Original Research Article

Comparative study of low dose magnesium sulphate regime with Pritchard regime in eclampsia

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Abstract

Introduction: Eclampsia is still a leading cause of maternal mortality and morbidity. Magnesium sulphate despite being an anticonvulsant of choice remains underutilized due to fear of toxicity. Average weight of Indian women is less than the western women due to which lower dose of magnesium sulphate can be used in treatment of eclampsia. The aim of the study was to compare the efficacy of low dose magnesium sulphate regimen with Pritchard regimen, in the control of convulsion in eclampsia. We also compared neonatal and maternal outcome in these two group. **Methodology:** This randomized control study was carried out at Emergency Labour room, Government Medical College, Nagpur. 160 patients of eclampsia were divided randomly into study group (n=80) receiving low dose MgSO4 and control group (n=80) receiving Pritchard regimen. The recurrence of convulsion, toxicity profile and maternal and fetal outcome was studied. **Results:** Majority of patients 73.75% were primigravida and 77.5% unbooked cases. 91.5% had antepartum/intrapartum eclampsia. 6 (7.5%) patients in study group had recurrence of convulsion as compared to 11 (13.75%) in Pritchard regimen group (p =0.31). Toxicity of MgSO4 in the form of lost tendon reflexes and respiratory depression was significantly less in those receiving Low dose of MgSO4 (p<0.001). Respiratory depression developed in one patient in control group and none in study group. Maternal mortality was 2.5% in both the groups. Perinatal mortality was 28.75% in the study group and 33.73% in control group. **Conclusions:** Low dose Magnesium sulphate regimen was equally effective in the control of convulsions in eclampsia and can be safely used in Indian women.

Key words: Eclampsia, Low dose, Magnesium sulphate

Introduction

Eclampsia is an obstetric enigma. It is one of the important causes of maternal and neonatal mortality and morbidity. Worldwide 50,000 deaths occurred due to eclampsia [1]. In developed country incidence had fallen considerably due to improved prenatal care. But in developing countries eclampsia incidence is still high. Reports published from 1976 to 2015 reveal that incidence of eclampsia in India ranges from 0.179 to 5%, the average being 1.5% [2]. Magnesium Sulphate is drug of choice and most preferred regimen is Pritchard regimen [3]. Jack A. Pritchard popularized magnesium sulfate therapy in eclampsia in modern obstetrics since 1975. But doubt still persists regarding suitable dose of $MgSO_4$ because serum magnesium level varies according to (maternal) weight [4]. Pritchard regime was formulated for woman weighing average 70 kg. But an Indian woman has an average weight of 49.4 ± 7.18 kg [5]. Witling also recommended an adjustment of dose according to patient's body mass index [6].

This initiated a research to modify the dose of magnesium sulphate in eclampsia.

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Materials and Methods

Study Design:-This randomized case-control study was carried out in the department of Obstetrics and Gynecology, Government Medical College & Hospital, Nagpur.

Study Setting:- Emergency Labor room/eclampsia room.

Study period:- June 2005 to November 2006

Approval was taken from Institutional Ethics committee of Government medical college Nagpur.

Study population/participants: All eclampsia patients, antepartum, intrapartum and postpartum, admitted in Emergency labor room.

Inclusion criteria: Diagnosed case of Eclampsia: Diagnosis of eclampsia has been established in accordance with National High Blood Pressure Working Group Report on High blood pressure in Pregnancy.

Exclusion Criteria: 1) Known case of epilepsy, 2) Meningitis and encephalitis, 3) Intracranial tumor or SOL.

Informed consent was obtained from the spouse or patient's nearest relative.

Detailed clinical examination was carried out in all the patient along with relevant investigation which include complete haemogram, KFT, LFT, Coagulation profile, fundus examination y & urine analysis.

Sample size- Sample size was calculated by assuming the power 80%. While considering the recurrence rate with Pritchard regime 10-20% and recurrence rate with low dose regime 7.89%, sample size was calculated as 160. According to randomization, they were allocated into 80 each in study and control group.

Randomization- At the time of admission the eclampsia patients were allocated to either study group or control group by tossing method.

Study group: Eclampsia patient received low dosage magnesium sulfate regime

Control group: received Pritchard regime.

***Protocol for low dose $MgSO_4$ [5]**

Loading dose: 4 gram (20%) of $MgSO_4$ (7.H2O) diluted in 12 cc of distilled water slowly intravenously over 15-20 minutes.

Maintenance dose: 2 gram (50%) of $MgSO_4$ given intramuscularly every 3 hourly was continued for 24hr after delivery or after last convulsion which ever occur later.

For Recurrence of convulsion: If the convulsion occurred half an hour after receiving loading dose called recurrence of convulsion, additional dose of 2 gm (20%) of $MgSO_4$ given I.V. diluted in 6 cc of distilled water. If again the recurrence of convulsion occurs, another anticonvulsant drug, Inj. Phenytoin Sodium 100mg was added intravenously.

Before giving each dose of $MgSO_4$ following parameter were checked

1. Knee Jerk (patellar reflex)
2. Urine output – It should be more than 100 ml in 4 hr or more than 30 ml/hr
3. Respiratory rate- more than 16

Anti hypertensive therapy: Nifedipine 10 mg was given either sublingually or orally as an adjuvant for control for hypertension. Hydration was maintained by Ringer lactate solution 1000cc over 24hr.

When the patient was stabilized obstetric management was carried out according to bishop score, gestation age & viability of fetus.

Outcome measures: (1) Recurrence of convulsion, (2) Toxicity profile, (3) Maternal mortality and morbidity, (4) HELLP, (5) DIC(Disseminated Intravascular coagulation), (6) Pulmonary edema, (7) Intra cranial hemorrhage, (8) Post partum hemorrhage.

Perinatal Outcome was measured as (1) Still birth, (2) Low birth weight and (3) Neonatal death.

Statistical Analysis: Mean, Standard deviation and P value was calculated using statistical formulas (epi-info software). T-test, z-test and Chi-square test was used. P value < 0.05 was called as statistically significant.

Results

There were 180 cases of eclampsia among 24,680 deliveries at our institute which gave an incidence of 0.72%.

Table-1: Demographic profile of cases & controls.

Variables	Study group Cases (n=80)	Control group(n=80)
Age(years) ± SD	23.5 ± 2.7	23.4 ± 3.04
Weight(Kg) ± SD	47.4 ± 4.35	48.37± 5.8
Gestational age(wks)	36.9	37
Unbooked patients (unsupervised) (%)	61 (76.25%)	63 (78.75%)
Primigravida (Parity)(%)	59 (73.75%)	58 (72.5%)

Patients were weighted on 3rd and 4th day of delivery when ambulatory. Average weight in study and control group was 47.4± 4.35kg and 48.37± 5.84 kg respectively. Weight distribution in study and control group was similar. Mean gestational age in the study and control group was 36.9 weeks and 37 weeks respectively. Most of eclapmsia patients were primigravida 73.75% and 72.5% in study and control group respectively. Most of the eclampsia patients, total 124 (77.5%) out of 160 had unsupervised pregnancy.

Table-2: Types of Eclampsia in Study and Control group.

Type of Eclampsia	Study group (n=80)	Control group (n=80)	TOTAL 160
Antepartum /Intrapartum	74 (92.5%)	72 (90%)	146 (91%)
Postpartum	6 (7.5%)	8 (10%)	14(9%)

74 (92.5%) patients of study group and 72 of control were having antepartum/ intrapartum eclampsia. Only 6 among the study group and 8 among control developed total 9% developed convulsions after delivery**.**

Table-3: Recurrence of convulsions in Study & Control group.

Convulsions	Study group (n=80)	Control group (n=80)	P val
None	74 (92.50%)	69 (86.25%)	
One	4 (5%)	11 (13.75%)	
Two	2 (2.50%)	0	p=0.31

Control of convulsions after receiving loading dose was 92.5% in study group and 86.25% in control group. 6 cases in study group and 11 in control group had recurrence of convulsions which was controlled with one or two additional doses of MgSO4 doses and the difference was statistically not significant.

Table-4: Toxicity profile in Study and Control group.

Toxicity profile	Study group (n=80)	Control group (n=80)	P value
DTR absent	6 (7.5%)	28 (35%)	**P <0.001**
Respiratory depression	0	1 (1.25%)	
Coma	0	0	
Total	**6**	**29**	

(DTR—Deep tendon reflexes)

D**ifference in toxicity was statistically highly significant (p < 0.001)** Absent DTR was in seen in 7.5% and 35% in study and control group respectively. One patient in control group developed respiratory depression needing assisted ventilation and calcium gluconate supplement. Thus the difference in toxicity was statistically **highly significant**.

Table-5: Maternal Complications.

Causes	Study group (n=80)	Controls (n=80)
1. Mortality	2 (2.5%)	2(2.5%)
2. DIC	5 (6.25%)	2 (2.5%)
3. Pulmonary odema	1 (1.25%)	2 (2.5%)
4. APH	0	2 (2.5%)
5. HELLP	1(1.25%)	3 (3.75%)
6. Intracranial Hemorrhage	1(1.25%)	0
7. LVF	0	1(1.25%)

(APH-Antepartum Hemorrhage, LVF-Left ventricular failure, DIC-Disseminated Intravascular coagulation)

Maternal mortality was equal in both group 2.5%. It was due to complication of eclampsia .In study group 8 patient & 10 patient in control group developed complication. The study group cause of death in first patient was HEELP with DIC with PCF (peripheral circulatory failure) and other had intracranial hemorrhage. Maternal mortality in the **control group** was **2 (2.5%).** Cause of death was LVF with pulmonary edema and other patient DIC (Disseminated Intravascular coagulation) with hypoxic brain injury. 5 cases in study group and 2 in control developed DIC.

Table-6: Perinatal Outcome.

	Preterm/Term	Study group (n=80)	Control (n=80)
1.Livebirth		64(80%)	61(73.50%)
	Preterm	10	7
	Term	47	48
2.Stilbirth		16 (20%)	22(26.50%)
	Preterm	12	13
	Term	4	9
3.Neonatal Death		7 (11.25)	6(7.22%)
	Preterm	5	5
	Term	2	1
4.Perinatal Mortality		23 (28.75%)	28 (33.73%)

(P value = 0.86)

64(80%) out of 80 in study group and 61(73.5%) out of 83 in control group had Live birth. Perinatal mortality in study group was **23 (28.75%)**. There were 16 Stillbirths, out of these 12 were preterm and 4 were IUD. 2 Intrapartum deaths, one due to complication of forceps and other due to birth asphyxia. Perinatal outcome in the form of live births was 80% and 76% respectively in study and control groups. In the control group perinatal mortality was **28 (33.73%)**. 22 were stillbirths out of them 13 were preterm and 9 were term. 10 were IUD. Maximum fetus weighted <1.5kg. 4 were intra-partum death. Neonatal deaths were 6; 5 were preterm and 1 was term. Cause of death in most of the neonates was prematurity.

Discussion

Magnesium sulphate has been recommended by WHO as the effective and safe drug for prevention and control of convulsions in eclampsia [7]. Suman Sardesai et al proved low dose Magnesium sulphate regimen was as effective as Pritchard regimen in control of convulsions in Indian women weighing average 48.4± 6.7 kg. Considering the effectiveness of this regimen the present study was undertaken [5]. Average maternal weight in the study and control group was 47.4± 4.35 kg and 48.37± 5.8 kg respectively. There was no statistically significant (p=0.23) difference. This was similar to mean weight reported in other Indian studies. Whereas due to good antenatal care in developed country like UK its 0.05%. Majority of cases in study

group were antepartum and intrapartum eclamsia. Similar observations were found in other Indian studies [8,9,10,11]. Eclampsia a disease of primigravida, incidence was 73.75% in our study, 89.7% in Jana et al, 75% in Pritchard. Similar observations were made by other authors [12,13,14,15].

Most of our patients of eclampsia were unbooked (unregistered with health system) and never received any antenatal checkup which remains the cornerstone in prevention of eclampsia. Similar observation were found in Ekelea et al and other studies [16,11,9].

Eclamsia is a sequel to uncontrolled and elevated blood pressure therefore regular ANC screening and treatment of pre-eclampsia remains the key factors in treatment of Eclampsia. The Collaborative group had concluded that there was compelling evidence in favor of magnesium sulphate for treatment of eclampsia but it was seen that healthcare personal are reluctant to administer it, prefer Diazepam or phenytoin sodium due to fear of potential toxicity of MgSO4. Timely managed (by giving loading dose) and early referral/ transportation of these patients to hospital could prevent maternal and foetal catastrophe, if MgSO4 given at primary health care in low dose without fear. Magnesium has narrow therapeutic index (4-7 meq/L). A higher number of patients lost DTR with Pritchard regimen than low dose regimen with Begum et al & Shilva et al [17].

Respiratory depression is a major threat while using MgSO4. One patient of control group developed respiratory depression while 3 cases developed respiratory depression with Pritchard regimen. None developed respiratory depression with low dose regimen in present study [4,8,9,18].

Seizures were well controlled in study group except in 7.5% who developed recurrence of convulsion. Similar observations seen in Suman Sardesai , Ruchira Nautiya while Begum et al reported only one case of recurrence. Recurrence rate with Pritchard regimen was 10 to 20% quoted by Pritchard et al and Sibai et al. It therefore seems that a lower dose of MgSO4 was equally effective in managing eclamptic convulsions [19].

Maternal mortality due to eclampsia ranges from 0.4-1.4% depending on severity of organ damage and delay in treatment. In present study maternal mortality was similar in study and control group. No maternal mortality was observed with Rashida et al and Ruchira et al. Jana et al observed low maternal mortality [8,9,12]. In present study perinatal mortality in study and control group was 28.75% & 33.73% respectively. Perinatal mortality was 16% with Rehan Ahmad, 33.78% Suman Sardesai and 32% Shiva [5,13,17].

Conclusions

1) Low dose regimen is a viable alternative to standard dose of Pritchard regimen in cases of eclamptic women in developing countries. It should be used in all general hospitals and tertiary care centers.

2) Due to low toxicity profile and equally effective compared to Pritchard regimen low dose MgSO4 should be used at primary health centre and rural hospitals before referrals.

3) Being a comparative study between two widely popular regimens with small sample the findings need to be confirmed in large multicentre trial.

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