Original Research Article

Neonatal effects of maternal magnesium sulphate in preeclampsia: a case control study

Karunaa Joe Sengottaian, Sheela Shivamonga Rangappa*

Department of Obstetrics and Gynaecology, Sri Devaraj URS Medical College, Tamaka, Kolar, Karnataka, India

*Correspondence:
Dr. Sheela Shivamonga Rangappa,
E-mail: drsrsheela@gmail.com

ABSTRACT

Background: Preeclampsia is a significant public health problem in developed and developing countries. It is a multi-organ system disorder, hence making it demanding to find out severity markers.[4] Awareness, recognition and knowledge of risk factors of preeclampsia will assist in predicting and lessen the recurrence of preeclampsia. In severe cases of preeclampsia and in eclampsia, magnesium sulfate is an effective anticonvulsant. Aims and objectives were: to document the clinical parameters of patients with or more than 28-week gestation having preeclampsia or eclampsia receiving magnesium sulphate and patients with or more than 28-week gestation having preeclampsia but not receiving magnesium sulphate; and to compare and study the obstetric and neonatal outcomes between the groups.
Methods: A case control study was performed among patients who delivered at RLJH hospital during study period (July 2020-July 2021), subjects who were administered magnesium sulphate due to maternal conditions were taken as cases and the subjects who did not receive magnesium sulphate were taken as controls. Obstetrical and neonatal outcomes were compared between both the groups. Data was entered in Microsoft excel sheet. Unpaired t test was performed. P value less than 0.0001 was considered significant.
Results: Magnesium sulphate did not have significant effects on the neonatal and obstetrical outcome.
Conclusions: The association between magnesium sulphate administration and neonatal outcomes were studied and it concludes that the administration of magnesium sulphate for the mother didn't have significant effects on the neonatal and obstetrical outcome.

Keywords: Preeclampsia, Neonate, Magnesium sulphate, Eclampsia

INTRODUCTION

Pre-eclampsia is a multiple system disorder taking place in pregnancy and puerperium which is identified by development of hypertension of 140/90 mmHg and above, after 20th week in a previously normotensive patient.[1] It accounts for about 2-8% of world population and 11-29% of Indian population.[2] It accounts for nearly 18% of all maternal deaths worldwide.[3] According to World Health Organization (WHO), incidence is 7 times greater in developing countries when compared to developed country.

Preeclampsia is a significant public health problem in developed and at the same time in developing countries.[4] It is a multi-organ system disorder, hence making it demanding to find out severity markers. Awareness, recognition and knowledge of risk factors of preeclampsia will assist in predicting and lessen the recurrence of preeclampsia.[12] In severe cases of preeclampsia and in eclampsia, magnesium sulfate administered parenterally is an effective anticonvulsant that avoids central nervous system depression in either the mother or the infant.

Present criteria for the diagnosis of preeclampsia is the presence of de novo hypertension (blood pressure of ≥140/90 mmHg), with proteinuria or any other multisystem complications, with onset after the 20th week of gestation.[1] Magnesium sulfate ($MgSO_4 \cdot 7H_2O$) is one of the most frequently used obstetric drugs and is the first line therapy for preventing eclampsia.[7] Magnesium sulfate has 8.12 mEq per 1 g. Parenterally administered magnesium is excreted almost totally by renal excretion, and magnesium intoxication is rare when the glomerular filtration rate is normal or very slightly decreased. Adequate urine output mostly correlates with good glomerular filtration rates. Magnesium excretion is urine flow reliant.[8] So, serum creatinine levels should be measured to rule out a decreased glomerular filtration rate.

Magnesium can cross the placenta, and fetal serum magnesium levels have been shown usually to correlate with maternal serum magnesium levels.[4] The use of magnesium sulphate as prophylactic anticonvulsant in severe preeclampsia and management of eclamptic seizures is well established and is proven to improve maternal outcomes[11]. The use of magnesium sulphate as a neuro-protective agent in preterm deliveries is also approved. So this study focuses on the neonatal effects among women receiving magnesium sulphate for maternal indications.[6] Eclamptic convulsions mostly prevented or arrested by plasma magnesium levels maintained between 4 to 7 mEq/l, 4.8 to 8.4 mg/dl, or 2.0 to 3.5 mmol/l.[14] Although laboratories interpret total magnesium levels, free or l ionized magnesium actively participate in suppressing neuronal d excitability.[5]

RLJH hospital being a tertiary care center the prevalence of preeclampsia and eclampsia is high. Magnesium sulfate is one of the most commonly used obstetric drugs and is the standard therapy for preventing eclampsia, data correlating neonatal outcomes in fetuses exposed to magnesium sulphate are lacking. This study is intended to study the neonatal effects among women receiving magnesium sulphate for maternal indications.

Objectives of the study

The aims and objectives of the study were as follows: to document the clinical parameters (patients with or more than 28-week gestation having preeclampsia or eclampsia receiving magnesium sulphate, and patients with or more than 28-week gestation having preeclampsia but not receiving magnesium sulphate); to compare the obstetric and neonatal outcomes between the above groups; and to study the association between magnesium sulphate administration and neonatal outcomes.

METHODS

Source of data

Preeclampsia and eclampsia patients delivered at RLJH hospital during the period of study.

Study design

It was a case control study.

Study period

The study period was from July 2020 – July 2021.

Method of collection of data

Data collected was entered in Microsoft excel spread sheet and unpaired t test was performed.

Inclusion criteria

Group A included 23 singleton pregnancy with hypertension developed after 20 weeks of pregnancy who was administered injection $MgSO_4$ in antepartum period or intrapartum period. Group B included 23 singleton pregnancy with hypertension developed after 20 weeks of pregnancy who have not received injection $MgSO_4$ in present pregnancy (according to ACOG guidelines; blood pressure (BP) ≥140/90 mmHg at 2 intervals 4 hours apart with or without significant proteinuria) and severe pre-eclampsia (according to ACOG guidelines, BP ≥160/110 mmHg and proteinuria >5 gm/24 hours), developing after 20 weeks of gestation, were included.

Exclusion criteria

Pregnancy less than 20 weeks of gestation; patient with coagulation disorders like idiopathic thrombocytopenia, sickle cell disease, viral hepatitis, cholestatic jaundice, acute fatty liver, malaria, and chronic hypertension.

Methodology

A cross sectional comparative study was conducted among pregnant women above 20 weeks of gestation, who were recruited from labour ward. Institutional ethics committee approval and a written informed consent was obtained from each patient before starting the study. Baseline demographic details along with pregnancy risk factors was taken into account. Blood pressure and proteinuria was estimated in all the subjects. Information on presence of nausea, vomiting, headache, urine output less than 400 ml/24 hours, haemogram, hypoproteinaemia, raised liver enzymes, deranged LFT, presence of haemolysis was observed and noted. Patients with preeclampsia/eclampsia receiving magnesium sulphate were included in one group (case). Patients with preeclampsia, not requiring magnesium sulphate, were included in the other group (control), fetal outcomes were studied in each group and was compared post-partum referrals.

Sample size

There are 2 groups: group A included 23 singleton pregnancy with hypertension developed after 20 weeks of pregnancy who was administered injection $MGSO_4$ in

antepartum period or intrapartum period group B included 23 singleton pregnancy with hypertension developed after 20 weeks of pregnancy who have not received injection MGSO$_4$ in present pregnancy.

$$n = \frac{2s_p^2 [z_{1-\alpha/2} + z_{1-\beta}]^2}{\mu_d^2}$$

$$s_p^2 = \frac{s_1^2}{s_2^2}$$

Where, s_1^2 is the standard deviation in the first group; s_2^2 is the standard deviation in the second group; μ_d^2 is the mean difference between the samples; α is significance level; and 1-β is power.

RESULTS

In the present study mean age of group A was 24.55±4.58 and the mean age of group B was 25.25±4.44.mean age between two groups is nearly closer together (Table 1).

Among the 23 participants of group A (43.5%) were primi (39.1%) were gravida 2 and (13%) were gravida 3 and (4%) were gravida 4. Among the participants of group B (34.8%) were primi (34.8%) were gravida 2 (21.7%) were gravida 3 and (8.7%) were gravida 4 (Table 2).

Among the 23 participants of group A (52.2%) belonged to 36 weeks to 40 weeks of gestation. Among the participants of group B (47.8%) belonged to 36 weeks to 40 weeks of gestation. Most of the case and controls are between 36 weeks to 40 weeks of gestation (Table 3).

In case group most common mode of delivery was LSCS (52.2%) and in controls most common mode of delivery was vaginal delivery (60.9%) but there is no statistical significance (Table 4). In case group most common mode of delivery was LSCS (52.2%) and in controls most common mode of delivery was vaginal delivery (60.9%) but there is no statistical significance.

In the present study in the case group the mean birth weight is 2.682 kg and mean birth weight in the control group is 2.931 kg and they are comparable (Table 5).

In the present study in the case group 47.8% babies were admitted in NICU due to various reasons and 52.2% of babies in control group were admitted in NICU. P value is 0.087 which is statistically not significant. It shows that there is no significant difference between the case group and control group in terms of NICU admission (Table 6).

In the present study respiratory distress among the case group is 56.5% and in the control group is 52.2%. There is no statistical significance between both the groups concerning to respiratory diseases (Table 7).

In the present study 52.2% of babies in the case group had passed meconium before birth and in the control group 39.1% of the babies had passed meconium before birth and there is no statistical significance between the groups pertaining to meconium passage before birth (Table 8).

Table 1: Comparison of age between case and controls.

Age (years)	Case		Control	
	Number	Percentage	Number	Percentage
18-20	3	13.0	4	17.4
21- 25	14	69.9	13	56.5
26-30	4	17.4	5	21.7
31-35	2	8.7	1	4.3
Total	23	100.0	23	100.0

Table 2: Comparison of parity between case and controls.

Parity	Case		Control	
	Number	Percentage	Number	Percentage
Gravida 1	10	43.5	8	34.8
Gravida 2	9	39.1	8	34.8
Gravida 3	3	13.0	5	21.7
Gravida 4	1	4.3	2	8.7
Total	23	100.0	23	100.0

Table 3: Comparison of period of gestation between case and controls.

Period of gestation	Case		Control	
	Number	Percentage	Number	Percentage
27-30 weeks of gestation	0	0	1	4.3

Continued.

Period of gestation	Case		Control	
	Number	Percentage	Number	Percentage
30 weeks 1 day-35 weeks 5 days of gestation	8	34.8	7	30.4
36-40 weeks of gestation	12	52.2	11	47.8
More than 40 weeks of gestation	3	13.0	4	17.4
Total	23	100.0	23	100.0

Table 4: Comparison of mode of delivery between case and controls.

Mode of delivery	Case		Control		P value
	Number	Percentage	Number	Percentage	
LSCS	12	52.2	9	39.1	
Vaginal delivery	11	47.8	14	60.9	
Total	23	100.0	23	100.0	0.789

Table 5: Comparison of birth weight between case and controls.

Birth weight	Case		Control	
	Number	Percentage	Number	Percentage
Less than 2 kg	5	21.7	3	13.0
2-2.5 kg	11	47.8	8	34.8
2.6-3 kg	3	13.0	8	34.8
3.1 - 3.5 kg	3	13.0	3	13.0
More than 3.5 kg	1	4.3	1	4.35
Total	23	100.0	23	100.0

Table 6: Comparison of NICU admission between case and controls.

NICU admission	Case		Control	
	Number	Percentage	Number	Percentage
Yes	11	47.8	12	52.2
No	12	52.2	11	47.8
Total	23	100.0	23	100.0

Table 7: Comparison of respiratory distress between case and controls.

Respiratory distress	Case		Control		P value
	Number	Percentage	Number	Percentage	
Yes	13	56.5	12	52.2	
No	10	43.5	11	47.8	
Total	23	100.0	23	100.0	0.088

Table 8: Comparison of meconium passage before birth between case and controls.

Meconium passage	Case		Control		P value
	Number	Percentage	Number	Percentage	
Yes	12	52.2	9	39.1	
No	11	47.8	14	60.9	
Total	23	100.0	23	100.0	0.789

DISCUSSION

Magnesium sulphate is well accepted as the treatment for prophylaxis of preeclampsia and for management of eclampsia.[22] Maternal adverse effects are less, and safety is well known. In preterm foetuses, antenatal magnesium sulphate acts as a neuro-protective agent and is now introduced in most guidelines.[23] However, systematic reviews opine that there is no evidence for administration of magnesium for neuro-protection of the term infant. Hence, the study of the neonatal effects of magnesium

sulphate—the apparently indispensable drug for maternal benefit—formed the basis of the study.[24] The administration of magnesium sulphate, hence, raises concerns not only for the doctors but also for nurses and midwives. In our study, the obstetric outcomes were comparable. Mode of delivery and birth weight remained comparable among the groups.

Neonatal effects of magnesium

NICU admission rate was 21.7%, in the control group not receiving magnesium sulphate. Greenberg et al even in his study there is a high rate of NICU admission.[25] Same results were identified by the same authors in two different study cohorts also.[26]

The rate of neonatal hypotonia was 17% in the study by Das et al. In a large retrospective cohort study by Abbasi-Ghanavati et al. Also, presence of neonatal hypotonia matched with the increasing neonatal magnesium levels.[26] In our study neonatal hypotonia was not taken into consideration. In our study, the occurrence of respiratory distress was comparable among both the case and control groups. However, this finding is different from the study of Greenberg and Riaz et al. In his study there was higher rate of respiratory distress.

The time of meconium passage was similar among both groups. However, the slowing down effect of magnesium on the gastrointestinal system of the neonate is already established, with a study by Havranek et al reporting effects on intestinal blood flow velocity.[21]

Relation of NICU admission rate to magnesium levels

In our study, NICU admission rate was higher in both the groups but there was no relation to the administration of magnesium sulphate but our findings are different from Greenberg et al. He identified duration and dose dependent increase in the rate of NICU admission.[25]

A study by Sherwin et al had found that foetal effects due to use of magnesium sulphate can be affected by magnesium levels. Increasing maternal magnesium levels showed increased foetal complications like lower Apgar score. It was also identified that maternal and neonatal magnesium levels are correlated well.[27] But a review article by Drassinower states that magnesium sulphate exposure do increase the need for neonatal resuscitation.

In our study, there was no increase in NICU admission magnesium sulphate adminision, yet it is recommended to have a trained neonatologist to be present when a baby is delivering.

Table 9: Comparison of neonatal outcomes between our study and other studies.

Parameters	Our study (%)	Wassie et al (%)	Nabrean et al (%)
NICU admission	47.8	18.4	18.8
Respiratory distress	56.5	41.1	-
Meconium passage before birth	52.2	-	-
Perinatal outcome	No significance	Significant increase in perinatal mortality and morbidity	No significance

Table 10: Comparison of neonatal outcomes like NICU admission, respiratory distress, meconium passage before birth and perinatal outcomes between our study and other studies.

Parameters	Our study (%)	Abalas et al (%)	Ambadkar et al (%)	Roy et al (%)
NICU admission	47.8	25.8	27.7	15.2
Respiratory distress	56.5	-	10	-
Meconium passage before birth	52.2	-	26	-
Perinatal outcome	No significance	Significant increase in perinatal morbidity	Significant neonatal morbidity	No significance

CONCLUSION

In the current study clinical parameters of patients with or more than 28-week gestation having preeclampsia or eclampsia receiving magnesium sulphate and patients with or more than 28-week gestation having preeclampsia but not receiving magnesium sulphate were documented obstetric and neonatal outcomes between the groups were compared. And the association between magnesium sulphate administration and neonatal outcomes were studied conclude in this study the administration of

magnesium sulphate for the mother did not have any significant effects on the neonatal and obstetrical outcome in terms of need for NICU admission and mode of delivery.

REFERENCES

1. Sibai BM. Hypertension in pregnancy. Clinical Obstet Gynecol. Am J Obstet Gynecol. 2004;190:1520.
2. World Health Organization. Make every mother and child count. Geneva: World health report. 2005. Available at: https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9241562900/en/. Accessed on 15 October 2021.
3. Khan KS, Wojdyla D, Say L, Gulmezoglu AM ,Van Look PF. WHO analysis of causes of maternal death: a systemic review. Lancet. 2006;367.
4. Hallak M, Berry SM, Madincea F, Romero R, Evans MI, Cotton DB. Fetal serum and amniotic fluid magnesium concentrations with maternal treatment. Obstet Gynecol. 1993;81:185-8.
5. Bain ES, Middleton PF, Crowther CA. Maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes: a systematic review. BMC Pregnancy Childbirth. BioMed Central. 2013;13:195.
6. Bain E, Bubner T, Ashwood P. Implementation of a clinical practice guideline for antenatal magnesium sulphate for neuroprotection in Australia and New Zealand. Aust N Z J Obstet Gynaecol. 2013;53(1):86-9.
7. Pryde PG, Mittendorf R. Contemporary usage of obstetric magnesium sulfate: indication, contraindication, and relevance of dose. Obstet Gynecol. 2009;114:669-73.
8. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D . Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;1:CD004661.
9. Lyell DJ, Pullen K, Campbell L, Ching S, Druzin ML, Chitkara U, et al. Magnesium sulfate compared with nifedipine for acute tocolysis of preterm labor: a randomized controlled trial. Obstet Gynecol. 2007;110:61-7.
10. Lyell DJ, Penn A, Caughey A, Kogut E, McClellan L, Adams B, et al. Neonatal outcomes following antenatal magnesium sulfate exposure: follow up from a magnesium vs nifedipine tocolysis RCT. Am J Obstet Gynecol. 2009;201:180.
11. Greenberg MB, Penn AA, Thomas LJ, El-Sayed YY, Caughey AB, Lyell DJ. Neonatal medical admission in a term and late-preterm cohort exposed to magnesium sulfate. Am J Obstet Gynecol. 2011;204:515.
12. American College of Obstetricians and Gynecologists. Diagnosis and management of pre-eclampsia and eclampsia. ACOG Practice Bulletin No. 33. Obstet Gynecol. 2002;99:159-1.
13. Lucas MJ, Leveno KJ, Cunningham FG. A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. N Engl J Med. 1995;333:201-5.
14. Coetzee EJ, Dommisse J, Anthony J. A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre-eclampsia. Br J Obstet Gynaecol. 1998;105:300-3.
15. Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet. 2002;359:1877-18.
16. Yilmaz Z, Yilmaz E, Kucukozkam T. Red blood cell distribution width: A simple parameter in preeclampsia. Pregnancy Hypertens. 2016;285-7.
17. Bain ES, Middleton PF, Crowther CA. Maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes: a systematic review. BMC Pregnancy Childbirth. BioMed Central. 2013;13:195.
18. Bain E, Bubner T, Ashwood P. Implementation of a clinical practice guideline for antenatal magnesium sulphate for neuroprotection in Australia and New Zealand. Aust N Z J Obstet Gynaecol. 2013;53(1):86-9.
19. Nguyen TMN, Crowther CA, Wilkinson D. Magnesium sulphate for women at term for neuroprotection of the fetus. Cochrane Database Syst Rev. 2013;2:CD009395.
20. Drinkwater J. Magnesium sulphate for pre-eclampsia: care of the neonate. Pract Midwife. 2011;14(11):17-9.
21. Havranek T, Ashmeade TL, Afanador M et al. Effects of maternal magnesium sulfate administration on intestinal blood flow velocity in preterm neonates. Neonatology. 2011;100(1):44-9.
22. Bain ES, Middleton PF, Crowther CA. Maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes: a systematic review. BMC Pregnancy Childbirth. BioMed Central. 2013;13:195.
23. Bain E, Bubner T, Ashwood P. Implementation of a clinical practice guideline for antenatal magnesium sulphate for neuro- protection in Australia and New Zealand. Aust N Z J Obstet Gynaecol. 2013;53(1):86-9.
24. Nguyen TM, Crowther CA, Wilkinson D, Bain E. Magnesium sulphate for women at term for neuroprotection of the fetus. Cochrane Database Syst Rev. 2013;2:CD009395.
25. Greenberg MB, Penn AA, Thomas LJ. Neonatal medical admission in a term and late-preterm cohort exposed to magne- sium sulfate. Am J Obstet Gynecol. 2011;204(6):515.

26. Greenberg MB, Penn AA, Whitaker KR. Effect of magne- sium sulfate exposure on term neonates. J Perinatol. 2013;33(3):188-93.

27. Sherwin CM, Balch A, Campbell SC, Fredrickson J, Clark EA, Varner M, Stockmann C, Korgenski EK, Bonkowsky JL, Spigarelli MG. Maternal magnesium sulphate exposure predicts neonatal magnesium blood concentrations. Basic Clin Pharmacol Toxicol. 2014;114(4):318-22.

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