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Original Research Article

Fetomaternal Outcome in Patients with Early Preterm Labour Following Administration of Magnesium Sulphate - A Hospital Based Observational Study

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Abstract:

Background: The disability known as cerebral palsy (CP) is more common in individuals who are preterm and have low birth weights (LBW). Numerous research indicate that providing magnesium sulfate (MgSO4) to expectant moms can enhance the neurodevelopmental result of their offspring. to evaluate magnesium sulfate's neuroprotective efficacy in cases of early preterm labor (28–32 weeks). The purpose of this study is to evaluate any negative effects magnesium sulfate may have on the mother or fetus.

Methods: This hospital based prospective observational study was conducted at Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital, Laheriasarai, Bihar from January 2021 to December 2021. At the beginning, 72 expectant mothers who had planned preterm births at 28 to 32 weeks of gestation because of maternal or fetal indications were chosen. Of the 37 women who got MgSO4, two were unable to be contacted for more information. Thus, 35 women in the study group (Group A) who received MgSO4 and 35 women in the control group (Group B) who did not received MgSO4 participated in the study. Both groups received corticosteroids.

Results: Compared to the MgSO4 group (3/35, 8.6%), the non-MgSO4 group had a substantially higher number of newborns that had IVH (5/35, 14.3%) (p Value = 0.452). In this study, compared to 2 (5.7%) in the MgSO4 group, 3 (8.6%) ELBW newborns in the non-MgSO4 group experienced IVH. One VLBW baby (2.9%) in the MgSO4 group and two (5.7%) in the non-MgSO4 group suffered IVH. 20% (7/35) of the newborns in the non-MgSO4 group who were between 28 and 30 weeks gestational age needed to be intubated, whereas only 4.4% (4/35) of the infants in the MgSO4 group needed to be. In the non-MgSO4 group, 5.7% (2/35) of the babies between 30 and 32 weeks needed intubation, whereas 14.3% (5/35) of the kids in the MgSO4 group needed it. (0.017 is the p-value). In the non-MgSO4 group, 5.7% (2/35) of babies born between 30 and 32 weeks gestation exhibited delayed milestones; in the MgSO4 group, no baby displayed any delayed milestones.

Conclusion: Prenatal magnesium sulfate (MgSO4) seems to reduce the risk of intraventricular hemorrhage, the need for ongoing respiratory assistance, and invasive mechanical ventilation. The effects of antenatal magnesium SO4 are comparable for a variety of preterm gestational ages.

Keywords: Preterm, Neuroprotective, Magnesium Sulfate.

Introduction

The primary cause of infant illness and death worldwide is preterm birth. Over 10 percent of all neonates born worldwide are prematurely born, with 15 million of them babies born early each year. [1] Although exact statistics on the prevalence of preterm birth around the world are not available at this time, estimates range from 5% in wealthy nations to 25% in underdeveloped nations. [2] The majority of growing nations like India bear the burden of premature delivery. [2] The incidence of premature birth in India is 23.3%. [3] Preterm delivery (before 32 weeks) causes 60% of perinatal deaths and almost all neurological morbidity; it makes up 1% to 2% of all births. [4] Worldwide, preterm birth rates are on the rise, potentially due to aging mothers, diabetes, and a higher prevalence of induction brought on by maternal indications such PIH. On the other hand, enhanced ICU care and treatments like surfactant and prenatal corticosteroids have increased the survival rate of premature babies. However, given that preterm delivery is linked to neurodevelopmental

impairments such neuromotor deficits, cognitive deficits, learning difficulties, behavioral and psychiatric illnesses, and neurosensory deficiencies, their long-term neurological outcome is still a significant cause for concern [5, 6].

Necrotizing enterocolitis, cerebral bleeding, and other respiratory and cardiovascular issues are examples of short-term consequences of premature birth. After overcoming these initial challenges, some people may experience long-term effects such as cognitive dysfunction, hearing loss, vision impairment, or intellectual disability. [7–9] In Indian contexts, 25% of very low birth weight infants followed for two years had aberrant neurological results [10].

Preterm newborn central nervous system difficulties are thought to be caused by two known patterns of injury: 1. intraventricular hemorrhage (IVH); and 2. white matter damage. These can cause neurodevelopmental issues and cerebral palsy (CP) later in childhood. Two to 2.5 out of every 1000 live newborns are affected by CP11. Due to frequent magnesium sulfate usage in eclamptic patients, several studies have demonstrated that infants born preterm to women with eclampsia had a decreased frequency of poor central nervous system outcomes [12, 13].

Nelson KB and Gretter JK first reported that very-low birth weight infants (less than 1.5 kg) with cerebral palsy responded less favorably to magnesium sulphate therapy for pre-eclampsia and tocolysis in utero (7.1 vs. 36%). This finding led to the discovery of magnesium's neuroprotective effects in preterm newborns. In order to reduce the likelihood of preterm neurodevelopmental issues, prospective research has been conducted to find a potential preventative medication with neuroprotective benefits, and magnesium sulphate (MgSO4) studies have shown promise [14]. In preterm newborns, magnesium sulfate restores infusion by lowering cerebral artery constriction, stabilizing blood pressure, and reducing brain metabolism [12]. We hypothesise that the use of intravenous magnesium sulfate in patients with early preterm birth can reduce the risk of neurological complications of preterm infants, and consequently reduce neonatal mortality and morbidity. This is based on the evidence that magnesium sulfate has neuroprotective effects with minimal and tolerable side effects [2,12,15].

Material and Methods

From January to December of 2021, a hospital-based prospective observational study was carried out in the Obstetrics and Gynecology department of Darbhabga Medical College and Hospital in Laheriasarai, Bihar. The first 72 pregnant women who went into preterm labor were chosen for planned preterm births between 28 and 32 weeks of gestation because of maternal or fetal indications. Of these, 37 women received MgSO4, of whom two could not be traced. Accordingly, 35 women in the study group (Group A) received MgSO4, while 35 women in the control group (Group B) did not get MgSO4. Each group received one course of corticosteroid.

Ultrasonography, clinical examination, and clinical history were used to diagnose premature labor. The patients' medical, obstetric, and demographic histories were evaluated using pre-made proforma.

15 minutes were allocated for a 4 gm intravenous loading dosage, after which a 1 g/hr infusion was started and continued for up to 24 hours, or until the baby was born, whichever occurred first (FOGSI FOCUS- Prevention of preterm labor, 2017). The maternal side effects that were assessed included hot flushes, nausea, vomiting, muscle weakness, and soreness at the injection site in addition to respiratory depression. Birth weight, Apgar scores at one and five minutes, admission to the intensive care unit, need for respiratory support, presence of IVH (identified by cranial USG performed within 14 days of birth), neonatal morbidities, adverse effects on the mother, neonatal signs and symptoms (weak cry, tachypnoea, chest retraction, lathery, seizure, hypotension, apnea, sepsis), neonatal morbidities (RDS, NEC, septicemia), and the baby's condition upon discharge were all examined and compared. A follow-up at six months was conducted to evaluate any early neurological problems. We evaluated these newborns' accomplishment of developmental milestones at two, four, and six months of corrected gestational age. These benchmarks were utilized for comparison at two months (social grin), four months (neck holding), and six months (sitting with support).

The Fishers exact test or chi square is used to assess the relationship between categorical variables. Using the Shapiro-Wilk and Kolmogorov-Smirnova tests, the normality of the data was examined. When comparing the mean difference between two groups, the independent T test is employed, provided that the continuous variable's normality condition is met.

Results

In the current investigation, compared to 3 (8.6%) of the kids delivered to mothers who got MgSO4, 5 (14.3%) of the babies born to mothers who did not receive MgSO4 suffered IVH (table 1).

Table 1: Incidence of IVH in MgSO4 (Group A) and non-MgSO4 group (Group B)

IVH	Group A	Group B	Total	Percentage	Group A%	Group B%	p-value
Absent	32	30	62	89%	91%	86%	0.452
Present	3	5	8	11%	9%	14%	
Total	35	35	70	100%	100%	100%	

In this study, compared to 2 (5.7%) in the MgSO4 group, 3 (8.6%) ELBW newborns in the non-MgSO4 group experienced IVH. Table 2 shows that of the VLBW newborns in the MgSO4 group, 1 (2.9%) had IVH and 2 (5.7%) had IVH in the non-MgSO4 group.

Table 2: Incidence of IVH in comparison to weight of the baby

Categories	Weight of baby	No	Yes	Total	No%	Yes%	Total%	p-value
Group A (MgSO4 group)	<1 kg	3	2	5	8.6%	5.7%	14.3%	<0.001
	1-1.5 kg	17	1	18	48.6%	2.9%	51.4%	
	>1.5 kg	12	0	12	34.3%	0.0	34.3%	
	Total	32	3	35	91.4%	8.6%	100.0%	
Group B (Non-MgSO4 group)	<1 kg	4	3	7	11.4%	8.6%	20.0%	<0.033
	1-1.5 kg	13	2	15	37.1%	5.7%	42.9%	
	>1.5 kg	13	0	13	37.1%	0.0	37.1%	
	Total	30	5	35	85.7%	14.3%	100.0%	

Of the 35 newborns in the nonMgSO4 group, 12 (34.3%) required intubation, while 6 (17.1%) of the 35 babies in the MgSO4 group needed intubation. Depending on gestational age, the two groups' CPAP requirements were comparable. In the non-MgSO4 group, 3 (8.6%) out of 35 newborns needed oxygen by hood, whereas in the MgSO4 group, 9 (25.7%) out of 35 kids needed oxygen between 28 and 30 weeks of gestation. In the nonMgSO4 group, 7 (20%) out of 35 newborns needed oxygen by the time they were 30 to 32 weeks gestated. Of the 35 infants in the MgSO4 group born between 30 and 32 weeks gestation, 6 (17.1%) needed oxygen via hood (table 3).

Table 3: Comparison of respiratory support with gestational age in babies born to mother who received MgSO4 and those did not

Categories	Gestational Age							
	Respiratory support	28-30 wks	30-32 wks	Total	28-30 wks%	30-32 wks%	Total%	p-value
Group A (MgSO4 group)	CPAP	7	2	9	20.0%	5.7%	25.7%	0.576
	Intubated	4	2	6	11.4%	5.7%	17.1%	
	Not required	2	3	5	5.7%	8.6%	14.3%	
	O2 by hood	9	6	15	25.7%	17.1%	42.9%	
	Total	22	13	35	62.9%	37.1%	100.0%	
Group B (Non-MgSO4 group)	CPAP	7	2	9	20.0%	5.7%	25.7%	0.677
	Intubated	7	5	12	20.0%	14.3%	34.3%	
	Not required	0	4	4	0.0	11.4%	11.4%	
	O2 by hood	3	7	10	8.6%	20.0%	28.6%	
	Total	17	18	35	48.6%	51.4%	100.0%	
Total	CPAP	14	4	14	20.0%	5.7%	20.0%	0.453
	Intubated	11	7	13	15.7%	10.0%	18.6%	
	Not required	2	7	16	2.9%	10.0%	22.9%	
	O2 by hood	12	1	37	17.1%	1.4%	38.6%	
	Total	39	31	70	55.7%	44.3%	100.0%	

Compared to the two (5.7%) kids whose mother did not get MgSO4, five (14.3%) ELBW babies (<1kg) born to mothers who got MgSO4 required intubation. Compared to two (5.7%) kids in the MgSO4 group, four (11.4%) VLBW newborns in the non-MgSO4 group needed to be intubated. Compared to the MgSO4 group, where none of the babies needed intubation, the nonMgSO4 group had two LBW babies (>1.5 kg) that needed intubation (table 4).

Table 4: Requirement of respiratory support according to birth weight in babies born to mother who received MgSO4 and those did not

Categories	Weight of baby									
	Respiratory support	<1 kg	1-1.5 kg	>1.5 kg	Total	<1 kg%	1-1.5 kg%	>1.5 kg%	Total%	p-value
Group A (MgSO4 group)	CPAP	2	5	2	9	5.7%	14.3%	5.7%	25.7%	
	Intubated	2	2	0	4	5.7%	5.7%	0.0	11.4%	0.011
	Not required	0	3	3	6	0.0	8.6%	8.6%	17.1%	
	O2 by hood	0	9	7	16	0.0	25.7%	20.0%	45.7%	
	Total	4	19	12	35	11.4%	54.3%	34.3%	100.0%	
Group B (Non-MgSO4 group)	CPAP	1	5	4	10	2.9%	14.3%	11.4%	28.6%	
	Intubated	5	4	2	11	14.3%	11.4%	5.7%	31.4%	0.002
	Not required	0	2	1	3	0.0	5.7%	2.9%	8.6%	
	O2 by hood	0	5	6	11	0.0	14.3%	17.1%	31.4%	
	Total	6	16	13	35	17.1%	45.7%	37.1%	100.0%	
Total	CPAP	3	10	6	14	4.3%	14.3%	8.6%	20.0%	
	Intubated	7	6	2	13	10.0	8.6%	2.9%	18.6%	<0.001
	Not required	0	5	4	16	0.0	7.1%	5.7%	22.9%	
	O2 by hood	0	14	13	27	0.0	20.0%	18.6%	38.6%	
	Total	10	35	25	70	14.3%	50.0%	35.7%	100.0%	

Three (8.6%) of the newborns in the MgSO4 group and five (14.3%) of the babies in the non-MgSO4 group had delayed milestones at the six-month mark, respectively. Three (8.6%) neonates in the current trial, who were between 28 and 30 weeks gestation, failed to meet milestones in both the MgSO4 and nonMgSO4 groups. Between 30 and 32 weeks of gestation, 2 (5.7%) of the kids in the non-MgSO4 group and none of the newborns in the MgSO4 group experienced delayed milestones (table 5).

Table 5: Comparison of gestational age with achievement of milestones at the end of 6 months in MgSO4 and non MgSO4 group

Categories	Outcome (milestone) 6 months							
		28-30 wks	30-32 wks	Total	28-30 wks%	30-32 wks%	Total%	p-value
Group A (MgSO4 group)	Achieved	19	13	32	54.3%	37.1%	91.4%	
	Not achieved	3	0	3	8.6%	0.0	8.6%	0.357
	Total	22	13	35	62.9%	37.1%	100.0%	
Group B (Non-MgSO4 group)	Achieved	14	16	30	40.0%	45.7%	85.7%	
	Not achieved	3	2	5	8.6%	5.7%	14.3%	0.729
	Total	17	18	35	48.6%	51.4%	100.0%	

After six months, LBW kids in the MgSO4 group did not exhibit delayed milestones at all, while LBW babies in the nonMgSO4 group did exhibit delayed milestones in 1 (3%). Two VLBW infants (6%) who did not meet milestones in the MgSO4 group and three (9%) in the non-MgSO4 group. Table 6 shows that 1(3%) of ELBW babies in the MgSO4 and nonMsSO4 groups experienced delayed milestones.

Table 6: Comparison of birth weight with achievement of milestones at the end of 6 months

Categories	Weight of baby								
	Outcome (Mile-stones) 6 months	<1 kg	1-1.5 kg	>1.5 kg	Total	<1 kg%	1-1.5 kg%	>1.5 kg%	Total%
Group A (MgSO4 group)	Achieved	3	17	12	32	9%	49%	34%	91%
	Not achieved	1	2	0	3	3%	6%	0	9%
	Total	4	19	12	35	11%	54%	34%	100%
Group B (Non-MgSO4 group)	Achieved	5	13	12	30	14%	37%	34%	86%
	Not achieved	1	3	1	5	3%	9%	3%	14%
	Total	6	16	13	35	17%	46%	37%	100%

Compared to the MgSO4 group, where 3 out of 35 kids (8.6%) had IVH, 5 (14.3%) of the 35 babies in the current trial who were not exposed to MgSO4 antenatally developed IVH. Of the kids born to moms who got MgSO4 and those who did not, 4 (11.4%) had NEC. Compared to 17 (48.6%) newborns in the non-MgSO4 group, 15 (42.9%) babies in the MgSO4 group had RDS. Compared to 2 (5.7%) of the kids in the non-MgSO4 group, 3 (8.6%) of the babies in the MgSO4 group experienced septicemia (table 7).

Table 7: Comparison of incidence of neonatal morbidities in babies born in mother who received MgSO4 (Group A) and those who did not (Group B)

Neonatal morbidities	Group A	Group B	Total	Group A%	Group B%	Total%
Necrotising enterocolitis	4	4	8	11.4%	11.4%	11.4%
RDS	15	17	32	42.9%	48.6%	45.7%
Septicaemia	3	2	5	8.6%	5.7%	7.1%
IVH	3	5	8	8.6%	14.3%	11.4%

Discussion

The primary risk factor for IVH in the current study was an infant's abnormally low birth weight (p value = <0.001). In 1992, Kuban and associates, as well as later Van de Bor et al and Levitron, discovered that providing MgSO4 to pre-eclamptic mothers decreased the likelihood of intraventricular hemorrhage in low birth weight infants [16].Comparable to what we discovered in our investigation, the Crowther 2003 and Rouse 2008 RCTs also reported a protective effect [17,18].

There was a protective effect of antenatal MgSO4 exposure against the need for respiratory assistance. In our investigation, MgSO4 demonstrated a protective effect against the requirement for invasive breathing, even in cases where birth weight or gestational age were lower. 20% (7/35) of the newborns in the non-MgSO4 group who were between 28 and 30 weeks gestational age needed to be intubated, whereas only 4.4% (4/35) of the kids in the MgSO4 group needed to be.

In the non-MgSO4 group, 5.7% (2/35) of the babies between 30 and 32 weeks needed intubation, whereas 14.3% (5/35) of the kids in the MgSO4 group did (p value = 0.017). Compared to 5.7% (2/35) of ELBW and 5.7% (2/35) of VLBW kids in the MgSO4 group, 14.3% (5/35) of ELBW babies and 11.4% (4/35) of VLBW babies in the nonMgSO4 group required intubation (p value = 0.011). No discernible variations were observed in the utilization of breathing assistance after birth or in the Apgar score at five minutes < seventeen by Crowther et al. (2017) in their meta-analysis. In a study on the effects of MgSO4 on newborns delivered to 6654 moms with preeclampsia, Mina Abbassi [19] found that hypotonia, lowered 1-minute and 5-minute Apgar scores, intubation, and NICU admission were enhanced.

At the end of the six-month research, we discovered more delayed milestones in the non-MgSO4 group (14%) than in the MgSO4 group (6%). In a 24-month follow-up analysis, Rouse et al. (2008) discovered that children in the magnesium sulfate group who survived had substantially lower rates of major gross motor impairment (3.4% vs. 6.6%; relative risk, 0.51; 95% CI, 0.29 to 0.91).18 Marret et al. [20] presented the results of a trial including 573 mothers over a 2-year period. Cerebral palsy rates among survivors were non-significantly lower in infants whose mothers received magnesium sulfate (7.0% vs. 10.2%; relative risk, 0.69; 95% CI, 0.41 to 1.16). The current study demonstrates enhanced neuroprotection in infants weighing over 1.5 kg. The infants' mean birthweight was similar in both groups. At the end of six months, 10.5% of VLBW kids in the MgSO4 group and 18% of VLBW babies in the nonMgSO4 group in this study had delayed milestones. While none of the LBW babies in the MgSO4 group showed delayed milestones, 7.6% of the LBW newborns in the nonMgSO4 group did. Nelson KB (1995) discovered that MgSO4 21 was exposed to 36% of the 75 VLBW controls and 7.1% of the 42 VLBW infants with CP. [21]

In both groups, 8.6% (3/35) of newborns born between 28 and 32 weeks gestational age exhibited delayed milestones. While no kids in the MgSO4 group experienced delayed milestones between 30 and 32 weeks of gestation, 5.7% (2/35) of the newborns in the non-MgSO4 group [Group A (p value = 0.357), Group B (p value = 0.729)] did. Jung EJ et al. (2017) demonstrated that for patients in the 28-30 weeks and 28-30 weeks subgroup, there was no discernible difference in developmental delay between the two groups. According to Rouse et al. (2008), at 24 months of age, 3.5% of the babies in the MgSO4 group and 2.5% of the newborns in the placebo group, aged 28 to 30 weeks, developed cerebral palsy.[18]

No cases of serious adverse effects required an early cessation of the magnesium sulfate infusion. In line with previous findings, our research indicates that administering MgSO4 to women for neuroprotection does not have a clinically meaningful effect on maternal morbidity. There were no statistically significant differences found in the examination of baby morbidities. Four (11.4%) of the eight neonates with NEC in this study were in the MgSO4 group, while the remaining four (11.4%) were in the non-MgSO4 group. No relationship between MgSO4 consumption and NEC was found. In his meta-analysis, Agustn Conde-Agudelo found that the MgSO4 group had a non-significantly higher incidence of necrotizing enterocolitis. [22] Although the difference was not statistically significant, the MagNET experiment raised concerns about MgSO4 potentially injuring infants. The research showed that 32% of neonates whose mothers received MgSO4 experienced more

adverse events than those whose mothers received a placebo (19%). [23]

Conclusion

Give magnesium sulfate to prevent cerebral palsy and lower the risk of fetal or infant death before preterm birth for fetal neuroprotection. Antenatal magnesium sulfate (MgSO4) is now well established as a neuroprotective drug to lower the incidence of cerebral palsy in preterm newborns, having undergone a number of major randomized control trials.

Regardless of the etiology of preterm delivery, there are positive effects that are noticed, and the protective effect is shown regardless of gestational age. Because of its affordability, ease of storage, and broad availability, magnesium sulphate presents a significant deal of potential for usage in resource-constrained environments.

We suggest the inclusion of such a low-cost, simple-to-administer treatment with negligible side effects for mothers in the national guidelines could significantly improve the prognosis for preterm infants and should be viewed as an integral part of the prenatal prophylactic treatment of preterm infants.

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