MAGNESIUM SULPHATE THERAPY IN ECLAMPSIA: A 5 YEARS EXPERIENCE AT A TEACHING HOSPITAL

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ABSTRACT

***Objective**: To describe the presentation of eclampsia, its management and associated outcomes using magnesium sulphate (MgSO4), over a five years period at a tertiary care hospital.*

***Methodology:** This descriptive study was conducted at Obstetrics and Gynecology unit, Hayatabad Medical Complex, Peshawar from January 2004 to December 2008. Data was collected from all patients presenting with eclampsia.*

***Results**: A total of 146 patients had eclampsia. Unbooked were 124 (84.93%). Mean age 23 years ± 5.3 years (range 18-38 years), primigravida were 69.17 %(101 cases). Antepartum fits in 72.6 % (106 cases), intrapartum 14 (9.58%) and 27(18.49%) postpartum. MgSO4 was used in all except 4 with oliguria, they were given diazepam. Recurrent fit occurred in only 20(13.69%). MgSO4 toxicity occurred as respiratory depression in 9 cases., depressed tendon reflexes in 10 and decreased urine output in 13 cases Total deliveries were 23021, prevalence of eclampsia was 0.63% .Mode of delivery was Vaginal in 97 (66.43%), instrumental in 29 (19.98%) and cesarean section in 20 (13.69%)cases. There were 26(17.2%) stillbirths and 4 neonatal deaths. Complications included HELLP in 17 (11.64%), pulmonary complications in 17, renal failure in 7(4.79%), DIC in 16(10.95%) and temporary blindness in 16 cases. Eleven (7.53%) maternal deaths occurred, causes included DIC in 1case, HELLP in 2, renal failure 1, cardiopulmonary failure in 2 and CVA (recieved deeply unconscious) in 5 cases. All were unbooked cases and with delay in reaching hospital.*

***Conclusion:** Eclampsia is common antenatally and in primigravidae, and a major cause of maternal morbidity and mortality in our region.It was effectively controlled with MgSO4, preventing recurrent fits and safe for both mother and fetus.*

***Keywords:** Eclampsia, Management, Outcome, Magnesium Sulphate (MgSO4) Anticonvulsant.*

This article may be cited as: Naz T, Hassan L, Rafique I. Magnesium Sulphate Therapy in Eclampsia: a 5 years experience at a Teaching Hospital. J Postgrad Med Inst 2012; 26(1): 84-90.

INTRODUCTION

Eclampsia, the occurrence of convulsions in association with pre eclampsia remains a rare but serious complication of pregnancy [1]. It is a common cause of maternal mortality worldwide but particularly in developing countries. It is estimated that every year eclampsia is associated with about 50,000 maternal deaths, most of which occur in developing countries [2] . Prenatal care that a woman recieves during pregnancy, labor and in the post partum period is vital for the survival of both the mother as well as the baby. In the developing countries, there is low utilization of both antenatal and intrapartum care and many pregnant patients present to the hospital only as a last resort, and thus the opportunity to detect women at the pre eclamptic phase is therefore usually lost.

The management is based on seizure control, prevention of recurrent fit, stabilization, monitoring and delivery. Magnesium sulphate(MgSO4) is the agent of choice for treatment and prophylaxis of eclampsia in patient with severe pre- eclampsia and its efficiency has been universaly proven[3,4,5,6]. It was first introduced

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Date Received: April 1, 2011
Date Revised: October 5, 2011
Date Accepted: October 13, 2011

to control convulsions in 1925 but its efficiency was confirmed in 1995 after the collaborative eclampsia trail(Magpie Trial)[7]. MgSO4 is not a benign drug and is associated with toxicity. After the Magpie trial, the fear of toxicity was laid to rest and the drug was monitored using clinical parameters i.e. knee jerk should be present, respiratory rate more then 16/min. and urine output more then 25 mls/hour. Serum magnesium level should be 2-3.5 mmol/litre. Most studies have shown that MgSO4 does not increase the duration of labour, maternal blood loss or cesarean section rate, but it does effect maternal and fetal parameters[4].

The use of MgSO4 as an anticonvulsant was started in our hospital in 2002, after the publication of Magpie trial. It was used according to Pritchard regieme and was found effective in treatment of eclampsia and prophylaxis of recurrent fit, as well as reduced maternal mortality when compared to diazepam.[8.] The present study analyses the clinical presentation, maternal and fetal outcome, and complications in patients of eclampsia, with MgSO4 therapy over a 5 years period in a tertiary health care facility.

METHODOLOGY

This is a descriptive study of all consecutive patients with eclampsia at the department of obstetrics and gynecology, Hayatabad Medical Complex, Peshawar, Pakistan. All patients admitted with eclamptic fits were included in the study. Eclampsia was diagnosed if there was generalized tonic-clonic convulsions, with elevated blood pressure and or proteinuria or if there was history of hypertension in pregnancy. Patients with previous history of seizures disorder like epilepsy or if there was doubt about diagnosis were excluded.

At admission patients' age, parity, booking status, duration of gestation, delay before reaching hospital, type of eclampsia, (antenatal, intrapartum or postpartum), blood pressure, detailed examination and presence of protienuria were recorded. Necessary baseline investigations including full blood count, platelet count, coagulation status, renal function tests, liver function test and fundoscopy were carried out. At admission each patient was provided emergency management including passing an intravenous line, airway, folley's catheter, loading dose of MgSO4 for control of seizures and blood pressure control. After stabilizing the patient, induction of labour or mode of delivery was decided. Pritchard regeime for administrating MgSO4 was used; 4 gm MgSO4 diluted were administrated slowly intravenously over 10 minutes and 5 gms given deep intramuscular in each buttock making a total loading does of 14 grams. Maintenance dose of 5 gm 4 hourly intramuscularly was then continued for 24 hours. Hydralazine injection was used as antihypertensive to control severe hypertension and was given as intermittent bolus doses to keep diastolic blood pressure at about 90 mmHg. Methyldopa and nifedipine were the long term antihypertensive used. Obstetric management included induction with prostaglandin E2 passery in those with unfavorable cervix but adequate pelvis with an aim to achieve delivery with in 24 hours. Those already in labour were augmented, monitored and allowed vaginal delivery. Cesarean section was done for obstetrical indications. Babies with birth asphyxia, poor apgar score, low birth weight were managed at the neonatal care unit. Patient's sociodomographic, clinical data and outcome were entered on a pre prepaired proforma. An effort was made to detect preventable factors responsible for adverse outcome.

Data sources included patient's attendants, obstetrics record charts, referal letters if any, and in case of those shifted to other departments, record of concerned departments (ICU). After data collection, it was analyzed and results presented as percentages.

RESULTS

There ware 146 patients who presented with eclampsia during the study period. Total deliveries during this period were 23,021 giving an incidence of 0.63% of eclampsia. One hundred and twenty-four (84.93%) patients had no antenatal care. The age range was from 18 to 38 years with a mean age of 23.9 years ±5.3 years. The highest frequency was recorded in primgravida (n=101, 69.17 %) where as multigravida were 45(30.82%) shown in Table I. Majority of the patients had eclampsia at term(75 cases, 51.36%) and only 2(1.36%) had post dated pregnancy. Premonitory symptoms in the form of headache, epigastric pain and or blurring of vision was present in 99 (67.80%) of women. Single fit was recorded in 35 (23.97%) cases, whereas in others, number of fits ranged from 3-5. Type of eclampsia included antepartum fits in 106 (72.60%), intrapartum in 14(9.58%) and postpartum in 27 (18.49%) cases as shown in Table I. In 66.6 %(88 cases) the BP on admission was more than 110 mmHg diastolic and in the remaining it ranged from 90-110 mmHg. History of hypertension in pregnancy was positive 56 (39.18%), while 3(2.05%) patients had eclampsia in the previous pregnancy. Urine albumin was tested on admission for all patients and only 28 (19.17%) cases had no albuminuria. $MgSO_4$ was used as anticonvulsant in 142 (97.27%) cases, 4 (2.73%) were given injection diazepam as urinary output was less on arrival.

Fifteen (10.27%) had recieved diazepam injection to control seizures at the local health facility and they were then started on Mg SO_4 here. Repeat fit occurred in 20 (13.69%) cases and they were given additional 2 gm MgSO4. Side effects of $MgSO_4$ included respiratory depression in 9 (6.16%), depressed tendon reflexes in 10 (6.84%), and decreased urinary output in 13 (8.90%) cases (Table II). Further doses of $Mgso_4$ were not given in these patients, serum Mg. levels were not done as this facility was not available.

Labour was induced in 40 (27.26%) cases with prostaglandin E2 pessaries; where as the rest of the eclamptic patients had good Bishop Score or were in labour. Ninety seven (66.43%) had a spontaneous vaginal delivery, in 29 (19.98%) cases delivery was assisted with forceps or vaccum and cesarean section was performed in 20(13.69%) cases as shown in table III. The neonatal outcome was comparable in vaginally delivered (98 (89%) alive babies) and those delivered by cesarean section (18 (86%) alive babies) and no statistically significant difference (P >0.05) was observed. There were 26 (17.12%) stillbirths and 4 early neonatal deaths. There were 4 cases of twin pregnancy, 7 cases of IUGR and respiratory distress occurred in 9 cases.

Majority of the patients suffered some sort of morbidity (n-104:71.24% cases). Pulmonary complications in 17 (11.64%) cases, HELLP (hemolysis, elevated liver enzymes, low platelet) in 17 (11.64%), renal failure in 7 (4.79%), DIC (disseminated intravascular coagulation) in 16 (10.95%) and temporary visual loss occurred in 16 cases as shown in table-IV. There were 11 maternal deaths giving a case fatality rate of 7.53%. Five of them were received deeply unconscious and expired with in 1-3 hours of arrival (3 of them came from Afghanistan and 2 from Waziristan) and were suspected of having

Table 1: Presentation and Symptoms (n= 146)

Presentation	No. of patients	Percentage
Type of eclampsia		
Antenatal	106	72.60
Intrapartum	14	9.85
Postnatal	26	18.49
Parity primigravida	101	69.17
Multigravidae	45	30.82
Premonitory symptoms		
Headache	41	28.08
Epigastric pain	25	17.12
Visual symptoms	33	22.60
None	47	32.19

Table 2: Side effects of MgSO4.

Anticonvulsant used	No. of patients	Percentage
MgSO4	127	86.98
MgSO4 & diazepam	15	10.27
Diazepam	4	2.73
Side Effects of MgSO4		
Respiratory depression	9	6.16
Depressed knee jerk	10	6.84
Urine output <30ml/hr	13	8.90

Table 3: Mode of Delivery (n=146)

Mode of delivery		Number of patients	Percentage
Spontaneous vaginal delivery		97	66.43%
Instrumental delivery		29	19.93
Cesarean section		20	13.69
Indications of Cesarean Section	Failed induction	9	-
	Failure to progress	7	-
	Breech	2	-
	APH	1	-
	Previous cesarean	1	-

Table 4: Morbidity and Mortality (n=146)

Morbidity / Mortality	Number of patients	Percentage
Pulmonary complications	17	11.64
Tongue bite	19	13.01
HELLP	17	11.64
DIC	16	10.95
Renal failure	7	4.79
Temporary Blindness	16	10.36
PPH	5	3.42
Uncontrolled B.P	15	10.27
Mortality	11	7.53
Causes: CVA/ deeply unconscious	5	3.42
DIC	1	0.68
Renal failure	1	0.68
HELLP	2	1.36
Cardiopulmonary failure	2	1.36

cerebrovascular accident (CVA). Other causes included DIC in 1 patient, renal failure in 1 case, HELLP in 2 and cardiopulmonary failure in another 2 patients. All the deaths were recorded in those patients who had no antenatal care. The association of mortality with late presentation and failure to book for antenatal care was statistically significant ($P<0.05$). Among the patients that expired, delay of more than 6 hours in reaching the hospital was also present in 8 cases.

DISCUSSION

The severe morbidity and mortality associated with eclampsia/ pre eclamsia are among the leading problems that threaten safe motherhood, particularly in developing countries. [9] In Europe and other developed countries eclampsia complicates about 1 in 2000 deliveries while, in developing countries it is 1 in 100 to 1 in 1700 deliveries[4].

The prevalence of eclampsia in our study was 0.63% which is comparable to 0.51% and 1.9% reported by other local studies[10,4]. Studies from developing countries have reported an incidence of 0.29% and 2.2%[11]. This figure is higher than that of developed countries, in UK incidence of eclampsia was 2.7 cases per 10,000

births[12]. However, from Nigeria and other African countries its incidence is reported as 9.42%, 5.2% and in one study as 7.8 per 1000 deliveries[2, 13, 14]. The calculated prevalence in this study was based on the number of hospital deliveries rather than being population based, thus it seems to underscore the magnitude of the disease.

Eclampsia was commoner among young maternal age, 135 (92.45%) cases were aged 18-30 years and 69.17% were primigravidae, where as in another study 54% patients were aged less then 20 years and 70.9% were primigravidas[10]. These findings are consistant with that of other studies[2,3,7,11,13]. Majority (84.93%) of patients in this study never utilized any form of antenatal care. Similarly 83.4% patients were unbooked in study by Ahmeed R[10]. Hypertension in pregnancy and pre eclampsia could have been detected and treatment offered before it progressed to eclampsia if these patients had utilized antenatal care. Other studies have also found lack of prenatal care to be strongly associated with eclampsia[13,14]. However Knight M, in a study from UK has reported that 38% of the women had established hypertension and protienuria in the week before their first fit[12]. Others have also reported that eclampsia was seen in some patients despite antenatal care, and within one week of the last visit[11]. Thus, routine screening helps to identify potential eclamptic women but ecalmpsia may not always be predictable and preventable, women with mild pre-eclampsia shall have continuous evaluation of symptoms before labour and intra partum to pick up impending eclampsia. However most patients with pregnancy induced hypertension do not progress to seizures[4, 15].

Fit occurred mostly antepartum, 106 cases (72.60%) as in another local study with 79.9% cases were antepartum[10]. Chaudery P, from Nepal has also reported 70.2% cases to be of antepartum eclampsia[11]. Eclampsia was commonest at term pregnancy (51.36%) and only 6 (5.47%) cases occurred before 30 weeks of gestation. This finding is consistant with those reported by other studies[4, 10, 11].

In our study 28 (19.17%) cases had no protienuria and another 19.86 %(29 cases) had no hypertention. Hypertension and protienuria are not necessarily the most important signs of pre eclampsia. Douglous and Reidman found that protienuria was the only premonitory sign in 10% of cases and one third of women had only mild hypertension before the onset of convulsions[4,16]. Renal function tests, thrombocytopenia and plasma concentrations of liver enzymes give important information about the extent to which maternal system is effected, these were done in all patients as baseline and for monitoring ,to pick up complications.

MgSO4 was used in 97.27% patients while 4 (2.73%) cases had oliguria and they were not given MgSO4, 15 patients had also recieved injection diazepam before arrival, they were given MgSO4 here. Only 20 (13.69%) patients had a repeat fit after the first dose of MgSO4. The aim in eclampsia is prevention of further fits as it is the recurrent fit that leads to significant cerebral anoxia and is associated with adverse outcome. In the Magpie Trial women treated with MgSO4 had a 52% and 67% lower recurrence of convulsions then those treated with diazepam and phenytoin respectively, as well as MgSO4 also reduced the risk of progress of severe pre-eclampsia to eclampsia by half and reduced maternal mortality[7, 17]. Retrospective studies in Thailand, Turkey and Dhaka have reported significant decline in maternal mortality with the use of MgSO4[3, 18].

Vaginal delivery was the main mode of delivery in 97(66.43%) cases, 29(12.92%) had instrumental vaginal delivery and cesarean section was performed in 20 cases. Similarly majority of women were delivered vaginally in other local studies[4,10]. While cesarean section was the main mode of delivery in studies from Nepal and Kuwait[11, 19]. There were 26 stillbirths and 4 infants died in neonatal period. The perinatal outcome was comparable to other local studies but higher then that reported from developed countries[10, 11, 12]. Late arrival of the patient after the onset of fits result in severe intrauterine fetal hypoxia and death. Eclampsia occurring preterm also necessitates preterm delivery, while available neonatal care facilities also determine the perinatal outcome.

There were 11 (7 .53%) maternal deaths due to eclampsia during the study period, which is high as compaired to other studies where no maternal death was reported[10,12,19]. While it is quite lower than 9.9 %, 10.6% and 28.3% reported from Africa and Nigeria [2,13,14]. Delay in reaching the hospital, severe hypertension, recurrence of fits and presence of severe complications were observed in patients suffering severe morbidity or mortality. In our study 104(71.24%) women developed some form of complications, of these 45 women had severe morbidity after eclamptic episode, 17 (11.64%) had HELLP, 16(10.95%) DIC, 7 (4.79%) had renal complications and 5(3.42%) had CVA (cerebrovascular accident), and required ICU care. Mg SO4 toxicity was observed as reduced tendon reflexes, oliguria and decreased respiratory rate in few cases, further doses of MgSO4 were with held in these patient. Most of the other studies have also demonstrated MgSO4 as an excellent drug with low toxicity and side

effects[3,12,19]. We used MgSO4 according to Pritchard regime, but a single loading does of 14 gm has been found equally effective in control of seizures in eclampsia as well as in prophylaxis of seizures in pre eclampsia[4,6,13]. At Dhaka Medical College Hospital a 10gm MgSO4 dose followed by 2.5 intramuscularly every 4 hours for 24 hours, while in another study only 1.5 gm maintenance dose was continued for 12 hours, was found effective[20,21]. However we have no experience with the low dose.

The main limitation of this study was that it was done in a single health care facility and was not population based. Another fact is delay in seeking medical care and late presentation and thus many women who had eclampsia may never have made it the hospital, hence we may not have the actual statistics to highlight the magnitude of the problem.

CONCLUSIONS

Eclampsia is still a major cause for both maternal and perinatal morbidity in our region. It is common in young and primigravidae. Lack of antenatal care and delay in seeking care, particularly after developing major complications is associated with increased morbidity and mortality. The current strategy of managing eclampsia with MgSO4 was safe for both mother and fetus, and effective in preventing recurrence of fit and complications. In addition high dependency care of patients is effective in reducing morbidity and mortality associated with eclampsia. These findings are consistent with the findings of randomized controlled trials of MgSO4 and show the benefits of incorporation of research into practice.

Community health education, better utilization of antenatal care, early recognition and referral, institutional delivery and MgSO4 therapy, will help to reduce the incidence and morbidity/ mortality associated with eclampsia.

Grant Support, Financial Disclosure and Conflict of Interest

None Declared

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CONTRIBUTORS

TN conceived the idea, planned the study and wrote the manuscript. LH provided guidance and helped in manuscript writing. IR did the data collection. All the authors contributed significantly to the research.