Eclampsia In Eastern India: Incidence, Demographic Profile And Response To Three Different Anticonvulsant Regimes Of Magnesium Sulphate

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Abstract

IntroductionEclampsia continues to be a major cause of maternal and perinatal morbidity and mortality in the developing world. We evaluated the incidence and outcome of women diagnosed with eclampsia in a tertiary referral centre in eastern India.MethodsThe prospective randomized study was carried out in the department of Obstetrics & Gynecology, MKCG Medical College and Hospital, Berhampur, Orissa, India, a tertiary level Government referral centre for whole of Southern Orissa, over a 2 year period. The incidence, demographics of women with eclampsia and response to three different regimens of magnesium sulphate was studied.Results160 women presented with convulsions against a background of preeclampsia of which 2 were diagnosed with cerebral malaria and hence excluded. Out of 4925 live births during the study period, there were 158 women with eclampsia, giving an incidence of 3.2 %. Majority were unbooked 154 (97.4%) and from rural areas 133 (84.2%). Antepartum eclampsia occurred in 21(13.3%) patients; antepartum / intrapartum eclampsia in 108(68.3%) while postpartum eclampsia occurred in 29 patients (18.4%). Primigravidas accounted for 105/129 cases with antepartum & intrapartum eclampsia while primiparas accounted for 25/29 cases with postpartum eclampsia. The all cause maternal mortality in the study period was 67, of which a total of 7 women died due to eclampsia, giving a case fatality rate of 4.4 % and maternal mortality ratio of 10.44%. Majority of the patients 75/158(47.45%) received magnesium sulphate at 4-8 hours after of onset of convulsions. 60 women received magnesium sulphate by Pritchard regimen (Group-A), while 49 each received magnesium sulphate by Zuspan regimen (Group-B) and Sibai regimen (Group-C) . There was no recurrence of convulsions in any patient after start of magnesium sulphate in both Groups A and C, whereas there was recurrence of convulsion in 1 patient in Group-B. There were a total of 50 still births and 5 neonatal deaths out of total of 167 deliveries in the 158 women with eclampsia. The maternal mortality and morbidity did not differ significantly between the three groups; neither did the perinatal mortality and morbidity.ConclusionEclampsia continues to be a major cause of both maternal and perinatal morbidity and mortality. Magnesium sulphate was equally effective in controlling seizures in the three groups.

INTRODUCTION

Eclampsia is an unpredictable, multisystem, life threatening emergency disorder unique to human pregnancy. It is defined as the occurrence of generalised convulsions associated with preeclampsia during pregnancy, labour or within 7 days of delivery and not caused by epilepsy or other convulsive disorders.[1] The incidence of eclampsia has often been viewed as an index of civilization in a country.[1]

Eclampsia probably accounts for 50,000 maternal deaths a year worldwide.[2] The maternal mortality in eclampsia ranges from less than 1% to nearly 20%, [3] while perinatal mortality ranges from 2 to 8.6% in the developed world [4] and upto 33.98% in the developing countries.[5] Serious complications occur in upto 35% of affected women.[6] Thus eclampsia remains one of the most common causes of maternal and perinatal mortality and morbidity. The primary aim of the study was to evaluate the incidence and demographics of patients with eclampsia in the southern part of Orissa, a state located in eastern India. Our secondary aim was to compare the obstetrical outcome with different regimens of magnesium sulphate therapy in eclampsia.

MATERIALS AND METHODS

The prospective randomized study was carried out in the department of Obstetrics & Gynecology, MKCG Medical

College and Hospital, Berhampur, Orissa, India, a tertiary level Government referral centre for whole of Southern Orissa over a 2-yr period. Ethics approval was obtained prior to starting the study and informed consent was obtained from all participants or their attendants (in case participants were unable to give consent).

All patients presenting with eclampsia during the said period were recruited into the study. Patients who were diagnosed with other causes of convulsions in pregnancy like cerebral malaria and epilepsy were excluded from the study. On admission, a detailed history was taken. Thorough clinical examination was done and a bedside test for proteinuria was performed. Laboratory investigations performed were complete blood count, liver function test, renal function test, fundoscopic examination and serum magnesium level determination (optional). Patients were randomly allocated by means of a random number generator into one of three anticonvulsant regimes as follows:

Group-A: Pritchard Regimen

Loading Dose: 4 g magnesium sulphate solution was given intravenously (i.v) over 3-5 minutes followed immediately by 5 g given by deep intramuscular (i.m) injection into each buttock (total 10 g).

Maintenance dose: 5 g magnesium sulphate solution was given i.m 4 th hourly till 24 hrs after delivery or after the last convulsion, whichever was later.

Group-B: Zuspan Regimen

Loading dose: 4 g magnesium sulphate diluted with 100 ml fluid was given i.v over 5-10 minutes.

Maintenance dose: 1 g magnesium sulphate was given i.v per hour till 24 hrs after delivery or after last convulsion, whichever was later.

Group-C: Sibai Regimen

Loading dose: 6 g magnesium sulphate diluted with 100 ml fluid was given i.v over 15-20 minutes.

Maintenance dose: 2 g per hour magnesium sulphate was given i.v till 24 hrs after delivery or after last convulsion, whichever was later.

In all the three groups, if convulsions persisted after 15 minutes of administrating the loading dose, 2 g of magnesium sulphate was given i.v at l g/minute. All patients were monitored on clinical criteria and maintenance dose was adjusted according to clinical response. Nifedipine was given orally as an adjuvant therapy in all patients who had systolic blood pressure (SBP) ≥160 mmHg and/or diastolic blood pressure (DBP) of ≥110 mmHg.

Patients with complications were managed jointly by obstetricians, nephrologists, cardiologists or ophthalmologist. The cause of death was determined from the clinical diagnosis. Postmortem examination was not undertaken in any case. Obstetric management was done as per the protocol in the department. Pearson's Chi-square test (χ^2) test was applied for statistical analysis in the three groups with respect to maternal mortality and morbidity and perinatal mortality and morbidity. A p value of < 0.05 was considered to be significant.

RESULTS

160 women presented with convulsions against a background of preeclampsia of which 2 were diagnosed with cerebral malaria and hence excluded. Patient demographics were similar in the three groups. Out of 4925 live births during the study period, there were 158 women with eclampsia, giving an incidence of 3.2 %. Majority were unbooked 154 (97.4%) and from rural areas 133 (84.2%). Patients in age group < 20 years were 70(44.3%), between 20-30 years, 85 (53.8%) & >30 years 3(1.9%).

Antepartum eclampsia occurred in 21(13.3%) patients; antepartum / intrapartum eclampsia in 108(68.3%) while postpartum eclampsia occurred in 29 patients (18.4%). Primigravidas accounted for 105/129 cases with antepartum & intrapartum eclampsia while primiparas accounted for 25/29 cases with postpartum eclampsia. In cases of antepartum &/ intrapartum eclampsia (129 cases), gestational age was between 28-34 weeks in 13 (10.0%), between 34-37 weeks in 27 (21.0%) & between 37-42 weeks (term) in 89 cases (69.0%). There was no post-term pregnancy in any group.

SBP was found to be normal (<160mm Hg) in 4/158 patients while DBP was normal (<90 mmHg) in5/158 patients. Proteinuria at admission was absent in 3/158 women. 1-2 episodes of convulsions occurred before start of anticonvulsant therapy in 24(15.2%) patients. 125/158(79.1%) patients had between 3-10 episodes of convulsions while 9(5.7%) patients had 11or more episodes of convulsions before start of anticonvulsant therapy.

There were 7 maternal deaths with 3 in Group A & 2 each in Groups B & C. Pulmonary edema accounted for majority (5/7) of these deaths (Table 1). Maternal morbidity was common with total combined morbidity occurring in 15(25.0%), 14(28.5%) & 13(26.55) women in each group (in Table 2).

Majority of the patients 75/158(47.45%) received magnesium sulphate at 4-8 hours after of onset of convulsions. 60 women received magnesium sulphate by Pritchard regimen (Group-A), while 49 each received magnesium sulphate by Zuspan regimen (Group-B) and Sibai regimen (Group-C) . There was no recurrence of convulsions in any patient after start of magnesium sulphate in both Groups A and C, whereas there was recurrence of convulsion in 1 patient in Group-B. Pain at the site of injection was present in 46/60 (76.6%) women in Group-A, 1 (2%), women in Group-B and 2 (4%) women in Group-C (Table 3). The dose of magnesium sulphate was temporarily suspended due to inadequate urination in 5 women in Group A, 3 in Group B and 4 in Group C. No other side effects were noted.

Vaginal delivery (including instrumental vaginal delivery) occurred in 46, 41 & 35 women in each of the three groups respectively (Table 4). Caesarean Section (CS) was done in 14(23.3%), 8(16.3) &13(26.55) women in the groups A, B & C respectively (Table 4). 167 babies were born to 157 mothers with 10 pairs of twins (Table 5). Babies with low birth weight were 43 (69.3%), 38(73.0%) & 40 (76.9%) in the groups A, B & C while the corresponding figures for live births were 46 (74.2%), 35(67.3%) & 36 (68.0%). 7 babies in Group A, while 6 each in Groups B&C were referred to neonatal intensive care unit of which 3 in Group A &1 each in Groups B & C expired.

The difference in rate of recurrence of convulsions between the three groups was not found to be statistically significant (observed value was 3.49 vs. value of χ^2 at p = 0.05 being 5.99). The difference in maternal mortality (observed value 0.67 vs. value of χ^2 at p = 0.05 being 5.99) as well as the maternal morbidity (observed value 0.2 vs. value of χ^2 at p = 0.05 being 5.99) was not found to be statistically significant. The perinatal mortality did not differ significantly between the three groups (observed value 1.69 vs. value of χ^2 at p = 0.05 being 5.99) and neither did the perinatal morbidity (observed value 0.10 vs. value of χ^2 at p = 0.05 being 5.99). The difference in the side effects of magnesium sulphate was statistically very significant (78.4 vs. value of χ^2 at p = 0.01 being 9.21), being maximum with Pritchard regimen and least with Zuspan regimen.

Figure 1

Table 1: Maternal mortality

Group	Cause of Death			Total
	Pulmonary Edema	ARF	CVA	
Pritchard (Group A=60)	2	--	1	3
Zuspan (Group B=49)	1	1	--	2
Sibai (Group C=49)	2	--	--	2
Total	5	1	--	7

ARF: Acute Renal Failure, CVA: Cerebrovascular Accident

Figure 2

Table 2: Maternal Morbidity

Morbidity	Regimen											
	Pritchard (Group A=60)				Zuspan (Group B=49)				Sibai (Group C=49)			
Liver Failure	13				14				12			
Renal Failure	10				12				13			
HELLP Syndrome	--				1				1			
Hypertensive Retinopathy (Grade)	I	II	III	IV	I	II	III	IV	I	II	III	IV
	4	-	-	1	1	1	-	-	1	-	-	-
Abruptio-Placentae	1				3				1			
PPH	-				-				1			
DIC	1				-				-			
MROP	1				-				-			
Chorio-Amnionitis	1				-				-			
Total	15				14				13			

HELLP: Hemolysis, Elevated Liver Enzymes, Low Platelets, PPH: Postpartum haemorrhage, DIC: Disseminated intravascular coagulation, MROP: Manual removal of placenta

Figure 3

Table-3: Side Effects of Magnesium Sulphate Therapy

Group	Regimen	Pain at Injection Site	Reduced Urinary Output
A	Pritchard (n=60)	46 (76.6%)	5 (8.3%)
B	Zuspan (n=49)	1 (2.0%)	3 (6.1%)
C	Sibai (n=49)	2 (4.0%)	4 (8.1%)

Figure 4

Table-4: Type of delivery

Group	Regimen	Vaginal delivery			Forceps	Ventouse	LSCS	Undelivered
		Delivered Outside	±MLE	Breech assisted				
A	Pritchard (n=60)	9	31	2	1	3	14(23.3 %)	-
B	Zuspan (n=49)	8	26	3	2	2	8(16.3 %)	-
C	Sibai (n=49)	9	23	1	1	1	13(26.5 %)	1

MLE: Mediolateral Episiotomy, LSCS: Lower Segment Caesarean Section

Figure 5

Table 5: Perinatal Outcome

Group	Regimen	No. of babies	BW <2.5kg	BW >2.5kg	LB	SB	Transfer to NICU	NND
A	Pritchard (n=60)	62	43	19	46	16	7	3
B	Zuspan (n=49)	52	38	14	35	17	6	1
C	Sibai (n=49)	53	40	13	36	17	6	1

BW: Birth Weight, LB: Live Birth, SB: Still Birth, NICU: Neontal Intensive Care Unit, NND: Neonatal Death

DISCUSSION

The incidence of eclampsia in our study was 3.2% or 1 in 44 maternities. Eclampsia complicates 1 in 2000 pregnancies in Europe [6] to 1 in 3250 pregnancies in the US[7] while in the developing world, its incidence is reported as 1 in 100 to 1 in 1700 pregnancies.[8, 9, 10] The incidence of eclampsia from other parts of Asia, notably Singapore is also quite low and parallels that of the developed world.[11, 12] The incidence in our study is higher than not only that of developed countries, but also that of most developing countries as well as the incidence reported in other parts of India. The only other study which gives an incidence higher than our study is the Dhaka Medical College and Hospital, Bangladesh which is the largest tertiary referral government hospital in Bangladesh and deals mostly with referral cases where the incidence of eclampsia is 9%.[13]

After the inception of the National Health Services in the United Kingdom, which allowed free comprehensive antenatal care for all, a significant reduction (90%) in the incidence of eclampsia occurred, probably as a result of early detection of preeclampsia and its management. In India, the incidence of eclampsia has varied, [5, 14] probably due to lack of a uniform national healthcare policy. The high incidence of eclampsia seen in our patients is indicative of major social deprivation similar to the Bangladesh population. Majority of our cases were unbooked; in unbooked cases, the signs and symptoms of preeclampsia remain unrecognised until severe complications such as eclampsia occur.[13]

The other important finding of our study was that magnesium sulphate administered according to the Zuspan regimen was as effective as Pritchard and Sibai regimen in controlling eclamptic seizures. Magnesium sulphate is not a conventional anticonvulsant. Its use gained worldwide popularity only after the publication of the landmark world health organization (WHO) sponsored Eclampsia Trial Collaborative Study[15] in 1995 which established the superiority of magnesium sulphate in preventing recurrent eclamptic seizures. However, it is a drug with a narrow therapeutic index. Besides, the long term effect on children whose mothers received magnesium sulphate is not very well known. Therefore it seems that administering the lowest effective dose would decrease the risks of overdose and side-effects.

The all cause maternal mortality in the study period was 67, of which a total of 7 women died due to eclampsia, giving a case fatality rate (CFR) of 4.4 % and maternal mortality ratio (MMR) of 10.44%, which is much less than that described by Chabbra and Kakani.[16] The difference in CFR was probably due to a larger sample size in the Chabbra study since the demographic profile was same in our study as compared to theirs. A recent Nigerian study, [17] showed a lower incidence of eclampsia (1.7%) as compared to our study. However, the CFR and MMR were much higher (20.65% and 20.7% respectively) in that study as compared to the present study, probably due to unavailability of magnesium sulphate.

Aspiration leading to pulmonary oedema was the major cause of maternal death in our study (57.1%). Majority of the women who died had complications other than convulsions .Liver failure was present in 6/7, renal failure in 6/7, HELLP syndrome 2/7, PPH 2/7 and DIC 1/7. Once a complication had already developed, magnesium sulphate could not prevent the sequelae of complications.[13]

Maternal morbidity was high (26.58%) and correlates with other studies.[6,13] There were a total of 50 still births and 5 neonatal deaths out of total of 167 deliveries in the 158 women with eclampsia; the proportion of perinatal mortality was not significantly different between the groups. The preferred mode of delivery in Western studies is CS even if estimated foetal weight is low, while the Indian trend continues to be more towards vaginal delivery, thus affecting the perinatal outcome.[14] Similarly in our study, the incidence of CS was less as compared to vaginal delivery.

Antenatal screening (by measurement of blood pressure and urine analysis) may prevent most eclampsia preceded by hypertension and proteinuria. However, as eclampsia with classic presentation is prevented, atypical presentation

becomes a proportionately greater problem. 4 of our patients had normal SBP on admission, 5 had normal DBP & 3 did not have proteinuria on admission. In the United Kingdom, 1/3 of women had only mild hypertension before the onset of convulsions.[6] In these cases there was often delay in diagnosis, apparently because of the belief that eclampsia "should" be associated with high blood pressures.

In view of the current theories of pathogenesis, the initial signs and symptoms of the syndrome are dictated by the site and extent of endothelial cell damage and not by a predetermined hierarchy.[6] Therefore, seizures may precede hypertension or proteinuria, i.e. in other words, the term preeclampsia is misleading because eclampsia can precede preeclampsia.[6] Hence, to achieve further reductions in the incidence of eclampsia, new screening and diagnostic tools need to be developed other than features of hypertension and proteinuria.[6]

In our study, only those women were classified as having antepartum eclampsia who were definitely not in labour at the time of admission to hospital. Eclampsia per se increases uterine contractility and labour may begin spontaneously shortly after convulsions ensue and progress rapidly.[17] As most of the women were received in labour with onset of convulsion - admission interval being 4-8 hours in majority, it could not be determined if the women had antepartum or intrapartum eclampsia. These women were classified as having antepartum / intrapartum eclampsia.

It is possible that these were actually cases of antepartum eclampsia with labour ensuing shortly, which cannot be verified. Preterm antepartum eclampsia is associated with higher rate of maternal complications and neonatal mortality.[6] Eclampsia is less severe when it develops post-partum.[6] We were not able to determine how many women had severe or mild preeclampsia before seizures occurred. It was also difficult to elicit history of premonitory symptoms in our patients with eclampsia.

The landmark WHO sponsored Eclampsia Trial Collaborative Study[15] established the superiority of magnesium sulphate in preventing recurrent eclamptic seizures. However, there is no consensus on the optimal dosage and concentration of magnesium sulphate for the management of eclampsia.[19] The most commonly used regimens are the Pritchard's [20, 21] and Zuspan's regimen, [22] also used in Collaborative Eclampsia Trial.[15] Besides, Sibai regimen is equally popular.[23] Various modifications of these regimens are also used.[24]

Magnesium sulphate when given by Pritchard regimen (Group A) and Sibai regimen (Group C) was 100% effective in controlling recurring convulsions and 98% effective in controlling convulsions in Zuspan regimen (Group B). Thus recurrent convulsions were controlled even with the low dose Zuspan regimen of magnesium sulphate in our study. The one patient who had recurrence of convulsions with Zuspan regimen had complications in the form of HELLP syndrome and ARF, and magnesium sulphate was omitted for a total of 8 hours before the recurrence of convulsion (1 episode) due to inadequate urination.

Our centre serves as a tertiary referral centre to the whole of southern Orissa and covers at least 6 districts within the state and one additional district in the adjoining state of Andhra Pradesh. The cohort of patients selected in this study can therefore be considered representative of the population. In conclusion, eclampsia continues to be a life threatening disease with significant morbidity and mortality. Magnesium sulphate was equally effective in controlling recurrent eclamptic seizures in the three groups.

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