ORIGINAL ARTICLE

Loading Dose of Magnesium Sulphate Versus Standard Regime for Prophylaxis of Pre-eclampsia

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ABSTRACT

Objective: To determine the efficacy of single dose of magnesium sulphate versus the standard Pritchard regime in the management of pre-eclampsia.

Study Design: Quasi-experimental study.

Place and Duration of Study: Jinnah Postgraduate Medical Centre, Karachi, from January 2004 to January 2006.

Methodology: All women with severe pre-eclampsia and impending eclampsia were included in the study. Patients with pregnancy induced hypertension and mild to moderate pre-eclampsia were excluded. From the 100 women included in the study, after matching for age, parity and gestational age, 50 were given only bolus dose of magnesium sulphate and 50 were given the standard regime. They were observed for one week for the number of convulsions. Fisher's exact test and Chi-square test were used to analyze results.

Results: There was no significant difference in the two groups in term of occurrence of seizures, one patient developed fit with Pritchard regimen. The rate of caesarean section was lower in group A, 12% versus 30% in group B (p=0.05). There was no significant difference in perinatal outcome in either group (82% live births in group A versus 72% amongst group B (p=0.2). Few side effects like vomiting, dizziness and irritation at the site of injection were observed when standard treatment was used. Single dose treatment was also found to be cost-effective costing Pak Rs. 45 (US $ 0.56) as compared to Pak Rs. 195 (US $ 2.4) in control group. No maternal death was observed in either group.

Conclusion: Having the equal effectiveness, ease of monitoring and cost-effectiveness, single loading dose of magnesium sulphate is preferable over the standard regime in the management of pre-eclampsia as a prophylactic measure for prevention of seizure.

Key words: *Pre-eclampsia. Magnesium sulphate. Loading dose. Pritchard regimen.*

INTRODUCTION

Pre-eclampsia and eclampsia are still a leading cause of maternal mortality throughout the world.[1,2] The efficacy of magnesium sulphate in the control of eclamptic seizure and seizure prophylaxis in pre-eclampsia has been proven universally.[3-5] The primary objective of magnesium sulphate prophylaxis in women with pre-eclampsia is to prevent eclampsia.[6,7] Secondary benefits include reduced maternal and perinatal mortality and morbidity even in women who do not develop convulsions.[1,8-10]

The use of magnesium sulphate as an anticonvulsant started in JPMC during the Magpie trial in 1998- 2001 when being one of the participating centres,[1] women with pre-eclampsia were randomized to receive magnesium sulphate or placebo. Its routine use as an anticonvulsant in the management of pre-eclampsia started in 2002 after publication of Magpie trial.[1] Magnesium sulphate was given according to Pritchard regime.[11] It was observed that many patients did not receive maintenance therapy due to suspicion of toxicity but they did not convulse any further. Later on, there was a period when magnesium sulphate was out of stock and it was almost impossible to get magnesium sulphate. At that time Pritchard regime could only be used in eclamptic women, whereas pre-eclamptics received only single bolus dose. It was observed that none of the patients with pre-eclampsia developed seizure even after the single bolus dose. 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.

METHODOLOGY

It was a quasi-experimental study and sampling technique was non-random purposive. Study population consisted of 100 severe pre-eclamptics. The study was conducted from January 2004 to January 2006 at the Department of Obstetrics and Gynaecology, Jinnah Postgraduate Medical Centre, Karachi. All women with severe pre-eclampsia and impending eclampsia with a blood pressure more than 140/100 mmHg, proteinuria ++ on dipstick or signs and symptoms of impending eclampsia like epigastric pain, nausea and vomiting,

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headache associated with severe hypertension were included in the study after taking informed consent from the patients. Patients with pregnancy induced hypertension and mild to moderate pre-eclampsia were excluded.

From the 100 women included in this study, 50 were given magnesium sulphate in a single bolus dose (group A) i.e. 4 gm intravenously and 10 gm intramuscularly and 50 were given complete standard regime (group B) according to the Pritchard regime i.e. 14 gm loading dose (4 gm by intravenous route over 20 minutes, and 10 gm intramuscularly) followed by 5 gm intramuscularly every 4 hours, for 24 hours.

Before giving magnesium sulphate, every time the clinician checked that knee or other tendon reflexes were present, respiratory rate was normal (more than 16 breaths per minute) and urine output more than 100 ml in last four hours or greater than 25 ml in last hour. Serum magnesium level was not measured routinely. Additional management of these women consisted of control of hypertension and delivery of the fetus. Number of fits was observed after magnesium sulphate was given. Side effects due to the drug, like vomiting, headache, pain or abscess at the site of injection was observed. Serious side effects (including respiratory distress, renal failure, and cardiac arrest) and immediate neonatal outcome was also measured. Cost in Pak Rs. and US dollors was determined. The study was reviewed and approved by ethical review committee of the institute. Fisher's exact and Chi-square tests were applied.

RESULTS

The patients were matched for age, parity and gestational age. The average age of patients in group A was 26.06±5.01 years ranging from 19-40 years with median age of 29 years. In patients given standard regime (group B), it was 28.06±5.5, ranging from 19-38 years with median age of 28 years. The average parity of patients in group A was 1.95±3.25, ranging from 0-13 compared to 2.46±1.54, ranging from 0-7 in group B. The mean gestational age at the time of onset of pre-eclampsia was 33.28±4.24 and 33.80±3.73 at delivery in group A. In group B, it was 34.43±2.50 at the onset of pre-eclampsia and 35.56±2.76 at the time of delivery. There was no significant difference in the two groups in term of occurrence of seizures (Table I). The rate of caesarean section was lower in group A, 12% versus 30% in group B (p=0.05). There was no significant difference in perinatal outcome in either group (82% live births in group A versus 72% amongst group B (p=0.2). No serious untoward effects (e.g. respiratory, renal failure) were observed in either group. However, few mild side effects were observed when standard treatment was used and the results were statistically significant (Table II). Single dose treatment was also found to be cost-effective costing Pak Rs. 45 (US $ 0.56) as compared to Pak Rs. 195 (US $ 2.4) in control group. No maternal death was observed in either group.

Table I: Development of eclampsia.

	Development of eclampsia	Patients who remained fit-free	Total n=100
Patients with single loading dose	0 0%	50 100%	50
Patients with standard regime	1 2%	49 98%	50

Chi-square=1.010; p=1

Table II: Side effects of magnesium sulphate.

	Patients with single dose	Patients with standard regime	p-value
Nausea and vomiting	5 (10%)	17 (34%)	0.01
Feeling of warmth and flushing	35 (70%)	40 (80%)	Less than 1
Dizziness	10 (20%)	28 (56%)	0.001
Irritation at inj. site	0 (0%)	10 (20%)	0.001

p=0.05

DISCUSSION

Pre-eclampsia continues to be a major cause of maternal death.[12] It complicates 2-8% pregnancies.[13] Management of pre-eclampsia is based on stabilization, continued monitoring and delivery at an optimal time for mother and her baby. A large randomized trial has shown that conservative management with close monitoring of mother and fetus has lowered neonatal complications.[14] In the present study, the severe pre-eclamptic patients were kept under observation unless delivery was required for maternal and foetal indications. There was no significant difference in the perinatal outcome in both groups since both the groups were managed on the same lines and this aspect could not be compared.

The incidence of seizures in untreated pre-eclamptic women is approximately 3-4%, whilst for those receiving magnesium sulfate, the rate is 0.8-1%.[1,15] The two widely used regimes for magnesium sulphate are continuous intravenous infusion,[16] and combined intravenous (IV) and intramuscular regime (IM).[11] The IV regimen achieves more stable serum levels of magnesium but requires the use of an infusion pump for safe delivery and has a greater potential for inadvertent overdose. In addition, the number of patients in this hospital was larger than the number of attending doctors making frequent monitoring sometimes difficult; therefore, the Pritchard regime was preferred.

The IM dosing regimen, while potentially safer, requires repeated painful IM injections. In the present study its efficacy as a single loading dose was compared versus the standard Pritchard regime and single dose was found equally effective in preventing seizures.

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.[17] It led to similar results in the management of pre-eclampsia. 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.[18] Only one patient, who received standard Pritchard regime developed fit in the study, which was controlled with additional dose of magnesium sulphate. Magnesium sulphate does not completely prevent seizure activity in pre-eclamptic patients and is associated with an appreciable failure rate of ~1%.[15] Even with therapeutic serum magnesium concentrations, seizures are possible.[19,20]

At therapeutic concentrations of magnesium, about one quarter of pregnant women experience nausea, emesis, flushing or weakness.[1] Magnesium therapy can also be associated with lethargy, blurred vision and urinary retention.[21] Toxic effects include loss of reflexes, respiratory depression, cardiac arrhythmias and cardiac arrest.[22]

Few side effects, which were observed in the present study, are mentioned in Table II. The effects of magnesium toxicity can be rapidly reversed with 1 gm intravenous calcium gluconate.

A study showed that women with gestational hypertension had obstetrical intervention rates much higher than normotensive subjects but similar to those with pre-eclampsia and chronic hypertension.[23] Frequency of ceasarean section was reduced in group A in this study, which could not be explained. It may be by chance.

No maternal death or any significant difference in perinatal outcome was seen in both the groups. Since both the groups were managed on the same lines, this aspect could not be compared. There were no documented long-term serious maternal or neonatal side effects.[24,25]

CONCLUSION

Considering the equal effectiveness, fewer side effects, ease of monitoring and cost-effectiveness of loading dose, single loading dose of magnesium sulphate in the management of pre-eclampsia is preferable to the standard regime of administration requiring multiple doses.

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