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RESEARCH ARTICLE

COMPARISON OF LOW DOSE, SINGLE LOADING DOSE AND STANDARD PRITCHARD REGIMEN OF MAGNESIUM SULPHATE IN ANTEPARTUM ECLAMPSIA

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ABSTRACT

Aims and Objectives: To determine the safety and efficacy of low dose, single loading dose and standard Pritchard regimen of magnesium sulphate in treatment of Antepartum Eclampsia. To compare maternal and perinatal outcome in above three regimen groups.

Methodology: The present study is a prospective study conducted in the department of Obstetrics and Gynaecology at Government General Hospital, Ananthapuramu, during the period of July, 2014 – June, 2015 after obtaining clearance from Hospital Ethical Committee.

Results: The three groups were compared in terms of safety and efficacy of treatment, serum magnesium level, magnesium delivery interval, maternal and perinatal outcome. Low dose regimen groups have prevented seizures effectively in 93.4% cases. $MgSO_4$ toxicity was found less in the low dose groups. In group A 83.3% cases, in group B 80% cases and in Group C 76.7% cases were delivered vaginally and caesarean section was done for fetal and obstetric indications in 16.7% cases in Group A, 20% in group B and 23.3% in Group C which did not differ much in the three groups. There was no maternal morbidity or mortality in this study. The Perinatal mortality was 50% in group A, 35.4% in group B and 29% in group C.

Conclusion: The present study provides further strong support for the routine use of magnesium sulphate for Eclampsia. As long as there is adequate urinary output, clinical monitoring appears to be sufficient with no difference in maternal outcome.

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INTRODUCTION

Eclampsia still continues to remain the common cause of maternal mortality in developing world (Cunningham *et al.,* 2010). It is estimated to complicate 1 in 2000 deliveries in developed countries and 1 in 100 to 1 in 1,500 deliveries in developing countries. The maternal mortality rate is 2% worldwide (Andersgard *et al.,* 2006). The perinatal mortality rate in developing countries is as high as 80 (or) more per 1000 live births. Following Collaborative Eclampsia Trial (CET) with Eclampsia, magnesium sulphate was regarded as agent of choice for Eclampsia. It was Pritchard who suggested that the dose of magnesium sulphate should be limited[3]. The present study was undertaken to know the safety and efficacy of reduced doses of Magnesium sulphate as compared to standard dose and the maternal and foetal outcome.

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MATERIALS AND METHODS

The present study is a prospective study conducted in the department of Obstetrics and Gynaecology at Government General Hospital, Ananthapuramu, during the period of July, 2014 – June, 2015 after obtaining clearance from Hospital Ethical Committee.

Inclusion criteria

All women with Antepartum eclampsia

Exclusion criteria

1. Women who received magnesium sulphate or other anticonvulsants before reaching the hospital.
2. Women with antepartum eclampsia complicated either by cerebrovascular accident, aspiration pneumonitis, HELLP syndrome or renal failure.

Table 1. Mode of Delivery

Mode of Delivery	Group –A		Group –B		Group –C	
	No.	%	No.	%	No.	%
Vaginal	21	70	22	73.3	20	66.7
Forceps	4	13.3	2	6.7	3	10
Caesarean	5	16.7	6	20	7	23.3
Df=4			X^2 value = 1.095			

P value = 0.89

Table 2. Fetal Outcome (N=92)

Fetal outcome	Group –A (n=30)		Group –B (n=31)		Group –C (n=31)	
	No.	%	No.	%	No.	%
IUD	3	10	4	12.9	3	9.7
Intrapartum death	8	26.6	3	9.7	3	6.5
Alive	19	63.3	24	77.4	25	80.6

Table 3. Neonatal mortality rate accoding to fetal maturity (N=68)

Gestational age (weeks)	Group –A (n=19)		Group –B (n=24)		Group –C (n=25)	
	Cases	PMR	Cases	PMR	Cases	PMR
32 – 36	6 (31.5%)	4 (21%)	12(50%)	4 (16.7%)	12 (48%)	3 (12%)
≥ 37	13 (68.4%)	0	12(50%)	0	13 (52%)	0

Table 4. Comparison of seizure recurrence rate in three Groups (Niraj *et al.*, 2009; Mc Regmi *et al.*, 2010)

Seizure recurrence rate	Joshi *et al.*			Seth *et al.*			Present study		
	Prichard	Low	Single dose	Prichard	Low	Single dose	Prichard	Low	Single dose
	3.5%	12%	12.7%	7.7%	5%	15%	3.3%	6.6%	6.6%

Table 5. Comparison of mode of delivery in three groups (Niraj *et al.*, 2009; Mc Regmi *et al.*, 2010)

Study	Mode of delivery		
	Vaginal delivery (includes instrumental)		Caesarean section
Bankura *et al*.	89.7%		9%
Joshi *et al.*	89.1%		10.9%
Shaha *et al*.	91.5%		7.5%
Seth *et al*.	Pritchard	80.7%	15.4%
	Low	80%	20%
	Single dose	76.7%	23.3%

Table 6. Comparison of perinatal mortality in three groups (Begum *et al.*, 2001; Niraj *et al.*, 2009; Bissallah *et al.*, 2009; Shikha Seth *et al.*, 2010; Mc Regmi *et al.*, 2010)

Regimen Group	Authors	Perinatal Motalty
	Desai *et al.*	33.8%
	Sardesai *et al.*	25%
Pritchard	Seth *et al.*	62.9%
	Present study	50%
	Sardesai *et al.*	25%
	Bangal *et al.*	33%
Low dose	Seth *et al.*	40%
	Present study	35.4%
	Joshi *et al.*	24.8%
Single Loading Dose	Seth *et al.*	38%
	Gaddi *et al.*	39.3%
	Present study	29%

History

A detailed history regarding age, parity, gestational age, number of convulsions, history of imminent symptoms was taken from close relatives and also from the patient if she is conscious or taken retrospectively from her. Any past history of hypertension, renal disease or eclampsia in previous pregnancy were elicited.

Clinical Examination

A thorough general examination and obstetric examination were done. On general examination conscious level, temperature, pulse rate, respiratory rate, blood pressure, cardiovascular system, respiratory system, presence of anaemia, degree of edema, fundus examination were done. Urine was examined for Proteinuria. Blood sample was sent for random blood sugar, renal function tests, liver function tests, coagulation profile and viral screening.

Magnesium Sulphate Regimens

Group-A : Pritchard regimen (Pritchard *et al.*, 1984)

Loading Dose: 4 gm 20% $MgSO_4$ IV- slowly over 5 – 10 minutes 5 gm 50% $MgSO_4$ - deep IM in each buttock.

Maintenance dose: 5 gm of 50% $MgSO_4$ -deep IM every 4 hours in alternate buttocks, until 24 hrs after delivery or last fit.

Group-B: Low dose regimen

Loading Dose: 4 gm of 20% $MgSO_4$ -IV slowly over 5 – 10 minutes 2 gm of 50% $MgSO_4$ solution -deep IM in each buttock.

Maintenance dose: 2 gm of 50% $MgSO_4$ - deep IM every 3 hours in alternate buttocks,

Group-C: Single loading dose regimen

Loading Dose: 4 gm of 20% $MgSO_4$- IV slowly over 5 – 10 minutes 5 gm of 50% $MgSO_4$-deep IM in each buttock

Obstetric management

After stabilizing the patient, termination done with Tab-Misoprostol or Oxytocin or emecredyl depending on period of gestation and Bishop score. Caesarean section was done for fetal and obstetric indications. Neonatal outcome was recorded in terms of Apgar score and birth weight. Primary outcome measures are recurrence of fits and magnesium related toxicity. Secondary outcome measures are maternal and perinatal mortality in all the three groups.

Statistical analysis

Chi-square and one way ANOVA tests were used for comparing nominal and parametric data among groups.

RESULTS AND ANALYSIS

During one year study period, 90 Antepartum eclampsia cases were randomly selected and grouped into three groups namely A, B and C.Group A received Pritchard regimen, Group B received Low dose regimen and Group C received Single dose regimen. Most of the study subjects, 17 (56.7%) in Group A, 18 (60%) in Group B and 16 (53.3%) in Group C were teenagers. Eclampsia was more common in primigravida (80%) than multi gravida (40%). Eclampsia was more common after 36 wks of gestation but a significant number of cases were found between 28 – 32 wks in all the three groups. Most of the cases, 11/30 in group A, 13/30 in group B and 12/30 cases in group C had GCS level of 15. In group A 10/30 cases, 9/30 cases in group B and 11/30 cases in group C had GCS level between 12 – 14. Rest of the cases had a level between 8 – 11. It was noticed that 60 patients (70%) had severe hypertension ($\geq$ 160/110 mm Hg) in all the three groups. 21 patients in group A, 20 in group B and 19 patients in group C. Remaining 30 patients (30%) had blood pressure $\leq$ 160/110 mm Hg on admission (Duley, 2003; Montan, 1997)

Serum magnesium levels in all the three groups was almost equal. The levels were 4.79 mg/dl in group A, 4.05 mg/dl in group B and 4.02 mg/dl in group C. Most of the cases were induced with Misoprostol and oxytocin (50% and 42.3%) in group A, (66.6% and 18.5%) in group B and (65.2% and 21.7%) in group C. Few cases were induced with Emecredyl (7.7%%, 1.4.8% and 13.6% in three groups respectively). The P value is 0.346, which is insignificant. Out of 90 cases, 72 cases (70%) were delivered by vaginal route which also includes delivery by forceps application and rest of the 18 cases (20%) underwent caesarean section for fetal and obstetric indications. Amongst 90 cases, 42 cases were delivered within 12 hours and 48 cases between 13 – 24 hours, i.e. 10 vs 20 in group A, 15 vs 15 in group B and 17 vs 13 in group C. The P value was 0.175 which was insignificant. $MgSo_4$ related toxicity was observed as loss of DTR in 5 cases (16.6%) in group-A, but no case in the other two groups had toxicity. But dose was deferred in 7 cases (23.3%) due to loss of DTR in five cases and oliguria in two other cases.

There was no maternal morbidity and mortality in the present study. A total of 92 fetuses (two twins) from 90 women were evaluated and stillbirths included both intapartum and intrauterine deaths. Of these, 19 (63.3%) in Group-A, 24 (77.4%) in group B and 25 (80.6%) in group C were alive. Out of 68 live babies preterm vs term babies in three groups were as follows – 6 vs 13 in group A, 12 vs 12 in group B and 12 vs 13 in group C. Of all the 68 live babies, APGAR score at 5 mins was <7 in 33 babies that required NICU admission i.e., 57.8%, 45.8% and 44% in three groups respectively. Rest of the 28 babies had 7 to 10 APGAR. The majority of the babies had birth weight more than 2 kgs in all the three groups (73.7%, 54.2% and 48% in three groups respectively) as most of the study subjects were presented with eclampsia after 36 wks of gestation. In group A, 4/6 (21%) babies were preterm, in group B 4/12 (16.7%) babies and in group C 3/12 (12%) babies asphyxiated due to pre-maturity. There were 4/5 babies below 2 kgs weight in group A, 4/11 in group B and 3/13 babies in group C that expired due to low birth weight. The overall neonatal mortality was 21.05%, 16.7% and 12% in three groups respectively (Sibai *et al.,* 1985b). Perinatal mortality was 50% in Pritchard group compared to 35.4% and 29% in the other two groups as most of the babies delivered after long magnesium delivery interval and had low APGAR scores (Single Dose MgSo4 Regime, 2013).

DISCUSSION

Prevention of further seizures in eclampsia is associated with a reduction in adverse outcomes.

Magnesium is an ideal drug, wide safety and a readily available antidote in the form of calcium gluconate. In the present study, the total dose of low dose regimen (24 gms) used was just over half the dose (44 gms) used by Pritchard in Collaborative Eclampsia Trial. Another group which received single loading dose (14 gms) was one third of the dose used by Prichard. In a study by Seth et. al 57.7% cases in Pritchard group, 80% cases in low dose group and 70% cases in loading dose group had severe hypertension. The present study had the following number of cases with severe hypertension i.e., 70%, 66.6% and 63.3% in the three groups respectively which were comparable to Seth *et al.* study

The mean serum magnesium levels in the present study were within the therapeutic range in all the three groups. In various other studies recurrence rate was as follows – Pritchard reported in 12% of cases, Sardesai *et al*. in 7.8% cases, Gaddi *et al*. in 9.2% cases, Abdul *et al*. in 4.2% cases. In the present study, seizures were controlled in 94.5% cases and the result was almost similar to Seth *et al.* study. In Pritchard group 16.6% cases had toxicity which was comparable to the other two groups which had no toxicity. Studies have reported that toxicity was more apparent with serum magnesium levels of > 4.2 mg/dl. Majority of women had induced vaginal delivery i.e., 83.3% vs 16.7% in Pritchard group, 80% vs 20% in low dose group and 76.7% vs 23.3% in single dose group. Similar results were observed in many other studies. The present study results were correlating with Seth *et al* study.

Comparison of maternal morbidity in three groups (Begum *et al.*, 2001; Niraj *et al.*, 2009)

In various studies by different authors stroke, post partum psychosis, cortical blindness, renal failure were causes for maternal morbidity but in the present study there was no maternal morbidity at time of discharge. There was no maternal mortality in the present study.

Perinatal Outcome

The present study results were correlating with Seth et. al study in the three groups.

Conclusions

Eclampsia is still one of the most serious obstetric emergency. Magnesium sulphate is regarded as the anti-convulsant drug of choice for eclampsia. The low dose Magnesium sulphate regimens prevent convulsions effectively with no magnesium related toxicity (Bangal *et al.,* 2009; Narayan Jana and Dasgupta, 2013). The present study provides further strong support for the routine use of magnesium sulphate for eclampsia. As long as there is adequate urinary output, clinical monitoring appears to be sufficient. There is no significant difference in magnesium delivery interval in the three groups. There is no difference in maternal morbidity or mortality in the three groups. The perinatal mortality is low in low dose regimen groups. Even though eclampsia is unpredictable it is preventable with proper antenatal care and intensive management will largely reduce the incidence of eclampsia.

In conclusion, seizures can be safely controlled in Eclamptic women with a lower dose of magnesium sulphate, with the advantage of a lower magnesium related toxicity. Single loading dose regimen has an added advantage that repeated painful intramuscular injections can be avoided and is cost effective in developing countries like India.

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