

EFFICACY OF SINGLE LOADING DOSE OF MAGNESIUM SULFATE IN ECLAMPSIA

Meenakshi S. Devarmani, Neeta Harwal

1. Professor. Department of Obstetrics & Gynecology, M.R. Medical College, Gulbarga, Karnataka.
2. Professor. Department of Obstetrics & Gynecology, M.R. Medical College, Gulbarga, Karnataka.

CORRESPONDING AUTHOR

Dr. Meenakshi S. Devarmani,
Professor, Department of Obstetrics & Gynecology,
M. R. Medical College, Sedam Road,
Gulbarga- 585 105, Karnataka, India.
E-mail: drssdevarmani@gmail.com
Ph: 0091 9845221901

ABSTRACT: BACKGROUND: Eclampsia is a life threatening condition and it varies from countries to countries. The incidence in our country varies from 5-10%. The first and foremost thing in management of eclampsia is control of convulsions. Magnesium sulphate has established itself as the drug of choice for the anticonvulsant management of eclampsia but the question as to what constitutes the Minimum effective dose remains unanswered which is evident from the different regimens used in clinical practice. Its narrow therapeutic range mandates that it only be used in the minimum doses which gives efficient control of convulsions and helps in improving maternal and fetal outcome. **Aims:** To study the efficacy and safety of single loading dose of magnesium sulphate in controlling and prevention of recurrence of convulsion in eclampsia, to reduce the adverse affects of magnesium sulphate and improve the maternal and fetal outcome with single loading dose. **Methods:** Prospective study of 100 cases with clinical diagnosis of eclampsia were given single loading dose of magnesium sulphate [4 g of 20% IV and 10 g of 50 % IM], there was no maintenance dose. The effect of single loading dose of magnesium sulphate in controlling convulsions, the recurrence rates, toxicity and the maternal and fetal outcome was studied. **Results:** The results showed a favorable outcome with the reduction of the dose and duration of magnesium sulphate therapy. The primary outcomes were comparable with all other regimens in use. With recurrence rate of 9% its efficacy was comparable with the other regimens in use. The cases that were on single dose regimen had a significantly lower incidence of cesarean section with up to 74% of the patients having vaginal deliveries. The maternal mortality was 3% and perinatal mortality was 29%. **Conclusions:** Single loading dose of magnesium sulphate is effective in controlling and prevention of recurrence of convulsions in eclampsia. The single most advantage of this regimen was the complete absence of any incidence of magnesium sulphate toxicity and it is easy to administer in any place. Painful injections and monitoring of magnesium sulphate toxicity seen in maintenance dose can be avoided with this regimen.

KEYWORDS: Eclampsia; Magnesium sulphate; Low dose magnesium sulphate.

INTRODUCTION: Eclampsia now a rare disease in developed countries (1:2000 deliveries) where modern antenatal care is available to all pregnant women, as a result preeclampsia is detected early and treated effectively so that the convulsive stage is seldom reached. The

picture is very different in many developing countries (1:100 to 1:1700) particularly in rural areas where eclampsia may present for treatment in deep coma after many fits at home.

The first and foremost principle of management of eclampsia is control of convulsions. In the recent years with many large studies demonstrating the superiority of magnesium sulfate over other drugs for preventing and controlling eclampsia, magnesium sulfate has become the first line and preferred drug of choice for treatment and prevention of seizures.¹

Various regimens with different dosages have "been used over the years, question still remains about the 'minimum effective dose' of magnesium sulphate. "If a woman is known to be or appear to be small, the dose should probably be limited".²

Materials and methods: The present study group was 100 patients with eclampsia admitted in the labour room of Basaveshwar teaching and general hospital and Sangameshwar hospital, Gulbarga attached to Mahadevappa Rampure medical college, Gulbarga. The study was started on January 2007. All women with clinical diagnosis of eclampsia were eligible for the study, irrespective of when or where the fits occurred, whether pregnancy was singleton or multiple. A clinical history, thorough physical examination and detailed investigations were carried out for each patient. All the patients were cared for in the eclampsia labour room with intensive monitoring and frequent observations for vital signs. The patients were shifted to postpartum ward only after complete stabilization. Serum magnesium levels were not done due to lack of facilities.

Patients who were throwing convulsions were placed in left lateral position, airway secured; throat suction done, oxygen given if necessary, IV line secured, and urinary catheter inserted mouth gag used to prevent injury to the tongue. Fluid balance was maintained with strict input and output chart. Antibiotic prophylaxis was given to all cases to prevent infection

The single dose magnesium sulphate regimen consisted of: 4 grams of magnesium sulphate as 20% MgSO₄ got by adding 4 ampoules of 50% MgSO₄ in 12 ml of distilled water as IV given slowly over a period of 3-5 minutes promptly followed by 5 grams of 50 % solution (5 ampoules of 50% MgSO₄) injected deep IM in the upper and outer quadrant of one buttock through a 3 inch long, 20 gauge needle.

The effect of single loading dose of magnesium sulphate in controlling convulsions, the recurrence rates, toxicity and the maternal and fetal outcome was studied.

Antihypertensive Management:

All the cases were given oral nifedipine, amlodipine and hydrochlorthiazide were used after the BP was stabilized.

Obstetric Management:

Depending on the favorable state of cervix induction was done using prostaglandin gel, misoprostol vaginal/oral tablets, ARM and oxytocin infusion was used for augmentation of labor. In unfavorable and unresponsive cervix and with other obstetric indications cesarean section was done.

RESULTS: Clinical features: Majority of the patients (55%) belonged to the age group between 21-29 years. 80 % of the cases belonged to the lower socioeconomic class. 70 % of the cases were not booked. 71% patients were primi-gravida. 9 Patients gave history of preeclampsia during their past pregnancy and 2 patients had history of eclampsia in the past. Headache was

ORIGINAL ARTICLE

the dominant premonitory symptom and it was present in 78 cases followed by vomiting. 5 cases had blindness before the onset of convulsion.

Physical examinations: Most of the patients had MAP between 110 -130 mm Hg (60%). Majority had less than 3 episodes of convulsion; only two cases had more than 10 episodes of convulsions. Majority of the patients (84%) of the patients were brought to the hospital within 6 hrs of onset of convulsion which shows the prompt referrals and improved transport facilities the deficiency of which were responsible for the poor outcome in earlier years. Majority (36%) were in the gestational age 33 to 36 weeks. Pedal edema was present in 72% of the patients.

Investigations: Renal parameters were raised in only 10 % of the patients. 46% had grade-1 hypertensive changes on fundoscopic examination, 5% had grade 3 changes one patient had retinal detachment, which improved on post-natal day 5 with conservative management.

Outcome: 76% of the cases delivered within 12 hours. Those who took longer time were remote from term. Out of 100, 26 patients underwent cesarean delivery whereas 74 delivered through vaginal route. Maternal complications were occurred in 41 patients with most post partum hemorrhage. None of the complications were directly related to magnesium sulphate except thrombophlebitis and injection abscess. 3 out of 100 cases of eclampsia died, one patient died because of intracranial hemorrhage on post natal day 4 (CT showed hemorrhage in the right frontoparietal region with intraventricular bleed). One patient died because of cortical venous thrombosis on postoperative day 6 (patient was in coma for three days). One patient died due to hypovolemic shock, she was G3P2L2 with intrauterine death with abruptio with severe anemia delivered a still born baby, patient had PPH and developed HELPP syndrome following delivery. Mortality was due to complications of eclampsia and not solely due to magnesium sulphate administration. The first case was switched over to Pritchards regimen as she had recurrence of convulsion after 6 hours. In the remaining two cases, only single dose magnesium sulphate was given. Fetal outcome: At delivery- 73 cases had live birth following delivery. 15 still born cases, 5 abortus and 7 IUD were found. Fetal weight- 55 were in range of 1.6-2.5 kgs, 22 babies were in 1-1.5 kgs. 9 babies were having <1kg weight. APGAR score in 48 cases was <5 at 1 min and 9 cases showed <5 at 5 minutes. Unfortunate outcome observed in 29 cases, out of which 13 were still births and neonatal death occurred in 16 cases.

DISCUSSION: The incidence varies from developing to developed countries. The incidence of eclampsia varies from 1 in 100 to 1 in 1700 in developing countries and 1 in 2000 in developed countries.³ The incidence of pregnancy induced hypertension varies from 5-10%, the incidence of preeclampsia varies from 2-8% (magpie), and the incidence in India varies from 1-5%.³

The developed world has a much lower rate of this complication incidence in UK 4.9/10,000 with a case fatality rate of 1.4%. (RCOG Guidelines 10;2005).⁴

More than half the cases are antepartum, and approximately 20% of the cases occurred post partum. Maternal Mortality is 4 to 6% and the perinatal loss is 45% and the perinatal loss is 45% (ICOG Study).⁴

The use of magnesium sulphate in treatment and monitoring of pregnant women with eclampsia and pre eclampsia is well known since centuries. Pritchard JA from U.S.A. in 1955 gets the credit of popularizing magnesium sulphate therapy for eclampsia and his regime is popularly known as "Pritchard's Regime introduced at the Parkland Memorial Hospital."⁵

The Collaborative Eclampsia Trial (CET) published in 1985 found a lowered risk of recurrent convulsions with little difference in maternal, perinatal morbidity and mortality comparing magnesium sulphate with diazepam and phenytoin and concluded that "that there is

ORIGINAL ARTICLE

now a compelling evidence in favour of magnesium sulphate rather than diazepam or phenytoin in treatment of eclampsia". Similar findings were also reported by Crowther et al⁶ in their study. Friedman et al, Appleton et al⁷ and Lucas et al⁸ in different studies established the superiority of magnesium sulphate over phenytoin validating its long practiced use.

In 1997 Suman Sardesai et al⁹ used the "Low dose magnesium sulphate regimen" in their care centre and published encouraging results with "reduced dose of magnesium sulphate". Our results in terms of clinical features were similar with that study.

In 2002 the results of the 'Magpie trial' another large multicentric trial was published which showed beyond any reasonable doubt the efficacy of magnesium sulphate in reducing the risk of eclampsia.

The present study was started to study the efficacy and safety of single loading dose magnesium sulphate in treatment and prevention of recurrence of convulsions in eclampsia. Results were correlated with other compatible similar studies which are mentioned in table no 1. 71 % of the patients had 3 or lesser number of convulsions, 24 % had 4-6 episodes of convulsions. Convulsions may vary from 1 or 2 in mild cases to even 100 or more in severe and untreated cases or status may ensue (Cunningham et al).¹⁰

92% of the patients had proteinuria. Proteinuria is a feature of glomerular dysfunction and its presence with hypertension doubles the risk of perinatal death (Athula Kaluarachchi 1998).

In the present study 09 cases out of 100 showed a recurrence of convulsions, which is comparable with any of the other standard regimens in use today. One patient had recurrence within one hour and she continued to convulse even after the standard regimen was followed. Details of single dose and recurrence are mentioned in table no 2.

The results showed a favorable outcome with the reduction of the dose and duration of magnesium sulphate therapy and raises questions about whether the high dose regimens are really necessary and safer. The single most advantage of this regimen was the complete absence of any incidence of magnesium sulphate toxicity. The cases that were on single dose regimen had a significantly lower incidence of cesarean section with upto 74% of the patients having vaginal deliveries.

The maternal and perinatal outcomes were also comparable with the other regimens. The maternal mortality was 3%. Perinatal mortality in the present series was 29 % which was comparable with the other regimens considering the fact that almost half of the patients being preterm.

CONCLUSION: Though there appears to be no doubt on magnesium sulphate being the first line drug, the question as to what constitutes the 'Minimum effective dose' remains unanswered which is evident from the different regimens used in clinical practice.

The pioneers of magnesium sulphate therapy like Pritchards and Sibai themselves have opined that each hospital should have their own protocol to suit their patients. The fact that magnesium sulphate is not a safe drug and its narrow therapeutic range mandates that it only be used in the minimum doses which gives efficient control of convulsions and helps in improving maternal and fetal outcome.

ORIGINAL ARTICLE

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Table no 1:

Study	Pritchard et al ⁵ (1955)	Sibai et al (1990) ¹¹	Magpie (2002) ¹²	Sardesai et al (2003) ¹³	Present study(2007)
Recurrence of convulsions	12.1	14.1	0.8	7.8	9
Maternal mortality	0.4	0.4	2.6	0.2	3
Perinatal mortality	15.7	11.8	11.4	28.5	29

*figures in the table are in percentage forms

ORIGINAL ARTICLE

Table no 2: details of single dose and recurrences

Total cases	No. of convulsions	Convulsion to admission interval	MAP on admission	Type of eclampsia	Therapy to delivery interval	Anticonvulsant used
<1 hour						
	12	2 hr	100	A	8 hr	Single dose+ Pritchard's regimen+ Phenytoin+ Diazepam
4 hours (3 cases)						
	4	6	140	A	7 hr	Single dose+ Pritchard's regimen
	5	4	126	A	8 hr	Single dose+ Pritchard's regimen + Phenytoin
	4	4	106	A	8hr	Single dose+ Pritchard's regimen
5-10 hours (4 cases)						
	4	8	140	A	8 hr	Single dose+ Pritchard's regimen
	4	1	123	A	9 hr	Single dose+ Pritchard's regimen
	5	6	116	A	8 hr	Single dose+ Pritchard's regimen +Phenytoin
	2	4	120	I	4hr	Single dose+ Pritchard's regimen
11-15 hours						
	5	2	113	A	10 hr	Single dose+ Pritchard's regimen