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Beneficial Effect of Intravenous Magnesium Sulphate in Term Neonates with Perinatal Asphyxia

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ABSTRACT

Objective: To compare the efficacy of intravenous (IV) magnesium sulphate in treating neonatal hypoxia and enhancing immediate neurological outcomes. **Study design:** Randomized controlled trials. **Settings:** Neonatal intensive care unit (NICU) of Balochistan institute of child and health services Quetta. **Study duration:** January to April 2025. **Materials & Methods:** A total of 104 patients (52 in each group), both male and female infants and gestational ages gestational age ≥ 37 weeks presented with perinatal asphyxia were included. Babies who delivered by mothers who have had pethidine, phenobarbitone, magnesium sulphate (for pregnancy-induced hypertension), or any other medications that may depress the unborn child, Premature babies and Babies with congenital malformations or syndromic features were not included. Using a computer-generated random number table, the patients were split into two equal groups at random. Newborns in group A received additional magnesium sulphate doses of 250 mg/kg immediately after birth, followed by 125 mg/kg at 24 and 48 hours. This was administered as a 30-minute intravenous infusion of 5% dextrose. Neonates in group B was given all NICU protocol for birth asphyxia like electrolyte monitoring, seizure control and therapeutic hypothermia except magnesium sulphate therapy. Neurological evaluation was done using the Sarnat Classification or Sarnat Grading Scale at the time of admission and after 72 hours, and then when they were discharged back home. Efficacy was assessed at 72 hours of age in terms of poor neurological status, presence of seizures, mean time to establish feed, need of respiratory support and mortality. **Results:** In our study, neurological improvement, were recorded in 69.23%, absence of seizures in 75%, need of respiratory support in 34.62% and mortality in 11.54% babies in group A and 40.35%, 46.15%, 57.69% and 25.0% respectively in group B (p-value <0.05). Additionally, mean time for establishment of full oral feedings through sucking was documented as 17.83 ± 6.73 and 31.35 ± 9.45 hours, respectively (p-value = 0.0001). **Conclusion:** 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.

INTRODUCTION

Neonatal mortality and morbidity are remarkably high in Pakistan. Along with preterm, infection, and other factors, perinatal asphyxia is one of the main causes of this.[1] In addition to causing short and long-term neurological issues, perinatal asphyxia; commonly known as hypoxic-ischemic encephalopathy (HIE), also causes mortality.[2] A moderate to severe case of birth asphyxia is to blame for roughly 40% of deaths and illnesses.[3] Due to the short-term disruption in the supply of oxygen to numerous organs, it is insulting to the fetus. In developed countries, the incidence of perinatal asphyxia is 1-2 per 1000 live births, whereas it can reach 5 per 1000 in underdeveloped countries.[4] It is well known that a biphasic pattern of neuronal cell death results from hypoxic-ischemic damage. Asphyxia causes primary neuronal injury, which includes cell swelling and necrosis, and it gets end when resuscitative measures are taken.[5] During the secondary phase of neuronal injury, which lasts for hours to days, excitotoxicity, inflammation, and oxidative stress culminate in cell death. One of the main excitatory amino acids in the brain is glutamate. It affects the brain's postsynaptic NMDA receptor (N-methyl-D-aspartate Receptor).[6] High levels of glutamate during hypoxia activate NMDA channels, allowing excessive calcium to enter the neurons and causing irreversible neuronal damage. Magnesium is an organic NMDA receptor antagonist that shuts down the NMDA ion channel while the brain is at rest.[7] When a hypoxic ischemic insult occurs, this voltage-dependent barrier is broken during axonal depolarization. An increase in magnesium concentration extracellularly is intended to relieve this blockage.[8] Only a few studies have shown that magnesium sulphate has a positive effect on full-term newborns who have perinatal hypoxia. Study conducted by Siddiqui et al demonstrated the efficacy of magnesium sulphate in treating perinatal asphyxia. According to him, neonates who have received magnesium sulphate found to have good neurological outcome (65%) compared to those who did not receive magnesium sulphate therapy (37.5%) respectively.[9]

The effects of MgSO4 injection in term infants with perinatal hypoxia on neurologic benefit, seizure reduction, improved feeding, and survival indicators are well documented, mainly in western settings. Magnesium sulphate is simply administered in neonatal settings and is both affordable and widely accessible. It may be helpful in managing HIE even in newborn units with limited resources due to its relative simplicity of usage. Despite its potential advantages, there aren't many local researches on its application. Conducting a study on the role of MgSO4 therapy in neonates with birth asphyxia is essential to explore its neuroprotective potential, establish its safety and efficacy, and optimize its use as a treatment option. This research has the potential to significantly improve the quality of life for neonates who suffer from birth asphyxia and reduce the burden on healthcare systems by preventing long-term disabilities.

MATERIALS AND METHODS

After receiving approval from the ethical review committee, this randomized controlled experiment was carried out from January to April 2025 at the Neonatal intensive care unit (NICU) of Balochistan institute of child and health services Quetta. Sample size was calculated by using Openepi, considering percentage of good neurological outcome of neonates in treatment group (65 %) compared to outcome of neonates in placebo group (37.5 %) with 80 % power of test and 95% confidence level.[9] The calculated sample size was 104 patients total with 52 in each group respectively. Both male and female term neonates (gestational age ≥ 37 weeks) presented with perinatal asphyxia (low APGAR scores of neonate at birth that is ≤ 3 in 1 minute and ≤ 7 in 5 minutes of age) were included. Babies who delivered by mothers who have had pethidine, phenobarbitone, magnesium sulphate (for pregnancy-induced hypertension), or any other medications that may depress the unborn child, Premature babies and Babies with congenital malformations or syndromic features were not included.

Parents of study participants were asked to sign a written informed consent form. After receiving parental approval, a detailed history and physical examination of the newborn was performed. These newborns were allocated randomly to receive either the treatment group (intravenous magnesium sulphate) or a comparison group using a random number table. The neonates in both the groups were treated according to the routine NICU protocol for birth asphyxia. Newborns in group A received additional magnesium sulphate doses of 250 mg/kg immediately after birth, followed by 125 mg/kg at 24 and 48 hours. This was administered as a 30-minute intravenous infusion of 5% dextrose. Neonates in group B was given all NICU protocol for birth asphyxia like electrolyte monitoring, seizure control and therapeutic hypothermia except magnesium sulphate therapy. All newborns were kept in incubators with their skin temperatures regulated at 36.5 C. When necessary, further supportive care was given, such as oxygen therapy, 10% dextrose solution, electrolytes, vasopressors, or ventilator support. Moreover, results were obtained from laboratory tests such as the arterial blood gas analysis, complete blood count, C-reactive protein, blood urea, serum creatinine, serum bilirubin, serum electrolyte, serum lactate, and Lactate Dehydrogenase (LDH) test. Serum magnesium level was obtained at 0, 24, 48, 72 hours of magnesium sulphate infusion. Within 72 hours of admission, cranial ultrasound and electroencephalography was done for the first time. When necessary, a head CT scan or a brain MRI may be performed. Examiners who were blinded to the groups to which the newborns belong, assessed the CT scan and the EEG. Furthermore, neurological evaluation was done using the Sarnat Classification or Sarnat Grading Scale at the time of admission and after 72 hours, and then when they were discharged back home. Efficacy was assessed at 72 hours of age in terms of poor neurological status, presence of seizures, mean time to establish feed, need of respiratory support and mortality. All the above mentioned information was recorded in a pre-design proforma.

A data base was developed on SPSS for windows version 26.0. Mean value and standard deviation or median (IQR) as appropriate were calculated for quantitative variables like age, weight, length, front-occipital circumference (FOC) and mean time to establish feed. Weight was measured by Camry analog weighing scale while height was measured by stadiometer. Normality of data was assessed by using shapiro wilk test. Frequencies with percentages were presented for qualitative variables like gender (male/female), neurological status (good/poor), and presence of seizures (yes /no), type of respiratory support (invasive/non-invasive) and mortality (yes /no) and were compared in two groups by applying chi square or fisher exact test. Normally distributed numerical variables such as mean time to establish feed was compared in both groups by independent sample T-test.

RESULTS

The male to female ratio of these 104 patients was 1.16:1, with 56 (53.85%) being male and 48 (46.15%) being female. Group A and Group B had mean gestational ages of 38.58 ± 1.42 weeks and 38.49 ± 1.24 weeks, respectively. The average weight for groups A and B was 2.62 ± 0.69 and 2.72 ± 0.63 kg, respectively. (Table 1).

As indicated in Table 2, the results, i.e., neurological improvement, were recorded in 69.23%, absence of seizures in 75%, need of respiratory support in 34.62% and mortality in 11.54% babies in group A and 40.35%, 46.15%, 57.69% and 25.0% respectively in group B (p-value <0.05). Additionally, mean time for establishment of full oral feedings through sucking was documented as 17.83 ± 6.73 and 31.35 ± 9.45 hours, respectively (p-value = 0.0001).

Table 1

Comparison of Different Variables in Both Groups.

Variables		Group A (n=52)	Group B (n=52)
GA (weeks)	37-39	42 (80.77%)	41 (78.85%)
	>39	10 (19.23%)	11 (21.15%)
Gender	Male	29 (55.77%)	27 (51.92%)
	Female	23 (44.23%)	25 (48.08%)
Weight (kg)	≤2.5	28 (53.85%)	29 (55.77%)
	>2.5	24 (46.15%)	23 (44.23%)

Table 2

Comparison of efficacy (n=104).

Variables		Group A (n=52)	Group B (n=52)	P-value
Good neurological status	Yes	36 (69.23%)	21 (40.38%)	0.003
	No	16 (30.77%)	31 (61.62%)	
Absence of seizures	Yes	39 (75.0%)	24 (46.15%)	0.003
	No	13 (25.0%)	28 (53.85%)	
Need of respiratory support	Yes	18 (34.62%)	30 (57.69%)	0.018
	No	34 (65.38%)	22 (42.31%)	
Mortality	Yes	06 (11.54%)	13 (25.0%)	0.0757
	No	46 (88.46%)	39 (75.0%)	
Mean time for establishment of full oral feedings through sucking (hrs)		17.83 ± 6.73	31.35 ± 9.45	0.0001

DISCUSSION

A problem with blood-gas exchange can cause asphyxia (too much carbon dioxide) and hypoxemia (too little oxygen). When hypoxia and ischemia happen at the same time, the body goes through a number of metabolic changes that kill brain cells and harm the brain. The main reason newborns choke is because their placental blood flow is limited, which causes anaerobic circumstances and leads to brain cell ischemia and anoxia. As a result, lactic acid builds up and adenosine triphosphate (ATP) levels drop a lot.[10]

In our investigation, the experimental and control groups were the same in terms of gender, gestational age, and birth weight. This study found that 53.85% of the babies were boys. Our results are similar to those of Mamo et al., who studied babies who were born with hypoxia and found that 61.7% of the cases were boys.[11] Bhat et al. say that 52.5% of babies who died of prenatal hypoxia were boys.[12] Mamo et al. also discovered that in 77.2% of cases of birth asphyxia, the baby's weight at birth was normal.[11] It was found that 45.19% of babies weighed at least 2.5 kg when they were born.

In our study, 69.23% of babies in group A had neurological improvement, 75% did not have seizures, 34.62% needed respiratory support, and 11.54% died. In group B, the numbers were 40.35%, 46.15%, 57.69%, and 25.0%, respectively (p-value <0.05). Also, the average time it took to start full oral feeding through sucking was 17.83 ± 6.73 hours and 31.35 ± 9.45 hours, respectively (p-value = 0.0001). A local study by Sajid et al. from Faisalabad found that 75.8% of patients with severe birth asphyxia who received IV magnesium sulfate had better neonatal reflexes than 45.4% of those in the control group (p=0.01).[13] For 75.7% of neonates, giving them magnesium sulfate by mouth was statistically far better than feeding them by mouth (p=0.002).[13] In the magnesium sulfate group, 84.9% of people had normal computed tomography (CT) brains, while only 51.5% of people in the control group did (p=0.003).[13] Siddiqui et al.'s study showed that magnesium sulfate works to cure neonatal hypoxia. He said that 65% of newborns who had magnesium sulfate had a good neurological prognosis, but just 37.5% of those who did not get magnesium sulfate therapy did.[9]

Nanda and colleagues found that neonates who were given magnesium sulfate were able to start eating much quicker than controls (32 hours vs. 63 hours, p<0.001).[14] A multi-center, randomized controlled experiment was done by Ichiba and others before. They also saw that giving magnesium sulfate to babies with severe birth hypoxia (250 mg/kg/day for three days) made them respond better.[15,16] Based on cranial CT, electroencephalogram (EEG), and the onset of oral feeding by day 14 it was thought that the magnesium group would have significant results more often than the control group.[15,16]

The current study found that neonates who had severe birth asphyxia and were treated with magnesium sulfate seemed to have a good sucking reflex. We provided magnesium sulfate in three doses of 250 mg/kg each, spaced 24 hours apart. This was because the effects on the neurons could linger for up to 72 hours.[17] Bhat et al. observed that magnesium sulfate infusion protected the brain in their study. This was shown by the fact that the treatment group had more babies who were able to eat by mouth when they left the hospital and fewer babies who had neurological problems.[12] There were 48 babies (60.0%) who showed overall efficacy. The magnesium sulfate group exhibited a far wider range of effectiveness when it came to the emergence of a good sucking response (75.0% vs. 45.0%, p=0.0062) than the control group.[18]

Bhat et al. say that term infants who had severe neonatal hypoxia had a 10% fatality rate overall. Several studies have found that neonates who are treated for hypoxic-ischemic encephalopathy have higher death rates.[19] Sreenivasa et al. found that 14% of newborns who were given magnesium sulfate for birth asphyxia died.[20] Magnesium sulfate has several other benefits besides making babies' sucking reflex stronger. Its neuroprotective effects, which are largely due to blocking NMDA receptors, may reduce brain damage and excitotoxicity. This could diminish the risk of long-term problems such cerebral palsy and cognitive impairments.[21] It also possesses anti-inflammatory and anticonvulsant effects that may help stop seizures and lower the number of inflammatory cascades that happen after a hypoxic-ischemic injury.[22] Magnesium sulfate may make animals more ready to eat and help them develop faster by regulating blood flow to the brain and making it work better. When used with other treatments like therapeutic hypothermia, it could lead to a multimodal strategy to treating severe birth asphyxia. This would minimize the risk of long-term problems and improve quality of life.[23]

One problem with our study was that we only used clinical markers to stage HIE, leaving out base deficit and umbilical cord pH. A multicentric experiment with a bigger sample size and long-term follow-up could give more clear results.

CONCLUSION

This study suggests that magnesium sulfate may be important for speeding up neurological recovery and getting babies ready to eat, which could lessen the risk of long-term developmental difficulties. Adding magnesium sulfate to the treatment approach for severe birth asphyxia may enhance the short-term and long-term neurodevelopmental health of affected newborns, especially in places with few resources.

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