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Research Article

Comparative Study of Loading Dose of Magnesium Sulphate versus Standard Regime for Prophylaxis of Severe Pre-Eclampsia

Dr Ratna Kanta Talukdar[1], Dr Dibyajyoti Gharphalia[2], Dr Zarna Pegu[3]
[1]Professor, Dept of OBG, Gauhati medical college and hospital, Guwahati, Assam
[2]Assistant Professor, Dept of OBG, Gauhati medical college and hospital, Guwahati, Assam
[3]Postgraduate trainee, Dept of OBG, Gauhati medical college and hospital, Guwahati, Assam

***Corresponding author**
Dr. Ratna Kanta Talukdar
Email: rktalukdar@gmail.com

Abstract: To determine the efficacy and safety of only loading dose of magnesium sulphate versus the standard regime in the patients of severe preeclampsia. Patients of severe preeclampsia were randomly allocated to Group-A (control group) (n=100) and Group-B (study group) (n=100). Patients in the study group received only the loading dose of magnesium sulphate and patients in the control group received 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. Chi-square test, Fisher's exact test and Student's t test was used for data analysis. There were three cases of convulsion in Group-A(control group) and no occurrence of convulsion in Group-B(study group)(P value- 0.2462).There were 8 cases of absent knee jerk(P value-0.006) and 4 cases of oliguria (P value-0.121) in those receiving the pritchard regimen but none of these complications were seen in those receiving only the loading dose. In case of serum magnesium level in our study, the Pritchard regimen produce mean magnesium levels that were significantly higher than that level obtained with only loading dose of magnesium sulphate (P value< 0.0001). There was no significant difference in the maternal and perinatal outcome in the study. Thus only loading dose of magnesium sulphate may be effective in preventing convulsion in the patients of severe preeclampsia with the added advantage of reduced toxicity and ease of monitoring.
Keywords: Severe pre-eclampsia, Magnesium sulphate, Pritchard regime, loading dose.

INTRODUCTION

Pre-eclampsia and eclampsia are important causes of maternal morbidity and mortality for women and her child, although outcome is often good [1]. Pre-eclampsia and eclampsia probably account for more than 50,000 maternal deaths a year [2]. In places where maternal mortality is high, most of these deaths are associated with eclampsia. Where maternal mortality is lower, a higher proportion will be due to pre-eclampsia. For example, in the UK pre-eclampsia and eclampsia together account for 15% of direct maternal deaths, and two-thirds were related to pre-eclampsia [1]. 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 [3]. In 1998 a systemic review of anticonvulsants [4] for women with pre-eclampsia identified four trials, comparing an anticonvulsant with placebo. The review concluded that the magnesium sulphate is a drug of choice for women with eclampsia and better than diazepam [5], phenytoin [6] or lytic cocktail [7]. As administration of magnesium sulphate requires regular supervision by trained staff, which is costly [8], 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. Routine use of Magnesium sulphate as an anticonvulsant in the management of pre-eclampsia started in 2002 after publication of Magpie trial [9]. Magnesium sulphate was given according to Pritchard regime. It was observed that many patients did not receive maintenance therapy due to suspicion of toxicity but they did not convulse any further. On the basis of this observation, this study was planned to compare the efficacy of loading dose of magnesium sulphate versus the standard regime in the management of pre-eclampsia to prevent fits.

MATERIALS AND METHODS

This study "Comparative Study of Loading Dose of Magnesium Sulphate Versus Standard Regime for Prophylaxis of Severe Pre-Eclampsia" was carried out in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati and covered a period of one year from 1st August 2014 to 31st July 2015. During the study period, 200 cases were

included to treatment with either Pritchard regimen (Group-A) or Loading dose of magnesium sulphate (Group-B) by randomisation.

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). A detailed history was taken from the patients and complete examination was done at the time of admission. Investigations done were, Blood grouping, Routine examination of blood, Platelet count, RBS, Blood urea, Serum creatinine, Serum uric acid, LDH, Liver function test, Coagulation studies if platelet count <1 lakh, ECG, Urine for albumin detection by heat coagulation test done for all cases, Evaluation of fetal size and well- being and amniotic fluid volume with sonography was done. After admission all the severe preeclampsia patient was assigned randomly to standard Pritchard regimen or loading dose of magnesium sulphate. In Group-A (control group) - The loading dose of 4g 20% magnesium sulphate was given intravenously, slowly over 10 minutes (diluted to 12 cc distilled water) and 10gm 50% magnesium sulphate intramuscularly followed by 5gm intramuscularly in alternate buttock every 4 hours for 24 hours after delivery or the last convulsion which ever was later [22]. In Group-B (study group) - The loading dose of 4gm 20% magnesium sulphate was given intravenously, slowly over 10 minutes (diluted to 12 cc distilled water) and 10gm 50% magnesium sulphate intramuscularly in each buttock. In both the control and study groups the magnesium sulphate therapy was monitored i.e. patellar reflex, respiratory rate, urine output. In case of recurrence of convulsion additional 2gm 20% magnesium sulphate was given slowly intravenously. The antihypertensive used were alpha methyl dopa and labetalol. Progress of labour was monitored by a partograph recording. Patients were either induced or allowed for spontaneous labour. The occurrence of convulsions and signs of magnesium toxicity like loss of knee jerk and oliguria were assessed. Neonatal outcomes were assessed by Apgar scores at 1 minute. After 24 hours of delivery with completion of maintenance dose of magnesium sulphate the patients were advised to do serum magnesium level. The data collected from the following observations were statistically analysed using Fischer's exact test, Chi- square test and student t test.

RESULTS

During the study period of 1 year, 100 patients of severe preeclampsia under the control group received the conventional 24 hour regime of magnesium sulphate and 100 patients of severe preeclampsia under the study group received only the loading dose of magnesium sulphate. Patients in both the groups were comparable in terms of age, and are depicted in Table-1. The occurrence rates were highest in age group below 24 years in both the groups. This is comparable to other studies which show the peak incidence of eclampsia in the teenage years and low twenties [10, 11]. In Group-A (control group), Mean age was 24.61 years± (4.410 SD), Median-24years. In Group-B (study group), Mean age was 24.74 years± (4.939 SD), Median-24 years. The distribution of patients based on numbers of previous pregnancies is depicted in Table-2. The incidence of severe pre-eclampsia in nulliparous population was 57% in Group-A and 55% in Group-B in our study. This is consistent with the high incidence and risk of pre-eclampsia in the nulliparous population. As mentioned in Table-3, in our study, in Group-A, 19% of the cases had severe preeclampsia preterm out of which 13% were between 33-36weeks. The mean duration of gestation was 38.71weeks± (2.815 SD). In Group-B, 21% of cases had severe preeclampsia preterm out of which 16% were between 33-36weeks. The mean duration of gestation was 38.53weeks± (2.935 SD). In the study by Seth et al 47% patients were over 36weeks and 31.8% were between 32-36weeks [12]. The disparity in gestational age in our study could be possibly due to late onset of severe pre-eclampsia in our study population. In our study, we observed that out of 100 patients treated with Pritchard regimen, 3 patients had convulsion. While out of 100 patients treated with only loading dose of magnesium sulphate, not even a single patient had convulsion (P value - 0.2462, considered not significant). The outcome is depicted in Table-4. In Group-A (control group), 8% of patients had absent knee jerk. But in Group-B (study group) ,no magnesium sulphate toxicity was seen(P value -0.006, considered extremely significant). Again in Group-A, 4% of patients had oliguria and in Group-B no toxicity was seen. But it was statistically not significant (P value-0.121). The outcome is depicted in Table-5. In Group- A, Mean magnesium sulphate was 4.599± (1.415 SD), Median-4.250 with maximum levels of 8.3mg/dl. In Group-B, Mean magnesium sulphate was 2.143± (0.4260 SD), Median-2.1 with maximum levels of 3.8mg/dl (P value< 0.0001, considered very significant). The outcome is delineated in Table-6.

Table 1: Age Distribution of Patients

Age Group	15-19	20-24	25-29	>29	Total
Group A(n-100)	7	43	35	15	100
Group B(n-100)	6	48	27	19	100

Table 2: Distribution of Patients Based On Parity

Parity	G1	G2	G3	G4	G5	G6	G7	G8	Total
Group- A(n-100)	57	23	13	4	0	2	0	1	100
Group- B(n-100)	55	21	13	7	2	0	2	0	100

Table 3: Duration of Pregnancy

Duration of Pregnancy	25-28wks	29-32wks	33-36wks	≥37wks	Total
Group- A(n-100)	1	5	13	81	100
Group- B(n-100)	2	3	16	79	100

Table 4: Occurrence of Convulsion in Both the Regimens

Occurrence Of Convulsion	Present	Absent	Total
Group-A(n-100)	3	97	100
Group-B(n-100)	0	100	100

P value -0.2462

Table 5: Magnesium Sulphate Toxicity

$MgSO_4$ Toxicity	Absent Knee Jerk	Oliguria	Total
Group-A(n-100)	8	4	12
Group-B(n-100)	0	0	0
P-Value	0.006	0.121	

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
Group-A(n-100)	42	55	3	0	0	0	0	100
Group-B(n-100)	0	11	29	26	16	12	6	100

P Value <0.0001

Table 7: Maternal Morbidity and Complications

Maternal Complications	Subdural Hematoma	Tah Due To Placenta Acreta	Hypertensive Retinopathy	Abscess In Buttock	Fulminant Cystites With Hematuria	Total
Group-A(n-100)	1	1	1	1	0	4
Group-B(n-100)	0	0	0	0	1	1

P Value-0.3687

DISCUSSION

Magnesium sulphate is the drug of choice for seizure prophylaxis in patients of severe preeclampsia [13]. Different studies were conducted to find out the least effective dosage of the drug which could simultaneously reduce the toxicity associated with the drug [14, 15]. Our study compared the efficacy and safety of Modified Pritchard's regime with the only loading dose and it was designed such that after an initial loading dose, subsequent doses of the drug were to be given only if the patient developed any convulsion. The incidence of seizures in untreated preeclamptic women is approximately 3-4%, whilst for those receiving magnesium sulphate; the rate is 0.8-1% [16, 17]. 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.;* 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.;* 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 [19]. 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%. 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[13]. 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 [20]. 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. On admission in Group-A (control group) the mean BP was 172.3± (11.179 SD) systolic and 118.8± (6.077 SD) diastolic and in Group-B ((study group) the Mean BP was 171.15±(10.672 SD) systolic and 117.1±(6.860 SD) diastolic. There was no significant difference seen in the distribution of systolic and diastolic blood pressure in both the groups. Douglas and Redman [21] reported mean systolic BP as 173 mmHg and mean diastolic BP as 97mmHg. In our study the frequency of ceasarean section was more in Group-A than in Group-B, even though it was insignificant statistically. The high operative interference in both the groups was due to fetal distress. The women allocated with magnesium sulphate had a small increase (5%) in the risk of ceasarean section (95% CI 1% to 10%) [22]. 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 (P value- 0.006) and oliguria (P value-0.121). In similar study by Hethyshi Ranganna *et al.;* [19] there was a significant reduction in the toxicity associated with the use of magnesium sulphate in the study group compared to the control group. However, Magpie trial [23] did not demonstrate any difference between the patients on magnesium sulphate and those receiving the placebo in terms of absent knee jerk and oliguria. In case of serum magnesium level in our study, the pritchard regimen produce mean magnesium levels that were significantly higher than those level obtained with only loading dose of magnesium sulphate (P value <0.0001, considered very significant). In our study no maternal death was seen in both the groups ,but there was an increased numbers of maternal complications in Group-A compared to Group-B, even though difference was not significant, as delineated in Table-7. Again in perinatal outcome there was no significant difference in both the groups.

CONCLUSION

Magnesium sulphate remains the drug of choice for both prophylaxis and treatment of women with eclampsia. Short regimen, minimizes the risk of toxicity since most patients would not need the maintenance doses. No maternal death or any significant difference in perinatal outcome was seen in both the groups. The efficacy of a single loading dose of magnesium sulphate in prevention of convulsion was simillar to the pritchard regimen in patients of severe preeclampsia, with the added advantages of reduced toxicity, fewer side effects, and ease of monitoring.

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