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Role of Intravenous Magnesium Sulphate in Term Neonates with Severe Birth Asphyxia in Terms of Immediate Neurological Outcome

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ABSTRACT

Introduction: Different treatment modalities are used worldwide for birth asphyxia, including initiation of therapeutic hypothermia within 3 hours after birth. Some modalities under research are intravenous magnesium sulphate, endogenous cannabinoids, stem cell therapy, xenon, argon, allopurinol, and topiramate. **Objectives:** To determine frequency of neurological outcome and mortality of term neonates with severe birth asphyxia treated with and without intravenous magnesium sulphate (MgSO4). **Methodology:** A total of 102 neonates were randomized equally to treatment and placebo groups (group A and B). Sampling technique used was non-probability consecutive sampling using simple randomization. Group A got two additional doses of magnesium sulfate at 24 and 48 hours after receiving an infusion of 250 mg/kg/dose in 10% dextrose to make volume equal to 3.0 mL/kg/dose over the course of an hour, after first dose at admission. 10% dextrose 3.0 mL/kg/dose was given to the control group over the course of an hour, with two further doses given at comparable intervals. Outcome was noted in both groups in terms of improvement in neurological findings and death of neonate during hospital admission. **Results:** Neurological improvement in terms of improvement in establishment of feed were recorded in 42 (82.35%) of the patients in group A and 33 (64.71%) of the patients in group B (p-value = 0.043). Additionally, death was documented in 04 (7.84%) and 12 (23.53%) patients, respectively (p-value = 0.029). **Conclusion:** The study indicated that magnesium sulfate had the potential to be used as a neuroprotective intervention in neonatal care since it greatly improved the appearance of a good sucking reflex in neonates with severe birth asphyxia.

INTRODUCTION

With an estimated 690,000 deaths annually, intrapartum-related events rank as the third most common cause of mortality for children under the age of five worldwide.[1] With a frequency of 3.94–5.12 per 1000 live births, intrapartum-related events rank second in terms of infant mortality (24%), after prematurity, despite improvements in obstetrical, perinatal, and neonatal care.[1,2] There is a dose-response gradient between the degree of asphyxia and the resulting complications, and the effects of birth asphyxia can range from minor to severe, including HIE, multi-organ dysfunction, and death.[3]

One of the main causes of newborn illness and mortality worldwide is birth asphyxia. Neonatal asphyxia accounts for 20.9% of neonatal deaths in Pakistan, where the neonatal mortality rate is 41.22 per 1,000 live births.[4] It continues to be a major source of fatalities and poor developmental outcomes. [2-4] According to estimates, infections account for 35% of neonatal fatalities worldwide, preterm births for 28%, and birth asphyxia for 23%.[5] As a result of the rising prevalence of risk factors, asphyxia is thought to occur more frequently in emerging nations. About 40% of deaths and morbidities are caused by moderate to severe birth asphyxia.[6]

Management of neonates with birth asphyxia is mainly supportive, including management of seizures and fluid electrolyte balance along with management of hematological and cardiovascular abnormalities. Different treatment modalities are used worldwide for birth asphyxia, including initiation of therapeutic hypothermia within 3 hours after birth. Some modalities under research are intravenous magnesium sulphate, endogenous cannabinoids, stem cell therapy, xenon, argon, allopurinol, and topiramate.[7]

The neuroprotective efficacy of magnesium sulfate has been explored in various international and local studies.[8] Studies done in two neonatal centers at Lahore, Pakistan have concluded that intravenous magnesium sulfate is safe and has beneficial effects on neurological outcome of neonates with birth asphyxia. Neurological status was normal in 26(65%) neonates with IV MgSO4 and

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15(37.5%) without IV MgSO4. 30(75%) neonates survived in IV MgSO4 group and 10(25%) without IV MgSO4 group. In-hospital mortality was 25% in IV MgSO4 group and 35% in control group.[6]

The rationale of the present research is to explore the beneficial role of intravenous magnesium sulphate as a neuroprotective therapeutic agent in neonates with birth asphyxia in resource limited tertiary care setup in Rawalpindi.

MATERIALS AND METHODS

With ethical review committee clearance, 102 neonates with gestational age >36+6 weeks having birth asphyxia (failure to initiate spontaneous respirations and/or 5 minutes Apgar score of less than 7) took part in this randomized controlled trial from January 1, 2025, to March 31, 2025 at Department of pediatric medicine, Holy family hospital Rawalpindi. The WHO sample size calculator was used to determine the sample size at 90% research power, 5% significance level, 65%[6] efficacy in the MgSO4 group, and 37.5%[6] efficacy in the control group. Patients with intrauterine growth retardation (weight less than 2.0 kg at birth), a history of prenatal magnesium supplementation by the mother, any congenital heart defects or malformations, newborn pneumonia, or sepsis were not included.

Before being included in the study, all parents gave their informed consent after being informed of its goals and assured of the confidentiality of the data. All data was entered into a proforma that had already been created. The pediatric department's inclusion criteria were used to choose the newborns. Sampling technique used was non probability consecutive sampling with simple randomization. Groups A and B were randomly assigned to receive therapy and a placebo. Group A got two additional doses of magnesium sulfate at 24 and 48 hours after receiving an infusion of 250 mg/kg/dose in 10% dextrose to make volume equal to 3.0 mL/kg/dose over the course of an hour. 10% dextrose 3.0 mL/kg/dose was given to the control group over the course of an hour, with two further doses given at comparable intervals. Every newborn was routinely evaluated neurologically while in the NICU. Outcome was noted in both groups in terms of improvement in neurological findings (presence or absence of neonatal reflexes of moro and suck, presence or absence of oral feed establishment, either mechanical ventilation needed or not). Outcome was noted in terms of death of neonate during that hospital admission, discharge from hospital.

Data was entered and analyzed using SPSS version 25. Numerical variable like age at presentation, weight, gestational age and duration of stay were summarized as mean and standard deviation. Qualitative variables like gender, mode of delivery, neurological improvement (presence of fits, neonatal reflexes, initiation of oral feed, need of mechanical ventilation) and outcome like discharge or mortality were presented in the form of frequency and percentages. Chi square test was applied to compare neurological improvement and outcome in both groups.

RESULTS

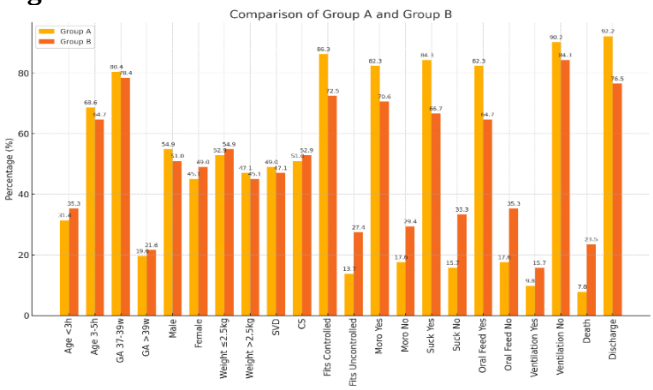
The study's age range was less than six hours after birth, with a mean age of 3.19 ± 1.23 hours. Neonates in groups A and B had mean ages of 3.22 ± 1.32 and 3.14 ± 1.20 hours, respectively. The male to female ratio of these 102 patients was 1.1:1, with 54 (52.94%) being male and 48 (47.06%) being female. Group A and Group B had mean gestational ages of 38.47 ± 1.21 weeks and 38.57 ± 1.17 weeks, respectively. The average weight for groups A and B was 2.55 ± 0.43 and 2.55 ± 0.44 kg, respectively. (Table 1).

Table 1

Comparison of Different Variables in Both Groups.

Variables		Group A (n=51)	Group B (n=51)	P-value
Age (hours)	<3	16 (31.37%)	18 (35.29%)	0.674
	3-5	35 (68.63%)	33 (64.71%)	
GA (weeks)	37-39	41 (80.39%)	40 (78.43%)	0.806
	>39	10 (19.61%)	11 (21.57%)	
Gender	Male	28 (54.90%)	26 (50.98%)	0.692
	Female	23 (45.10%)	25 (49.02%)	
Weight (kg)	≤2.5	27 (52.94%)	28 (54.90%)	0.842
	>2.5	24 (47.06%)	23 (45.10%)	
Mode of delivery	SVD	25 (49.02%)	24 (47.06%)	0.843
	CS	26 (50.98%)	27 (52.94%)	
Fits	Controlled	44 (86.27%)	37 (72.55%)	0.086
	Uncontrolled	07 (13.73%)	14 (27.45%)	
Moro reflex	Yes	42 (82.35%)	36 (70.59%)	0.161
	No	09 (17.65%)	15 (29.41%)	
Suck reflex	Yes	43 (84.31%)	34 (66.67%)	0.038
	No	08 (15.69%)	17 (33.33%)	
Oral feed established	Yes	42 (82.35%)	33 (64.71%)	0.043
	No	09 (17.65%)	18 (35.29%)	
Need for mechanical ventilation	Yes	05 (9.80%)	08 (15.69%)	0.373
	No	46 (90.20%)	43 (84.31%)	
Outcome	Death	04 (7.84%)	12 (23.53%)	0.029
	Discharge	47 (92.16%)	39 (76.47%)	

Figure 1



The figure illustrates a comparative bar chart showing the percentage distribution of various clinical and demographic variables between Group A and Group B.

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Most characteristics, such as age, gestational age, gender, weight, and mode of delivery, show similar distributions between the two groups. Notably, differences are more prominent in outcomes like suck reflex, oral feed establishment, and mortality rates. These variations highlight potential clinical differences impacting patient outcomes.

DISCUSSION

There were no differences between the experimental and control groups in our study with regard to mean age of intervention, gender, gestational age, birth weight, or mode of delivery. 52.94% of the infants in this study were male. Our results are in line with those of Mamo et al., who looked at neonates who had birth asphyxia and found that males made up 61.7% of the cases.[9] 52.5% of infants with perinatal asphyxia were male, according to Bhat et al.[10] Additionally, Mamo et al. found that in 77.2% of birth asphyxia instances, the birth weight was normal. [10] It was shown that 46.08% of infants weighed at least 2.5 kg at delivery.

Neonatal reflexes in patients with severe birth asphyxia were improved in 75.8% of subjects receiving IV magnesium sulphate compared to 45.4% in the control group, according to a local study conducted by Sajid et al. from Faisalabad (p=0.01). For 75.7% of newborns, oral feeding with magnesium sulfate was shown to be statistically substantially better than 39.4% (p=0.002).[13] Siddiqui et al. demonstrated that magnesium sulphate was superior in causing improvement in sucking reflex and reducing the amount of time it took for seizures to stop in infants with birth asphyxia.[6]

Neonates given magnesium sulfate were able to start feedings far faster than controls (32 hours vs. 63 hours, p<0.001), according to research by Nanda and colleagues.[12] Ichiba et al. previously conducted a multi-center, randomized controlled experiment. Furthermore, they observed that postnatal magnesium sulphate infusion therapy (250 mg/kg/day for three days) improved the response of neonates with severe birth hypoxia.[13,14] It was predicted that the magnesium group will experience significant improvement in results more frequently than the control group based on cranial CT, electroencephalogram (EEG), and the start of oral feeding by day 14.[13,14]

According to the current study, babies with severe birth asphyxia who received magnesium sulphate treatment appeared to have a good sucking reflex. We gave magnesium sulfate in three doses (each 250 mg/kg) spaced 24 hours apart because the duration of any subsequent neuronal impairment could last up to 72 hours.[15] Bhat et al. found that magnesium sulphate infusion was neuroprotective in their study, as demonstrated by the fact that the treatment group had more neonates receiving oral feedings at the time of discharge and fewer newborns with neurologic abnormalities.[10] Overall effectiveness was noted in 48 infants (60.0%). In comparison to the control group, the magnesium sulphate group had a considerably greater distribution of efficacy in terms of the appearance of a satisfactory sucking reflex (75.0% vs. 45.0%, p=0.0062).[16]

Four neonates (7.84%) in group A (magnesium sulphate) and twelve (23.53%) in group B (control group) died, respectively (p-value = 0.029). According to Bhat et al., term infants with severe neonatal hypoxia had an overall death rate of 10%.[10] Higher mortality rates among newborns treated for hypoxic-ischemic encephalopathy have been reported by several investigations.[17] Sreenivasa et al. discovered that neonates treated with magnesium sulphate for birth asphyxia had a 14% fatality rate.[18]

Beyond enhancing the sucking reflex in newborns, magnesium sulfate has a number of wider benefits. Its neuroprotective qualities, which are mostly achieved via NMDA receptor blockage, may lessen neuronal damage and excitotoxicity, which could lower the chance of long-term issues including cerebral palsy and cognitive impairments.[19] Additionally, it has anti-inflammatory and anticonvulsant properties that may help reduce inflammatory cascades linked to hypoxic-ischemic injury and prevent seizures.[20] Magnesium sulphate may increase feeding readiness and overall growth trajectories by stabilizing cerebral perfusion and improving brain functioning. Its use as a supplemental treatment in conjunction with methods such as therapeutic hypothermia may result in a multimodal approach to treating severe birth asphyxia, lowering the risk of long-term impairments, and enhancing quality of life.[21]

One of our study's drawbacks was that we exclusively used clinical markers to stage HIE, excluding base deficit and umbilical cord pH. More definitive results could be obtained from a multicentric trial with a larger sample size and long-term follow-up.

CONCLUSION

The study indicated that magnesium sulfate had the potential to be used as a neuroprotective intervention in neonatal care since it greatly improved the appearance of a good sucking reflex in neonates with severe birth asphyxia and improved survival rates. According to this research, magnesium sulfate may be essential for improving neurological recovery and early feeding readiness, which may lower the chance of long-term developmental problems. Including magnesium sulfate in the treatment plan for severe birth asphyxia may help afflicted neonates' short-term results and long-term neurodevelopmental health, particularly in environments with limited resources. Larger sample numbers and more extensive multi-center trials are needed to confirm the results of this investigation.

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