanson RB, Duley L. Role of magnesium sulphate in seizure prevention in patients with eclampsia and pre eclampsia. Drug saf 1996;15(3):188-99.

3. Duley L, Henderson-Smart D. Magnesium sulphate versus diazepam for eclampsia (Cochrane review). In the Cochrane library, issue 3, 2003 Oxford.

4. Sibai BM. Magnesium sulphate is the ideal anticonvulsant in pre eclampsia-eclampsia. Am J Obst Gynecol 1990;162:1141-5.

5. Belfort MA, Moise KJ. Effect of Magnesium sulphate on maternal brain blood flow in pre eclampsia. A randomized Placebo controlled study. Am J Obst Gynecol 1992;167:661-6.

6. Burrows RF, Burrows EA. The feasibility of a control population for a randomized control trial of seizure prophylaxis in the hypertensive disorders of pregnancy. Am J Obst Gynecol 1995;173:929-35.

7. Duley L. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. The Lancet. 1995; 345:1455-63.

8. Duley L. Do women with pre-eclampsia and their babies benefit from Magnesium sulphate? The MagPie Trial: a randomized placebo-controlled trial. Lancet 2002;359:(9321):1877-90

9. Katz VL, Farmer R, Kuller JA. Pre eclampsia into eclampsia. Towards a new paradigm. Am J Obst Gynecol 2000;182:1389-96.

10. Pritchard JA, Cunnigham FG, Pritchard SA. Parkland Memorial Hospital Protocol for treatment of Eclampsia.Evaluation of 245 cases. Am J Obst Gynecol 1984;148:951-63.

11. Fugate SR, Chow GE. Eclampsia. Retracted from e-Medicine. May 13, 2003.

12. Mattar F, Sibai BM. Risk factors for maternal morbidity. Am J Obst Gynecol 2000; 182:307-12.

13. Appleton MP, Kuchl TJ, Rebel MA, Adams HR, Knight AB, Gold WR. Magnesium sulphate versus Phenytoin for Seizure Prophylaxis in pregnancy induced hypertension. Am J Obst Gynecol 1991;165:907-13.

14. Douglas KA, Redman CWG. Eclampsia in the United Kingdom. BMJ 1994; 309:1395-1400.

15. Steer PJ. The definition of pre eclampsia. Commentary. Br J Obstet Gynecol 1999;106:753-5.

16. Schendel DE, Berg CJ, Allsopp MY, Boyle CA, Decoufle P. Prenatal Magnesium Sulphate Exposure and the risk for Cerebral Palsy or Mental Retardation among very Low birth weight Children aged 3 to 5 years. JAMA 1996;276:1805-10.

17. Nelson Kb, Grether JK. Can Magnesium sulphate reduce the risk of cerebral palsy in very Low birth weight infants? Pediatrics 1995;95:263-9.

18. Duley L. Magnesium sulphate regimen for women with eclampsia. Messages from the collaborative Eclampsia trial. Br J Obstet Gynecol 1996;103:103-5.

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