International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2017; 1(2): 05-08
Received: 02-09-2017
Accepted: 04-10-2017

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Use of loading dose of magnesium sulphate versus standard regime for prophylaxis of severe Pre-Eclampsia- A comparative study

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Abstract
Background: Preeclampsia is a pregnancy specific multi organ disease process characterized by de novo development of hypertension and proteinuria after 20 weeks of gestation. Preeclampsia complicates 2-8% of pregnancies. Present study is carried out to determine the efficacy and safety of only loading dose of magnesium sulphate versus the standard regime in the patients of severe preeclampsia.
Materials and Methods: Severe preeclampsia patients were randomly categorised into Group-A (control group) (n=50) and Group-B (study group) (n=50). Patients in the study group received only the loading dose of magnesium sulphate and in the control group the loading dose of magnesium sulphate followed by the maintenance dose every four hourly. Patients in both the groups were monitored closely after the initiation of therapy. Results obtained were statistically analyzed.
Results: The mean age of the patients was respectively 24.3 years and 24.60 years. It was observed that most of the patients were primigravidas. In regard to their gestation age, the majority were of term gestation with mean gestation age between 37-40 weeks in both the groups. Out of 50 patients who received prophylactic dose nobody had convulsions whereas 2 patients had convulsions in the group who didn't receive. There was significant difference of knee jerk and oliguria among patients receiving Modified Pritchard's and Loading dose only. 8 babies were admitted in NICU who had received injection magnesium sulphate whereas 13 babies had NICU admission in those who didn't receive the injection. There was no significant difference in the maternal and perinatal outcome in the study.
Conclusion: Loading dose of magnesium sulphate is an efficient prophylactic in preventing convulsion in severe preeclampsia patients

Keywords: Loading dose, Magnesium sulphate, pre-eclampsia

Introduction
Preeclampsia is a pregnancy specific multi organ disease process characterized by de novo development of hypertension and proteinuria after 20 weeks of gestation. They are important causes of maternal morbidity and mortality for women and her child, although outcome is often good [1].

Together preeclampsia – eclampsia account for 40,000 maternal deaths every year with most of the mortalities occurring in the developing countries. In India, they account for 5% of all maternal deaths with most of them occurring due to eclampsia [2].

Seizure prevention is an integral part of preeclampsia management apart from the control of blood pressure and delivery of the feto – placental unit. For decades anticonvulsant drugs have been given to women with pre-eclampsia in the belief that they reduced the risk of seizure and so improve outcomes. Magnesium sulphate is the drug of choice for women with eclampsia [3].

The conventional regime of magnesium sulphate is an empirical approach developed over the years based on its clinical efficacy. These regimes which were initially used for the treatment of eclampsia were empirically extended to the management of preeclampsia, although the rationale was unclear. Administration of magnesium sulphate requires regular supervision by trained staff, which is costly, and higher doses may be associated with a greater risk of side effects, it is particularly important to assess the minimum effective dose and duration of treatment [4].

Furthermore with a randomised controlled trial showing that seizures can be effectively controlled in cases of eclampsia by giving only the loading dose, it can be hypothesised that there is role of less doses of magnesium sulphate than the existing regimes in the prevention of seizures in patients of severe preeclampsia. Hence, present study was aimed to compare the efficacy of loading dose of magnesium sulphate versus the standard regime in the management of pre- eclampsia to prevent seizures.

Materials and methods

Present study was carried out in the Department of Obstetrics and Gynaecology over a period of one year. During the study period, Severe preeclampsia patients were randomly categorised into Group-A (control group) (n=50) and Group-B (study group) (n=50) by randomisation. Ethical clearance was taken before the commencement of the study.

Pre-eclampsia is considered severe in patients beyond 20weeks of pregnancy or during labour having one or more of the following criteria- Systolic BP of 160mmHg or higher and diastolic BP of 110mmHg or higher in two occasions at least 6 hours apart while the patient is at bed rest, proteinuria of 5g or higher in 24 hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart (even if BP is in the mild range), oliguria or less than 500ml in 24 hours, cerebral or visual disturbance, including altered consciousness, persistent headache, scotoma or blurred vision, pulmonary oedema, epigastric or right upper quadrant pain or elevated serum liver transaminases without a known cause, impaired liver function, thrombocytopenia, with platelet count ≤ 100,000/µl, fetal growth restriction, micro angiopathic hemolytic anaemia (raised bilirubin >1.2mg%, LDH >600IU/L, low haptoglobin).

One group received 4 gm intravenous MgSO4 on admission which was prepared by diluting in 10 ml normal saline and was given over 10-12 minutes slowly with strict vitals monitoring. 50 patients of severe pre-eclampsia with BP>160/110 mm of Hg were given the prophylactic dose and rest 50 acted as controls. Strict monitoring of BP, urine output; respiratory rate and FHS was done. Detailed history, clinical examination and investigations (complete blood count, urine analysis for proteinuria, liver and renal function tests, serum LDH, coagulation profile, evidence of hemolysis in peripheral blood smear, obstetric ultrasound with colour doppler). Daily BP, urine output, urine albumin and FHS record were strictly monitored from admission up to 2 days after she delivered. Patients with chronic hypertension and those with pre-existing renal compromise were excluded from the study. The data collected from the following observations were statistically analyzed using Fischer's exact test, Chi- square test and student t test.

Results

The mean age of the patients was respectively 24.3 years and 24.60 years. It was observed that most of the patients were primigravidas (48% in cases and 52% in controls) (Table 1). (Table 1).

In regard to their gestation age, the majority were of term gestation with mean gestation age between 37-40 weeks in both the groups (Table 1).

Out of 50 patients who received prophylactic dose nobody had convulsions whereas 2 patients had convulsions in the group who didn't receive. (Table 2)

There was significant difference of knee jerk and oliguria among patients receiving Modified Pritchard's and Loading dose only. (Table 3)

8 babies were admitted in NICU who had received injection magnesium sulphate whereas 13 babies had NICU admission in those who didn't receive the injection. (Table 4) Maximum systolic and diastolic blood pressure in both the groups is shown in Table 5.

Table 1: Distribution of Baseline patient characteristics

Age	Patient who received magnesium sulphate	Patient who did not received magnesium sulphate	P value
<20	15	10	
20-25	20	21	
26-30	11	12	
>30	4	7	0.85
Mean	24.30±2.25	24.60±3.45	
Gravida-Status			
Primigravida	24	26	
Gravida-II	14	13	
Gravida-III	10	6	0.42
Gravida-IV	2	5	
Gestational age			
<28 weeks	0	1	
28 to 34 weeks	4	1	
34 to 37 weeks	8	12	
37 to 40 weeks	30	23	0.46
40 to 42 weeks	8	13	

Table 2: Occurrence of Convulsion in Both the Regimens

Occurrence Of Convulsion	Present	Absent	Total
Group-A(n-50)	2	48	50
Group-B (n-50)	0	50	50

Table 3: Morbidity due to use of magnesium sulphate

Morbidity	Modified Pritchard's (n=50) (%)	Loading dose only (n=50) (%)	p-value
Absent knee jerk	8(16)	0	0.016
Oliguria	4(8)	0	0.026

Table 4: Neonatal outcome.

	Received MgSO4	Did not receive MgSO4
NICU admissions	08	13
FSB	02	04

Table 5: Maximum systolic and diastolic blood pressure.

Max systolic BP in mm of Hg	Modified Pritchard (n = 50) (%)	Loading dose only (n = 50) (%)	p- value
< /= 160	28	36	0.085
> 160	22	14	

Max diastolic BP in mm of Hg	Modified Pritchard (n = 50) (%)	Loading dose only (n = 50) (%)	p- value
</= 110	34	38	0.410
> 110	16	12	

Table 6: Serum Magnesium Level

Serum Magnesium Level	1-2mg/dl	2.1-3mg/dl	3.1-4mg/dl	4.1-5mg/dl	5.1-6mg/dl	6.1-7mg/dl	>7.1mg/dl Total	Total
Group-A (n-100)	21	6	4	0	0	0	0	50
Group-B (n-100)	0	5	15	13	8	6	3	50

Discussion

Magnesium sulphate is the drugs of choice for seizure prophylaxis in patients of severe pre-eclampsia. World over different regimes are being used. Our study consisted of using lowest dose of magnesium sulphate to have maximum benefits with least toxicity. The primary objective of our study was to prevent or reduce the rate of eclampsia with least toxicity. The secondary benefit of this drug was to reduce maternal and perinatal mortality and morbidity.

The incidence of seizures in untreated preeclamptic women is approximately 3-4%, whilst for those receiving magnesium sulphate; the rate is 0.8-1% [5].

In our study, in Group-A, 3% of the patients had occurrence of convulsion after completion of Pritchards regimen. But in Group-B there was no occurrence of seizures in not even a single patients.

In a similar study done by Shoaib T *et al.* [6]; 2009, 2% of the patients had developed convulsion in a group with standard regimen and 100% of the patients remained fit free in the group with single loading dose [18]. In a study done by Hethyshi Ranganna *et al.* [7]; the risk of occurrence of seizures was similar in both the groups, i.e. one patient in each group threw a fit when on therapy. In the magpie trial the incidence of seizures in patients of severe preeclampsia including those with impending eclampsia (n = 2174) receiving the placebo was 3.12% [8]. This risk was reduced to 1.09% in patients of severe preeclampsia including those with impending eclampsia (n = 2107) who were given magnesium sulphate. The trial concluded that there was a reduction of 58% in the risk of occurrence of seizures regardless of the severity of the disease by using magnesium sulphate. The trial by Coetzee *et al.* [9] included 822 randomized women, there were no cases of eclampsia seen when magnesium sulphate prophylaxis was used in severe preeclampsia cases.

There are different studies following different regimens for the administration of injection magnesium sulphate. Various trials have adopted different routes, dosages and time to start therapy. Among the trials using intra-venous regime, the loading dose ranged from 4-6 gm and the maintenance dose ranged from 1-2 g/hour Coetzee *et al.* [9] Shah R [10].

The effectiveness of loading dose versus standard regime in the management of eclampsia has been documented where loading dose was found equally effective for control of seizures in eclampsia [11]. It led to similar results in the management of preeclampsia. Single loading dose was also tried in Peshawar and the researchers also appreciated the omission of multiple injections after bolus dose with the same efficacy.

Present study showed no significant difference seen in the distribution of systolic and diastolic blood pressure in both the groups.

In our study magnesium sulphate toxicity was seen in 12 cases in Group-A, which was significantly high when compared to Group-B. The toxicity was in term of absent knee jerk and oliguria. Similar results were obtained by Hethyshi Ranganna *et al.* [7] whereas Magpie trial revealed non significant difference between the patients on magnesium sulphate and those receiving the placebo in terms of absent knee jerk and oliguria [8].

The limitation of this study was sample size was small so further studies are warranted to know the efficacy of the drug.

Conclusion

Magnesium sulphate remains the drug of choice for both prophylaxis and treatment of women with eclampsia. With minimal monitoring required this can be adopted in peripheral centres which can help to reduce maternal mortality and morbidity and improve perinatal outcome.

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