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Enhancing Neonatal Sucking Reflex: A Study on the Efficacy of Magnesium Sulphate in Severe Birth Asphyxia

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ABSTRACT

One of the main causes of prenatal deaths and a known factor in neuromotor disabilities is perinatal asphyxia. **Objectives:** To compare the efficacy of magnesium sulphate on the appearance of a good sucking reflex in cases of birth asphyxia with controls (without magnesium sulphate). **Methods:** This randomized controlled trial was conducted at the Department of Neonatology, The Children's Hospital and the Institute of Child Health, Multan, from January 2024 to June 2024. A total of 80 full-term newborns of both genders with severe birth asphyxia admitted within six hours of life were randomly assigned to either the study group or the control group. The study group received 3 doses of magnesium sulphate 24 hours apart by intravenous infusion at 250 mg/kg/dose, and the control group did not receive this treatment. Supportive care was given to both study groups. Both groups were examined for sucking reflexes. **Results:** 46 (57.5%) were male, while 43 (53.8%) had a body weight of ≥2.5 kg. The mean age at the time of presentation was 3.2 ± 1.5 hours. Overall efficacy was observed in 48 (60.0%) babies. The distribution of efficacy in terms of the appearance of a good sucking reflex was significantly better in the magnesium sulphate group versus the control group (75.0% vs 45.0%, p=0.0062). **Conclusions:** It was concluded that magnesium sulfate was found to significantly improve the appearance of a good sucking reflex among newborns with severe birth asphyxia, highlighting its potential as a neuroprotective intervention in neonatal care.

INTRODUCTION

Perinatal asphyxia is a leading cause of prenatal deaths and a significant contributor to neuromotor disabilities. Research in neurobiology has elucidated mechanisms underlying neuronal death following hypoxic-ischemic insult, highlighting the brain as the organ most vulnerable to hypoxia. Asphyxia fatalities are often characterized by respiratory arrest accompanied by bradycardia and asystole, due to the failure of the brainstem's respiratory centers caused by hypoxia [1, 2]. These adverse outcomes underscore the critical need for effective interventions in managing birth asphyxia. Among the mechanisms mediating hypoxic-ischemic neuronal death, glutamate plays a central role [3]. Glutamate-induced neuronal death occurs through two primary pathways: instantaneous cell death due to glutamate receptor activation and delayed cell death, which unfolds over hours and is predominantly mediated by the activation of N-Methyl-D-aspartate (NMDA) receptors [4-7]. Magnesium (Mg), a natural NMDA receptor antagonist, has been shown to block the NMDA ion channel at rest by occupying a binding site within the channel [8]. Hypoxia-ischemia, however, disrupts this voltage-dependent blockade by causing axonal depolarization. Increasing extracellular magnesium concentrations has been suggested as a means to restore this blockade and protect neurons. Experimental evidence from animal models has demonstrated that systemic magnesium treatment can reduce neuronal damage following simulated hypoxic-ischemic insults [9, 10]. Despite promising preclinical findings, evidence regarding the clinical use of magnesium sulfate for treating birth

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asphyxia remains inconsistent. Prior studies have been limited by methodological variability and small sample sizes, which have hindered conclusive outcomes [11]. Neurological assessment of newborns with birth asphyxia often includes the elicitation of a good sucking reflex. In a study by Kumar P *et al.*, neonates treated with magnesium sulfate demonstrated better outcomes, with 71.4% capable of oral feeding compared to 33.3% in the control group [12]. In South Punjab, Pakistan, where poverty and limited healthcare resources prevail, birth asphyxia represents a significant challenge. At Children's Hospital Multan, a tertiary care teaching hospital, approximately 30.6% of neonatal admissions are due to birth asphyxia [13]. This high burden underscores the urgent need for locally relevant evidence to guide clinical management.

This study aims to investigate the effectiveness of magnesium sulfate in managing severe birth asphyxia. We hypothesize that neonates treated with magnesium sulfate will demonstrate improved neurological outcomes, as assessed by the elicitation of a good sucking reflex, compared to untreated neonates. The findings from this study aim to provide a local reference for managing birth asphyxia, potentially improving outcomes in this underserved population.

METHODS

This randomized control trial was conducted at the Neonatology Unit, Department of Neonatology, "The Children's Hospital and the Institute of Child Health, Multan", Pakistan, from January 2024 to June 2024. The Institutional Ethical Committee obtained the study's approval before its commencement (letter number: 2354). RCT no (NCT06468475). A sample size of 80 (40 in each group) was calculated considering the percentage of neonates capable of having feed by mouth in the magnesium sulfate-treated group (P1) as 71.4% and the percentage of neonates capable of having feed by mouth in the control group (P2) as 33.3% [12]. The confidence interval was kept at 95% and the power of the study at 90%. Sample selection was made using a simple random sampling technique. The inclusion criteria were full-term babies (≥37 weeks of gestation) of both genders with severe birth asphyxia, admitted within six hours of life. The exclusion criteria were babies who were premature or had congenital malformations. The babies born to mothers receiving general anesthesia or whose mothers received magnesium sulfate, pethidine, and other drugs (likely to depress the baby) were also excluded. Severe birth asphyxia was described as a 1-minute Apgar score between 0 and 3 (as per the medical record) [14]. Informed and written consents were obtained from the parents or caregivers after describing the study objectives, safety, and data secrecy to them. Once the patients were enrolled, necessary demographics were recorded, and then the babies were randomly assigned to the study group (n=40) and control group (n=40). Randomization was performed using the lottery method, where sealed opaque envelopes containing group assignments were shuffled and picked by an independent staff member not involved in the study. This ensured allocation concealment and minimized selection bias. The study group received 3 doses of magnesium sulphate 24 hours apart by intravenous infusion at 250 mg/kg/dose (0.5 mL/kg/dose of injection magnesium sulphate 50% w/v diluted in 5 mL/kg of 5% glucose) over half an hour by an infusion pump, and the control group did not receive this treatment. Both groups received supportive care as per standard practice for birth asphyxia. Both groups were examined daily in the morning for sucking reflexes. The sucking reflex is an involuntary sucking movement of the lips of a newborn elicited by touching the lips or skin near the mouth. After washing hands, the infant was placed in the supine position, the index finger (pad towards the palate) was placed in the infant's mouth, and the power of sucking movements was judged after 5 seconds. If the sucking reflex appeared, it was said to be effective. This was noted after 72 hours of treatment in both study groups. All the data were analyzed by "IBM SPSS Statistics" version 26.0. The mean and standard deviation were shown for quantitative variables whereas frequency and percentage were calculated for categorical data. Comparison of Outcomes variables like the appearance of good sucking reflex and mortality were compared by applying a chi-square test between both study groups. For all inferential statistics, $p<0.05$ was considered significant.

RESULTS

Out of a total of 80 babies, 46 (57.5%) were male. The mean body weight was noted to be 2.5 ± 0.5 kg, while 43 (53.8%) babies had a body weight ≥2.5 kg. The distribution of age at the time of presentation showed that 9 (11.3%) babies were presented within 2 hours following birth, 23 (28.8%) between 2 and <4 hours and the remaining 48 (60.0%) were presented between 4 and 6 hours following birth. The mean age at the time of presentation was 3.2 ± 1.5 hours. Overall, mean gestational age was 37.8±1.0 weeks, whereas gestational age was between 37 and 39 weeks in 65 (81.2%) cases. Comparisons of baseline characteristics among newborns of both study groups are shown in Table 1.

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Table 1: Frequency Distribution of Study Characteristics in Both Groups(n=80)

Characteristics		Total	Groups		p-Value
			Magnesium Sulphate (n=40)	Control (n=40)	
Age Groups (Hours)	<2	9 (11.2%)	6 (15.0%)	3 (7.5%)	0.338
	2 to <4	23 (28.8%)	9 (22.5%)	14 (35.0%)	
	4-6	48 (60.0%)	25 (62.5%)	23 (57.5%)	
Gestational Age Groups (Weeks)	37-39	65 (81.3%)	30 (75.0%)	35 (87.5%)	0.152
	>39	15 (18.7%)	10 (25.0%)	5 (12.5%)	
Gender	Male	46 (57.5%)	24 (60.0%)	22 (55.0%)	0.651
	Female	34 (42.5%)	16 (40.0%)	18 (45.0%)	
Body Weight (Kgs)	<2.5	37 (46.2%)	16 (40.0%)	21 (52.5%)	0.262
	≥2.5	43 (53.8%)	24 (60.0%)	19 (47.5%)	

Efficacy in terms of the appearance of a good sucking reflex was observed in 48 (60.0%) babies. Mortality was reported in 9 (11.3%) cases during the study period. No treatment-related complications or side-effects were observed in both study groups. Distribution of efficacy in terms of the appearance of a good sucking reflex in both study groups revealed that the appearance of a good sucking reflex was significantly better in magnesium sulphate group versus control group (75.0% vs 45.0%, p=0.0062), as shown in table 2.

Table 2: Distribution of Appearance of Good Sucking Reflex after 72 Hours in Both Groups(n=80)

Appearance of Good Sucking Reflex	Groups		p-Value
	Magnesium Sulphate (n=40)	Control (n=40)	
Yes	30 (75.0%)	18 (45.0%)	0.0062
No	10 (25.0%)	22 (55.0%)	

Stratification of study variables concerning the appearance of good sucking reflex showed that there existed no significant differences concerning age groups (p=0.422), gestational age (p=0.559), and gender (p=0.518). Birth weight ≥2.5 kg was significantly associated with the appearance of good sucking reflex (p=0.001), and the details are shown in table 3.

Table 3: Association of Appearance of Good Sucking Reflex with Characteristics of Neonates(n=80)

Characteristics		Appearance of Good Sucking Reflex		p-Value
		Yes (n=48)	No (n=32)	
Age Groups (Hours)	<2	6 (12.5%)	3 (9.4%)	0.422
	2 to <4	16 (33.3%)	7 (21.9%)	
	4-6	26 (54.2%)	22 (68.8%)	
Gestational Age Groups (Weeks)	37-39	40 (83.3%)	25 (83.3%)	0.559
	>39	8 (16.7%)	7 (16.7%0	
Gender	Male	29 (61.4%)	17 (60.4%)	0.518
	Female	19 (39.6%)	15 (39.6%)	
Body Weight (Kgs)	<2.5	15 (31.2%)	22 (68.8%)	0.001
	≥2.5	33 (68.8%)	10 (31.2%)	

No statistically significant differences were noted between both study groups concerning mortality (p=0.2885), and the details are shown in table 4.

Table 4: Distribution of Mortality in Both Groups(n=80)

Mortality	Groups		p-Value
	Magnesium Sulphate (n=40)	Control (n=40)	
Yes	3 (7.5%)	6 (15.0%)	0.2885
No	37 (92.5%)	34 (85.0%)	

There was no significant association of mortality with age groups (p=0.084), gestational age (p=0.234), and gender (p=0.191). Low birth weight (<2.5 kg) was associated with significantly higher mortality rates (77.8% vs. 42.3%, p=0.044), and the details are shown in table 5.

Table 5: Association of Mortality with Characteristics of Neonates(n=80)

Characteristics		Mortality		p-Value
		Yes (n=9)	No (n=71)	
Age Groups (Hours)	<2	3 (33.3%)	6 (8.4%)	0.084
	2 to <4	2 (22.2%)	21 (29.6%)	
	4-6	4 (44.4%)	44 (62.0%)	
Gestational Age Groups (Weeks)	37-39	6 (66.7%)	59 (83.1%)	0.234
	>39	3 (33.3%)	12 (16.9%)	
Gender	Male	7 (77.8%)	39 (54.9%)	0.191
	Female	2 (22.2%)	32 (45.1%)	
Body Weight (Kgs)	<2.5	7 (77.8%)	30 (42.3%)	0.044
	≥2.5	2 (22.2%)	41 (57.7%)	

DISCUSSION

Hypoxemia (lack of oxygen) and hypercapnia arise from impaired blood-gas exchange, which causes asphyxia (accumulation of carbon dioxide). Hypoxia and ischemia, when present together, cause the body to experience a cascade of metabolic changes that culminate in the loss of neuronal cells and brain injury [14]. The fundamental factor causing neonatal asphyxia is a blockage in placental blood flow, which causes brain cell ischemia and anoxia and sets off anaerobic conditions. As a result, Adenosine triphosphate (ATP) stores are heavily used, and lactic acid builds up [15]. In the present study, 57.5% of babies were male. Our findings are consistent with Mamo *et al.*, examining neonates with birth asphyxia, where they noted 61.7% of cases to be male [16]. Bhat *et al.*, noted 52.5% of babies with perinatal asphyxia to be male [17]. Mamo *et al.*, also revealed that birth weight was normal in 77.2% of cases of birth asphyxia [16]. It was found that 53.8% of babies had a birth weight of ≥2.5 kg. In this study, the distribution of efficacy in terms of the appearance of a good sucking reflex was noted to be statistically significantly better among babies who were given magnesium sulphate versus controls (75.0% vs 45.0%, p=0.0062). A local study done by Sajid *et al.*, from Faisalabad showed that neonatal reflexes among patients with severe birth asphyxia were improved in 75.8% of subjects using IV magnesium sulphate in comparison to

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45.4% in the control group (p=0.01). Oral feeding was found to be statistically significantly better with magnesium sulphate for 75.7% of babies in comparison to 39.4% (p=0.002) [18]. Normal computed tomography (CT) brain was seen in 84.9% of subjects in the magnesium sulphate group in comparison to 51.5% in the control group (p=0.003) [18]. Siddiqui *et al.*, showed that magnesium sulphate was better in exhibiting the appearance of a sucking reflex and minimizing the time taken to seizure cessation among babies born with birth asphyxia [19]. Nanda and colleagues documented that neonates who were administered magnesium sulphate were able to initiate feeds significantly quicker than controls (32 hours vs. 63 hours, p<0.001) [20]. Previously, a multi-center, randomized controlled experiment was carried out by Ichiba *et al.* Additionally, they noticed that newborns with severe birth hypoxia responded better to postnatal magnesium sulphate infusion therapy (250 mg/kg/day for 3 days) [21]. As per cranial CT, electroencephalogram (EEG), and the initiation of oral feeds by day 14, it was projected that the magnesium group had significant outcomes more frequently than the control group [21, 22]. Current study shows that magnesium sulphate treatment improved the appearance of a good sucking reflex among newborns with severe birth asphyxia. Due to the potential for subsequent neuronal damage to extend up to 72 hours, we administered magnesium sulphate in three doses (each 250 mg/kg) at 24-hour intervals [23]. Magnesium sulphate infusion was discovered by Bhat *et al.*, to be neuroprotective in their study, as evidenced by the fact that there were fewer newborns with neurologic irregularities and more babies taking oral feedings at the time of discharge in the therapy group [17]. An overall mortality rate of 11.3% was noted in present study, while there was no statistically significant difference between groups (p=0.2885). Bhat *et al.*, noted an overall mortality rate of 10% among term neonates with severe perinatal asphyxia [17]. Some researchers have found higher mortality rates among neonates treated for hypoxic-ischemic encephalopathy [24]. Sreenivasa et al., found a mortality rate of 14% among neonates with birth asphyxia who were managed with magnesium sulphate [25]. Magnesium sulfate offers several broader implications beyond improving the sucking reflex in neonates. Its neuroprotective properties, primarily through NMDA receptor blockade, may reduce excitotoxicity and neuronal injury, potentially lowering the risk of long-term complications like cerebral palsy and cognitive delays [26]. It also exhibits anticonvulsant and anti-inflammatory effects, which could prevent seizures and mitigate inflammatory cascades associated with hypoxic-ischemic injury [27]. By stabilizing cerebral perfusion and enhancing neural functions, magnesium sulfate may improve feeding readiness and overall growth trajectories. Its integration as an adjunct therapy alongside approaches like therapeutic hypothermia could create a multimodal strategy for managing severe birth asphyxia, reducing long-term disabilities and improving quality of life [28].

CONCLUSIONS

It was concluded that magnesium sulfate was found to significantly improve the appearance of a good sucking reflex among newborns with severe birth asphyxia, highlighting its potential as a neuroprotective intervention in neonatal care. This finding suggests that magnesium sulfate could play a vital role in enhancing early feeding readiness and neurological recovery, potentially reducing the risk of long-term developmental impairments. Incorporating magnesium sulfate into the management protocol for severe birth asphyxia, especially in resource-limited settings, may improve short-term outcomes and contribute to better long-term neurodevelopmental health in affected neonates. Further large-scale metacentric trials with larger sample sizes are required to validate the findings of this study.

Authors Contribution

Conceptualization: MA[1]
Methodology: MA[1], ARM, MA[2], RTA
Formal analysis: MA[1]
Writing review and editing: MA[1]

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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