ORIGINAL ARTICLE

Efficacy of Magnesium Sulphate as an Adjuvant to Antenatal Steroids in Prevention of Intraventricular Hemorrhage in Preterm Infants

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ABSTRACT

Objective: To evaluate the efficacy of magnesium sulphate as an adjuvant to antenatal steroids in the prevention of intraventricular hemorrhage (IVH) in preterm babies.

Study Design: Prospective observational cohort study.

Place and Duration of study: Hameed Latif Hospital, Lahore from August 2022 – July 2024

Material and Methods: We enrolled 300 mothers who delivered between 26-34 weeks gestation. Their neonates were segregated into two groups: Group A (n = 195) comprised of babies born to mothers receiving magnesium sulphate and antenatal steroids, and Group B (n = 105) had babies born to mothers receiving only antenatal steroids. The primary outcome, intraventricular hemorrhage (IVH), was assessed by cranial scans on the third day of life and at discharge. SPSS 20 software was used to analyze the data, and a p-value ≤ 0.05 was considered significant.

Results: On day 3, IVH occurred in 14.9% of Group A and 38.1% of Group B infants (absolute risk reduction 23.2%, calculated as the difference in proportions, p<0.001, 95% CI: 12.8–33.6). At discharge, normal scans were more frequent in Group A (80.5% vs 71.4%; p=0.099), and severe IVH (Grades III–IV) remained significantly reduced (1.0% vs 6.7%; p=0.010). Multivariate logistic regression showed magnesium sulphate as an independent protective factor against IVH (adjusted OR = 0.28; 95% CI 0.12–0.65; p<0.0010).

Conclusion: Antenatal MgSO4 when used with steroids, decreases risk of IVH in premature infants.

Key Words: *Magnesium sulphate, Intraventricular hemorrhage, Antenatal steroid, Preterm*.

INTRODUCTION

Intraventricular hemorrhage (IVH) is a serious neurological complication that primarily affects premature infants, resulting from the rupture of fragile vessels in the germinal matrix and subsequent bleeding into the cerebral ventricles. It remains a major cause of neonatal morbidity and long-term neurodevelopmental impairment despite advances in perinatal care.[1]

The risk of IVH is influenced by several factors, including fluctuations in cerebral blood flow,

fragility of germinal matrix vasculature, and impaired venous drainage.[2]

The Papile classification divides IVH into four grades based on severity.[3]

- Grade I – Bleeding limited to the germinal matrix
- Grade II – IVH with no ventricular dilation.
- Grade III - IVH with ventricular dilation, occupying more than 50% of the ventricle
- Grade IV – IVH with intraparenchymal hemorrhage

Antenatal corticosteroids are well-established in reducing the incidence of IVH and respiratory distress in preterm infants by enhancing pulmonary maturity and improving cerebrovascular stability. A Cochrane review reported a 42% reduction in IVH when a full course of corticosteroids was administered 1–7 days before delivery.[4] However, despite this benefit, IVH still occurs in a considerable proportion of preterm neonates, indicating a need for additional neuroprotective strategies.

Recent studies have explored the potential synergistic role of magnesium sulphate with corticosteroids in improving neonatal neurological outcomes. Magnesium sulphate widely used for preterm labour and preeclampsia, exerts neuroprotection by stabilizing cerebral blood flow, blocking calcium channels, and reducing oxidative and excitotoxic neuronal injury.[5,6,7,8] Evidence suggests that antenatal magnesium exposure independently decreases the risk of severe IVH and cerebral palsy in preterm infants [9,10,11]

In preterm neonates born before 34 weeks, prenatal exposure to magnesium sulphate was independently associated with a decreased likelihood of brain injury. Lower incidence of severe (grade 3-4) IVH and better cognitive and motor development was observed in infants who received magnesium sulphate.[12, 13, 14]

This study was designed to evaluate the combined effect of magnesium sulphate and antenatal corticosteroids on the prevention and severity of IVH in preterm neonates compared with corticosteroids alone.

MATERIAL AND METHODS

The prospective observational cohort study was conducted from August 2022 to July 2024 at the Neonatology Department of Neonatology Hameed Latif Hospital, Lahore and its affiliated institute in Lahore, after obtaining approval from the Institutional Human Ethical Committee (Approval No. HLH/HDM/IRB/IRB 2022-016) and obtaining informed consent from the parents. The sample size was calculated using the WHO sample size calculator, 300 pregnant females delivering between 26–34 weeks of gestation during the study period were included using a consecutive sampling technique. Exclusion criteria consisted of those preterm neonates who did not survive during or shortly after birth, had incomplete clinical data and those preterm with complex congenital anomalies.

The neonates of these mothers were segregated into two groups: Group A (n = 195), whose mothers were given magnesium sulphate (4g IV over 30 minutes, within 24 hours before delivery. ACOG Committee Opinion No 455), along with antenatal steroids (betamethasone 12 mg IM, two doses, 12 hour apart), and Group B (n=105), whose mothers received only antenatal steroids. As this was an observational study, the administration of magnesium sulphate was at the discretion of the attending obstetrician based on maternal condition and anticipated risk of preterm birth.

The primary outcome was the occurrence and severity of intraventricular hemorrhage (IVH), assessed by cranial ultrasound (CUS) on the third day of life and at discharge. IVH was graded according to the Papile classification (Grades I–IV). The secondary outcomes included mortality and length of hospital stay.

Data was recorded and analysed using SPSS version 20. Mean and standard deviation were used for numerical variables such as maternal and gestational age, while categorical variables like gender and maternal risk factors were summarized using frequencies and percentages. The findings were presented in tables for clarity. The groups were compared using Student's t-test and chi-square test. Multivariate logistic regression was used to adjust for gestational age and maternal age. A p-value of ≤ 0.05 was considered significant.

RESULTS

The study involved 300 pregnant females between 26-34 weeks of gestation and their

neonates were segregated into two groups. Group A comprised 195 neonates whose mothers received both magnesium sulphate and antenatal steroids, while Group B included 105 neonates whose mothers were given only antenatal steroids. There was no significant difference in baseline maternal and neonatal characteristics between two groups ($p > 0.05$), as shown in **table 1 and 2.** Cranial ultrasound examinations on third day of life revealed following findings **table 3**.

TABLE 1: Baseline maternal and neonatal characteristics of study groups

Variable	Group A (n=195)	Group B (n=105)	p-value
Maternal age (years)	28.44 ± 4.25	28.85 ± 4.42	0.431
Gestational age (weeks)	31.31 ± 2.10	31.03 ± 2.47	0.307
Gender (Male)	122 (62.6%)	64 (61%)	
Gender (Female)	73 (37.4%)	41 (39%)	0.784

TABLE 2: Maternal risk factors associated with preterm birth in study groups

Risk factor	Group A n=195 (%)	Group B n=105 (%)	p-value
Pregnancy-induced hypertension (PIH)	42 (21.5)	22 (21.0)	0.915
Gestational diabetes mellitus (GDM)	20 (10.3)	09 (8.6)	0.639
Premature rupture of membranes (PROM)	4 (2.1)	03 (2.9)	0.678
Polyhydramnios	12 (6.2)	08 (7.6)	0.647
Placental abruption	18 (9.2)	06 (5.7)	0.279
Reduced amniotic fluid index (AFI)	09 (4.6)	12 (11.4)	0.032
Overall comparison			0.378

TABLE 3: Cranial scan at day 3

Variable	Group A (Mg + steroids) n = 195 (%)	Group B (Steroids only) n = 105 (%)	Absolute difference % (A − B)	95% CI (%)	p-value
Normal scan (no IVH)	166 (85.1)	65 (61.9)	+23.2	12.8 to 33.6	<0.001
Any IVH (Grades I–II)	29 (14.9)	40 (38.1)	−23.2	−33.4 to −12.8	<0.001
Severe IVH (Grades III–IV)	0 (0.0)	0 (0.0)	—	—	—

Group A demonstrated a significantly higher proportion of normal scans and a lower frequency of Grade 1 and 2 IVH compared to Group B ($p < 0.001$, 95% CI for difference in normal scans: 12.8%–33.6%).Most infants in the magnesium group demonstrated normal cranial ultrasound findings (85.1 % vs 61.9 %), indicating a substantial protective association between antenatal magnesium exposure and early IVH occurrence. No cases of severe IVH (Grades III–IV) were detected in either group on day 3, suggesting that early postnatal scans primarily reflected mild to moderate bleeds.

At the time of discharge, normal cranial ultrasound findings are as follows **table 4.**

TABLE 4: Cranial scan at discharge

IVH grade / scan finding	Group A n = 195 (%)	Group B n = 105 (%)	Absolute difference % (A−B)	95% CI (%)	p-value
Normal scan	157 (80.5)	75 (71.4)	+9.1	−1.2 to 19.4	0.099
Grade I IVH	12 (6.2)	8 (7.6)	−1.5	−7.6 to 4.6	0.694
Grade II IVH	21 (10.8)	10 (9.5)	+1.2	−5.9 to 8.3	0.772
Grade III IVH	0 (0.0)	3 (2.9)	−2.9	−6.0 to 0.3	0.042
Grade IV IVH	2 (1.0)	4 (3.8)	−2.8	−6.7 to 1.1	0.189
Severe IVH (Grades III + IV)	2 (1.0)	7 (6.7)	−5.6	−10.6 to −0.7	0.010

At discharge, the overall proportion of normal cranial ultrasound scans remained higher among infants in the magnesium + steroid group (80.5 % vs 71.4 %), although this difference did not reach statistical significance (p = 0.099).

When IVH severity was analysed separately, severe IVH (Grades III–IV) was significantly less frequent in the magnesium group (1.0 % vs 6.7 %; p = 0.010).

Grade III hemorrhage was absent in Group A but occurred in 2.9 % of Group B infants (p = 0.042), while Grade IV hemorrhage was also lower (1.0 % vs 3.8 %, p = 0.189).

These findings suggest that antenatal magnesium sulphate, when used alongside corticosteroids, may reduce the likelihood of both early and severe IVH in preterm neonates.

A multivariate logistic regression model was applied to assess the independent predictors of IVH, incorporating magnesium sulphate administration, gestational age, and maternal age as covariates. After adjusting for potential confounders, magnesium sulphate administration remained a significant protective factor, associated with a 72% reduction in the likelihood of IVH (adjusted odds ratio [aOR] = 0.28, 95% confidence interval [CI]: 0.12–0.65; p< 0.001) **fig 1**

Gestational age also demonstrated a statistically significant independent effect, with each additional week of gestation corresponding to a 26% decrease in the odds of IVH (aOR = 0.74, 95% CI: 0.60–0.90; p = 0.002). In contrast, maternal age did not exhibit any meaningful association with IVH risk (aOR = 0.98, 95% CI: 0.88–1.08; p = 0.60

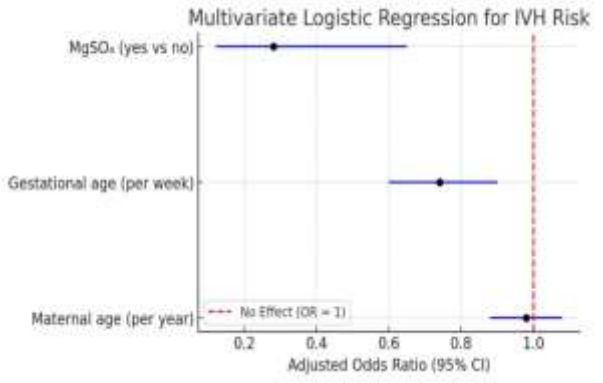

Fig 1: Multivariate logistic regression analysis

Mortality occurred in 3 neonates (1.5%) in Group A and 5 neonates (4.8%) in Group B. These differences were not statistically significant (p = 0.19, 95% CI: –1.5% to 8.2%).

The mean hospital stay was 8.48 ± 5.84 days (range: 3–27 days). Most neonates (74%) were discharged within 10 days, and only 6% required hospitalization beyond 20 days.

The mean corrected gestational age (CGA) at discharge was 35.4 ± 2.65 weeks, with most infants discharged near term-equivalent age, the youngest discharged at about 30 weeks and the oldest at nearly 39 weeks**.**

DISCUSSION

The present study observed that preterm neonates born to mothers who received both magnesium sulphate and antenatal corticosteroids had a lower incidence and severity of intraventricular hemorrhage (IVH) compared to those whose mothers received corticosteroids alone. These findings support an association between combined antenatal therapy and improved short-term neuroprotective outcomes.

Comparable results have been reported in several studies. Patel et al.[15] demonstrated that administration of magnesium sulphate in conjunction with antenatal steroids before 32 weeks' gestation significantly reduced the risk of IVH and periventricular leukomalacia. Similarly, Gentle et al.[16] found that dual therapy was associated with a lower rate of severe neurodevelopmental impairment or death in extremely preterm infants. Bansal and Desai.[17] also reported nearly a 50% reduction in IVH among infants whose mothers received magnesium sulphate. These results collectively strengthen the evidence that magnesium sulphate enhances the neuroprotective benefits of corticosteroids.

Regionally, Pakistani studies have independently evaluated the roles of antenatal corticosteroids and magnesium sulphate in preterm neuroprotection. Fatima et al.[18] showed that corticosteroids significantly reduced the risk of IVH, while Mazhar et al.[19] confirmed that magnesium sulphate lowered neurological complications in imminent preterm deliveries. However, the combined effect of these

interventions on IVH prevention has not been extensively investigated within Pakistan, highlighting the value of the present study.

In addition to a lower overall incidence of intraventricular hemorrhage, our study also observed a marked reduction in the severity of IVH. The frequency of Grade 3–4 IVH was significantly lower among neonates exposed to both magnesium sulphate and antenatal corticosteroids compared with those who received steroids alone (1.0% vs. 6.7%, p = 0.036). This finding supports an association between combined antenatal therapy and reduced risk of severe hemorrhagic brain injury. Similar trends have been reported in international studies, suggesting that magnesium's vasodilatory and neuroprotective properties may contribute to stabilizing fragile germinal matrix vasculature and mitigating the progression of minor bleeds into severe IVH.[20.]

Limitations: This study has several limitations that should be acknowledged.

- It was an observational, single-center design, which restricts the ability to infer causality and may limit the generalizability of the findings to other settings.
- Selection bias could not be fully excluded, as the decision to administer magnesium sulphate was based on the clinical discretion of the attending obstetrician rather than random allocation.
- Although baseline characteristics between groups were comparable, potential confounding factors such as maternal comorbidities, antenatal complications, mode of delivery, and neonatal hemodynamic instability were not adjusted for in multivariate analysis.
- Long-term neurodevelopmental outcomes were not assessed; therefore, the sustained neuroprotective impact of magnesium sulphate beyond the neonatal period remains uncertain.

CONCLUSION

The combined use of antenatal magnesium sulphate and corticosteroids was associated with a reduced incidence and severity of intraventricular hemorrhage among preterm neonates. This suggests a potential additive neuroprotective benefit when both agents are administered before preterm birth. However, as this was an observational study, causality cannot be inferred. Future multicentred randomized controlled trials with standardized dosing protocols and long-term neurodevelopmental follow-up are required to confirm these findings and guide clinical practice.

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REFERENCES

1. Moradi Y, Yousef M, et al. The effect of antenatal magnesium sulphate on intraventricular haemorrhage in premature infants: a systematic review and meta-analysis. Obstet Gynecol Sci. 2020;63(4):395–406. doi:10.5468/ogs.19210
2. Tsao PC. Intraventricular hemorrhage (IVH) and post hemorrhagic hydrocephalus (PHH) in preterm infants. J Korean Neurosurg Soc. 2023;66(3):228–238. doi:10.3340/jkns.2022.0288
3. Starr R, De Jesus O, Shah SD, et al. Periventricular and intraventricular haemorrhage. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [updated 2023 Aug 23; cited 2025 Oct 9]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538310/

4. Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2020;(12):CD004454.
5. Stark MJ, Clifton VL, Wright IM. Effects of antenatal magnesium sulphate treatment for neonatal neuroprotection on cerebral oxygen kinetics. Pediatr Res. 2015;78(3):310–314. doi:10.1038/pr.2015.96
6. Killion MM. Magnesium sulphate for neuroprotection. MCN Am J Matern Child Nurs. 2015;40(6):394. doi:10.1097/NMC.0000000000000187
7. Chollat C, Sentilhes L, Marret S. Fetal neuroprotection by magnesium sulfate: from translational research to clinical application. Frontiers in neurology. 2018 Apr 16;9:247.
8. Koning G, Leverin AL, Nair S, Schwendimann L, Ek J, Carlsson Y, Gressens P, Thornton C, Wang X, Mallard C, Hagberg H. Magnesium induces preconditioning of the neonatal brain via profound mitochondrial protection. Journal of Cerebral Blood Flow & Metabolism. 2019 Jun;39(6):1038-55.
9. Hirtz DG, Nelson KB, Grether JK, et al. Antenatal magnesium and cerebral palsy in preterm infants. J Pediatr. 2015;167(4):834–839.e3. doi:10.1016/j.jpeds.2015.06.067
10. Petrova A, Mehta R. Magnesium sulphate tocolysis and intraventricular haemorrhage in very preterm infants. Indian J Pediatr. 2012;79(1):43–47. doi:10.1007/s12098-011-0440-y
11. Mittendorf R, Dambrosia J, Pryde PG, Lee KS, Gianopoulos JG, Besinger RE, Tomich PG. Association between the use of antenatal magnesium sulfate in preterm labor and adverse health outcomes in infants. American journal of obstetrics and gynecology. 2002 Jun 1;186(6):1111-8.
12. Shepherd E, Salam RA, Middleton P, et al. Antenatal magnesium sulphate and adverse neonatal outcomes: a systematic review and meta-analysis. PLoS Med. 2019;16(12):e1002988. doi:10.1371/journal.pmed.1002988
13. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: a systematic review and metaanalysis. American journal of obstetrics and gynecology. 2009 Jun 1;200(6):595-609.
14. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, Iams JD, Wapner RJ, Sorokin Y, Alexander JM, Harper M. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. New England Journal of Medicine. 2008 Aug 28;359(9):895-905.
15. Patel D, Vora A, Goyal P, Dubey P. Effects of antenatal steroids with magnesium sulphate on intraventricular hemorrhage and periventricular leukomalacia in neonates born below 32 weeks of gestation. Natl J Med Res. 2024;14(1):1–5.
16. Gentle SJ, Carlo WA, Tan S, Gargano M, Ambalavanan N, Chawla S, et al. Association of antenatal corticosteroids and magnesium sulfate therapy with neurodevelopmental outcome in extremely preterm children. Obstet Gynecol. 2020;135(6):1377–1386.
17. Bansal V, Desai A. Efficacy of antenatal magnesium sulphate for neuroprotection in extreme prematurity: a comparative observational study. J Obstet Gynaecol India. 2022;72(Suppl 1):36–47. doi:10.1007/s13224-021-01531-9
18. Fatima F, Ajmal F, Shaukat F, Waqar H. Intraventricular haemorrhage amongst preterm babies—preventive role of dexamethasone. Proc Shaikh Zayed Postgrad Med Inst. 2010;24(2):61–65.
19. Mazhar T, Rauf S, Ambareen A, Nadir S. The efficacy and safety of magnesium sulphate for neonatal neuroprotection in patients with imminent preterm deliveries: experience at a tertiary care hospital. J Med Sci. 2023;31(2):1–7.
20. Ayed M, Ahmed J, More K, Ayed A, Husain H, AlQurashi A, Alrajaan N. Antenatal magnesium sulfate for preterm neuroprotection: a single-center experience from Kuwait Tertiary NICU. Biomedicine hub. 2022 Jun 30;7(2):80-7.

Authors' contribution

SI: Patient diagnosis & management, literature search, data collection manuscript.
SR: patient management, literature search, data collection, manuscript.
ZS: Patient diagnostic & management, manuscript writing.
SI: Patient diagnostic & management, manuscript writing.
MR: Patient management, literature search, data collection, manuscript writing.

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.