https://doi.org/10.29309/TPMJ/2024.31.07.8135

The Professional Medical Journal
www.theprofesional.com
2024, Volume, 31 Issue, 07

ORIGINAL ARTICLE

Efficacy of antenatal magnesium sulfate in the prevention of necrotizing enterocolitis: A randomized case-control study in preterm neonates.

Sabika Iftikhar[1], Mayda Riaz[2], Sajjad Rafique[3]

Article Citation: Iftikhar S, Riaz M, Rafique S. Efficacy of antenatal magnesium sulfate in the prevention of necrotizing enterocolitis: A randomized case-control study in preterm neonates. Professional Med J 2024; 31(07):1018-1022. https://doi.org/10.29309/TPMJ/2024.31.07.8135

ABSTRACT… Objective: To assess the efficacy of administering antenatal magnesium sulfate in reducing the occurrence of necrotizing enterocolitis in preterm infants. **Study Design:** Randomized Case-control study. **Setting:** Hameed Latif Hospital Lahore. **Period:** August 2023- February 2024. **Methods:** The study including 80 preterm neonates (26 to 32 weeks gestation) was conducted at Neonatology & Gynaecology Unit Hameed Latif Hospital, Lahore. These neonates were divided into two groups: Group A included infants whose mothers were given magnesium sulfate before preterm birth, while Group B comprised of infants whose mothers did not receive magnesium sulfate. The primary outcome was the incidence of NEC in infants born to mothers exposed to magnesium sulfate, with secondary outcomes covering other neonatal morbidities and maternal side effects. Data analysis utilized SPSS Statistics software version 24, employing t-tests and multivariate logistic regression to evaluate the association between antenatal magnesium sulfate exposure and NEC incidence, considering a significant p-value of ≤ 0.05. **Results:** The overall NEC incidence was 5%(n=2). No NEC cases were reported in the control group. The difference in neonatal outcomes between both groups was statistically insignificant (p>0.05). **Conclusion:** Administering antenatal magnesium sulfate has no effect in decreasing the incidence of NEC in preterm infants.

Key words: Magnesium Sulphate, Necrotizing Enterocolitis (NEC), Preterm.

INTRODUCTION

Necrotizing enterocolitis (NEC) is a severe gastrointestinal condition affecting preterm infants, often leading to serious consequences. The incidence rate of NEC ranges from 2% to 7% in neonatal intensive care units (NICUs).[1] NEC is a leading cause of morbidity and mortality among premature neonates.[2] Despite considerable advancements in neonatal care, the etiology of NEC remains multifactorial and elusive, involving factors such as prematurity, immaturity of the gastrointestinal tract, and microbial colonization.[3] NEC presents a substantial burden, necessitating innovative approaches for prevention.

Antenatal magnesium sulfate, a medication primarily used to prevent cerebral palsy and to manage eclampsia in pregnant females[2,4], has exhibited potential benefits beyond its primary indications. However, its role in the prevention of intestinal morbidities in neonates remains controversial.[5] The mechanism through which magnesium sulfate confer its protective effects is by improving blood flow, reducing oxidative stress, and modulating the inflammatory response, all of which are key factors in the pathogenesis of NEC.[6-7]

Antenatal magnesium sulfate reduced intestinal morbidities in preterm infants requiring surgeries (adjusted OR 0.234, 95% CI 0.060–0.922).[8] According to a study conducted by Prasath et al MgSO4 administered during pregnancy decreased the incidence of necrotizing enterocolitis in preterm infants with reduced gastrointestinal related mortality (n = 29,506 OR:0.74; 95% CI: 0.62–0.90, ARR: 0.47%).[9] Whereas another study showed that rate of NEC between infants unexposed and exposed to antenatal MgSO4 was insignificant (5.1% vs.

1. FCPS (Pediatrics), Fellow Neonatology/ Senior Registrar, Hameed Latif Hospital Lahore.
2. FCPS (Pediatrics), FCPS (Neonatology), Assistant Professor Neonatology, Children Hospital and Institute of Child Health Faisalabad.
3. MRCPCH, Consultant Pediatric and Neonatology, Hameed Latif Hospital Lahore.

Correspondence Address:
Dr. Sabika Iftikhar
Department of Pediatrics
Hameed Lateef Hospital, Lahore.
sabikaiftikhar06@gmail.com

Article received on: 02/02/2024
Accepted for publication: 25/04/2024

3.6%, p =0.369).[10]

Magnesium sulphate is an underrated drug but has a number of benefits in the field of neonatology. The role of magnesium sulfate in the prevention of NEC is argumentative. In Pakistan it has not been used routinely by the gynecologists before preterm birth despite its proven benefits in literature.[11,12] This study is aimed to find out whether magnesium sulfate confers any benefit against protection of NEC in premature babies, that carries a significant cause of morbidity in preterm neonates in our country.

METHODS

A randomized case control trial was conducted at Hameed Latif Hospital Gynaecology and Neonatal Unit, Lahore from August 2023 to February 2024.

All preterm neonates between 26-34 weeks of gestation were enrolled after obtaining informed consent. Females with multiple pregnancies, who are contraindicated to use of MgSO4, fetuses with congenital abnormalities and babies who died immediately after the delivery were excluded. Medical record of mother and baby was examined before by obstetrician and neonatologist.

The neonates were divided into two groups (A and B). The neonates of group A whose mothers received antenatal magnesium sulfate at a dose of 4-grams per kg over 4-hours before preterm birth were compared to the neonates in Group B whose mothers did not receive magnesium sulfate, in terms of incidence of NEC in both groups.

Maternal demographic characteristics such as maternal age at delivery, parity and mode of delivery were included. Neonatal outcome measures such as gestational age at delivery, gender, Apgar scores and birth weight were recorded.

The incidence of NEC in the infants born to mothers exposed to magnesium sulfate was the primary outcome. Secondary outcomes may include other neonatal morbidities and maternal side effects. Collected data was entered in the proforma.

Ethical approval for conducting the study was taken from the ethical committee IRB 2023-16. A written consent was taken from the parents for participation in the study.

Obtained data was analyzed using SPSS Statistic software version 24. Independent t-tests, and multivariate logistic regression was used to assess the association between antenatal magnesium sulfate exposure and NEC incidence P-value of ≤ 0.05 was considered significant.

RESULTS

In this study, in the MgSo4 group, the mean age of mothers was 28.53 ± 4.57 years and in control group, the mean age of mothers was 29.05 ± 3.83 years. The mean gestational age at enrollment was 31.30 ± 2.20 weeks vs. 31.23 ± 2.36 weeks, while mothers were delivered at mean gestational age of 31.35 ± 2.23 vs. 31.25 ± 2.30 weeks. In MgSO4 group, 20 (50%) mothers were primigravida, and 5 (12.5%) were grand multipara. In control group, 22 (55%) mothers were primigravida, and 1 (2.5%) were grand multipara. Antenatal steroid cover was given to 40 (100%) mothers in MgSo4 group while to 37 (92.5%) mothers in control group were given antenatal steroids. In MgSO4 group, 14 (35%) mothers underwent elective cesarean section, 22 (55%) had emergency cesarean section and 4 (10%) had spontaneous delivery. In control group, 22 (55%) mothers underwent elective cesarean section, 11 (27.5%) had emergency cesarean section, 6 (15%) had spontaneous delivery and 1 (2.5%) had hysterotomy.

In MgSO4 group, the mean birth weight of neonates was 1.64 ± 0.47 kg. In control group, the mean birth weight of neonates was 1.61 ± 0.47 kg. In both groups, 25 (62.5%) were males and 15 (37.5%) were females. In MgSo4 group, the mean Apgar score of neonates at 1 minutes was 6.18 ± 1.34, while at 5 minutes was 7.60 ± 0.90. In control group, the mean Apgar score of neonates at 1 minutes was 6.58 ± 1.13, while at 5 minutes was 7.88 ± 0.99. On day 3, cranial scan of neonates was done and observed that scan

was normal in 38 (95%) cases but intraventricular hemorrhage was observed in 2 (5%) cases in MgSo4 group. In control group, cranial scan was normal in 36 (90%) cases but intraventricular hemorrhage was observed in 4 (10%) controls. On day of discharge, cranial scan of neonates was done and observed that scan was normal in 36 (90%) cases but intraventricular hemorrhage was observed in 4 (10%) cases, and 1 (1.3%) was expired during follow-up. In control group, 34 (85%) of the cranial scans at discharge were normal and 6 (15%) had intraventricular hemorrhage, while 1 was expired. In MgSO4 group, the mean hospital stay was 7.68 ± 6.07 days and in control group, the mean hospital stay was 6.43 ± 4.79 days. In MgSo4 group, 19 (47.5%) had respiratory distress syndrome and 9 (22.5%) required mechanical ventilation. In control group, 18 (45%) had respiratory distress syndrome and 14 (35%) required mechanical ventilation. In MgSo4 group, Patent ductus arteriosus was developed in 10 (25%) cases, 13 (32.5%) developed neonatal jaundice, 7 (17.5%) had sepsis, neonatal hypotension occurred in 6 (15%) neonates and neonatal hypothermia developed in 1 (2.5%) cases. No neonate showed Periventricular leukomalacia. Necrotizing enterocolitis occurred in 2 (5%) cases. In control group, Patent ductus arteriosus was developed in 6 (15%) cases, 16 (40%) developed neonatal jaundice, 12 (30%) had sepsis, neonatal hypotension occurred in 8 (20%) neonates and neonatal hypothermia developed in 1 (2.5%) cases. No neonate showed Periventricular leukomalacia or Necrotizing enterocolitis. The difference in both groups for neonatal outcome was insignificant (p>0.05). Table-I

DISCUSSION

	Group		P-Value
	MgSO4	Control	
Birth weight (in kg)	1.64 ± 0.47	1.61 ± 0.47	0.784
Gender			
Male	25 (62.5%)	25 (62.5%)	
Female	15 (37.5%)	15 (37.5%)	
Apgar after 1 minute	6.18 ± 1.34	6.58 ± 1.13	0.152
Apgar after 5 minutes	7.60 ± 0.90	7.88 ± 0.99	0.198
Cranial scan on day 3 of birth			
Normal	38 (95%)	36 (90%)	0.6712
IVH	2 (5%)	4 (10%)	
Grade 1 IVH	1 (2.5%)	2 (5%)	
Grade 2 IVH	1 (2.5%)	2 (5%)	
Cranial scan on discharge			
Normal	36 (90%)	34 (85%)	0.7353
IVH	4 (10%)	6 (15%)	
Grade 1 IVH	0 (0%)	1 (2.5%)	
Grade 2 IVH	4 (10%)	1 (2.5%)	
Grade 3 IVH	0 (0%)	1 (2.5%)	
Grade 4 IVH	0 (0%)	2 (5%)	
Expired	0 (0%)	1 (2.5%)	
Hospital stay (days)	7.68 ± 6.07	6.43 ± 4.79	0.310
Respiratory distress syndrome	19 (47.5%)	18 (45%)	0.823
Need for mechanical ventilation	9 (22.5%)	14 (35%)	0.217
Patent ductus arteriosus	10 (25%)	6 (15%)	0.264
Neonatal jaundice	13 (32.5%)	16 (40%)	0.485
Sepsis	7 (17.5%)	12 (30%)	0.189
Neonatal hypotension	6 (15%)	8 (20%)	0.556
Neonatal hypothermia	1 (2.5%)	1 (2.5%)	>0.999
Periventricular leukomalacia	0 (0%)	0 (0%)	NA
Necrotizing enterocolitis	2 (5%)	0 (0%)	0.152

Table-I. Outcome of neonates delivered to mothers who received MgSO4 (n = 80)

In this study, we tried to investigate the effect of antenatal magnesium sulfate in the protection of NEC in preterm infants. We found that overall incidence of NEC is 5% (n=2), which is consistent with results of Neu etal who found the incidence to be 2% to 7%.[1] In our study, Magnesium sulfate is found to have no statistically significant effect in the prevention of NEC in preterm infants. These results are consistent with other randomized control trials that show no difference in incidence of NEC among neonates whose mothers were exposed and those who were not exposed to MgSO4 antenatally.[14,16]

We concluded in this study that there was no significant decrease in the incidence of NEC in group A preterm neonates. This is in contrast to the results mentioned by Constantine etal.[11] Despite the fact that in our study, more cases of NEC were seen in the group A neonates, serious adverse effects such as SIP were not noted and none of the neonates required surgical intervention. This sheds light on the fact that although not statistically significant but magnesium sulfate does offer protection against complications of NEC in infants, as mentioned in previous studies.[13,14]

Our study showed that there was no significant difference between the incidence of RDS, PDA, need of mechanical ventilation, JNN, neonatal sepsis, neonatal hypothermia and neonatal hypotension , days of hospital stay in both MgSO4 exposed and non exposed groups. These results are in comparison with those concluded by Bansal et al.[15]

In our study, IVH was less frequently observed and was less severe in babies exposed to antenatalMgSO4 as compared to non exposed group. This is in comparison to results given by Bansal etal.[13] However in our study there was no statistically significant difference in incidence of IVH among both groups. This might be attributed to low sample size in our study.

The optimal dose of antenatal magnesium sulfate is not yet established.[17] In our trial we administered the mothers, a loading dose of 4grams magnesium sulfate over a period of 20 minutes immediately before the preterm birth to avoid any drug related complications. It has been shown in a study that higher doses of magnesium sulfate (6grams loading and 2g maintenance) is associated with adverse neonatal outcomes in the form of NEC and SIP as compared to low dose magnesium sulfate (4grams loading and 1gram maintenance for 24 hours).[18]

We also concluded in our study, that magnesium sulfate can be safely administered to the mothers before preterm birth without having adverse outcomes. There were no serious adverse events noted in the mothers receiving magnesium sulfate bolus and later on after the birth of the baby.[16]

The limitation of this study is that it's a single centered study and its sample size is low. More studies need to be conducted on larger scale to establish the dose and efficacy of MgSO4 in order to prevent morbidity in preterm neonates.

CONCLUSION

We concluded that antenatal administration of MgSO4 to expecting mothers, is not efficacious in prevention of NEC among preterm babies. Despite the fact that more cases of NEC were found in MgSO4 group, no serious adverse effects were noted, suggesting potential protective benefits of magnesium sulfate against NEC complications. Nonetheless, this single-centered study underscores the need for further research to establish optimal dosing regimens and prevent morbidity in preterm neonates.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Neu, Josef, and W Allan Walker. **Necrotizing enterocolitis.** The New England Journal of Medicine. 2011; 364(3):255-64. doi:10.1056/NEJMra1005408Neu J, Walker WA.

2. Neu J, Walker WA. **Necrotizing enterocolitis.** New England Journal of Medicine. 2011 Jan 20; 364(3):255-64.7.

3. Lin, Patricia W, and Barbara J Stoll. **Necrotizing enterocolitis.** Lancet (London, England). 2006; 368(9543):1271-83. doi:10.1016/S0140-6736(06)69525-1.

4. Wu YW, Colford JM. **Chorioamnionitis as a risk factor for cerebral palsy: A meta-analysis.** JAMA. 2000; 284:1417-24.

5. Garg BD. **Antenatal magnesium sulfate is beneficial or harmful in very preterm and extremely preterm neonates: A new insight.** The Journal of Maternal-Fetal & Neonatal Medicine. 2019 Jun 18; 32(12):2084-90.

6. Rantonen TH, Grönlund JU, Jalonen JO, Ekblad UU, Kääpä PO, Kero PO, Välimäki IA. **Comparison of the effects of antenatal magnesium sulphate and ritodrine exposure on circulatory adaptation in preterm infants.** Clinical Physiology and Functional Imaging. 2002 Jan; 22(1):13-7.

7. Suzuki-Kakisaka H, Sugimoto J, Tetarbe M, Romani AM, Ramirez Kitchen CM, Bernstein HB. **Magnesium sulfate increases intracellular magnesium reducing inflammatory cytokine release in neonates.** American Journal of Reproductive Immunology. 2013 Sep; 70(3):213-20.

8. Kim SH, Kim YJ, Shin SH, Cho H, Shin SH, Kim EK, et al. **Antenatal magnesium sulfate and intestinal morbidities in preterm infants with extremely low gestational age.** Pediatric Neonatal. 2021; 62:202-7.

9. Prasath A, Aronoff N, Chandrasekharan P, Diggikar S. **Antenatal Magnesium Sulfate and adverse gastrointestinal outcomes in Preterm infants—a systematic review and meta-analysis.** J Perinatal. 2023; 43:1087-1100. https://doi.org/10.1038/s41372-023-01710-8

10. Hong JY, Hong JY, Choi YS, Kim YM, Sung JH, Choi SJ, et al. **Antenatal magnesium sulfate treatment and risk of necrotizing enterocolitis in preterm infants born at less than 32 weeks of gestation.** Scientific Reports. 30 Jul 2020; 10(1):12826. doi:10.1038/s41598-020-69785-3.

11. Costantine, Maged M. **Physiologic and pharmacokinetic changes in pregnancy.** Frontiers in Pharmacology. 3 Apr 2014; 5:65. doi:10.3389/fphar.2014.00065

12. Capsasso L, Borrelli AC, Cerullo C. **Magnesium sulfate in preterm birth: A narrative review.** Front Pharmacol. 2020; 11:596174.

13. Bansal V, Desai A. **Efficacy of antenatal magnesium sulfate for neuroprotection in extreme prematurity: A comparative observational study.** The Journal of Obstetrics and Gynecology of India. 2021; 1-2.

14. Downey LC, Cotten CM, Hornik CP, Laughon MM, Tolia VN, Clark RH, et al. **Association of in utero magnesium exposure and spontaneous intestinal perforations in extremely low birth weight infants.** Journal of Perinatology. 2017 Jun; 37(6):641-4.

15. Shalabi M, Mohamed A, Lemyre B, Aziz K, Faucher D, Shah PS. **Canadian Neonatal Network Investigators. Antenatal exposure to magnesium sulfate and spontaneous intestinal perforation and necrotizing enterocolitis in extremely preterm neonates.** American Journal of Perinatology. 2017 Oct; 34(12):1227-33.

16. Shepherd E, Salam RA, Manhas D, Synnes A, Middleton P, Makrides M, et al. **Antenatal magnesium sulphate and adverse neonatal outcomes: A systematic review and meta-analysis.** PLoS Medicine. 2019 Dec 6; 16(12):e1002988.

17. Bain E, Middleton P, Crowther CA. **Different magnesium sulphate regimens for neuroprotection of the fetus for women at risk of preterm birth.** Cochrane Database of Systematic Reviews. 2012; (2):CD009302.

18. Kamyar M, Clark EA, Yoder BA, Varner MW, Manuck TA. **Antenatal magnesium sulfate, necrotizing enterocolitis, and death among neonates< 28 weeks gestation.** American Journal of Perinatology Reports. 2016 Mar; 6(01):e148-54.

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Sabika Iftikhar	Patient diagnosis and management, Data collection, Literature search, Manuscript writing.	
2	Mayda Riaz	Patient diagnosis and management, Data collection, Literature search, Manuscript writing.	
3	Sajjad Rafique	Patient diagnosis and management, Data collection, Literature search, Manuscript writing.	