Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1199
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1199*
Original Research Article

EFFECTIVENESS OF MAGNESIUM SULFATE IN TERM NEONATES HAVING PERINATAL ASPHYXIA

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(Received, 24th June 2024, Revised 25th October 2024, Published 19th October 2024)

Abstract: *In Pakistan, neonatal mortality and morbidity are remarkably high. Birth asphyxia (perinatal asphyxia) is one of the main contributors to this, apart from prematurity, sepsis and other causes.* ***Objective:*** *To assess the effectiveness of magnesium sulfate in term neonates having perinatal asphyxia* ***Methods:*** *This Randomized Controlled Trial was carried out at the Department of Pediatrics, Sheikh Zayed Hospital Rahim Yar Khan from July 2023 to December 2023. The overall sample size was 130 patients (65 patients in each group). Neonates in group A received MgSO through I/V, 3 doses 250mg/kg/dose, 24 hours apart along with standard treatment. Group B was a control group that received 20 ml of normal saline infusion at the same interval with similar supportive and symptomatic treatment with regular monitoring. The outcome in terms of mortality, seizure, early initiation of feed, time to the establishment of full oral feeding, duration of seizures and duration of hospital stay were assessed. All the data was analyzed by using SPSS version 25.****Results:*** *In the current study, a total of 130 neonates were enrolled. Among them, moderate asphyxia was observed in 90 (69.23%) patients whereas severe perinatal asphyxia was observed in 40(30.77%) patients. In group A, the mean level of serum magnesium in neonates with moderate asphyxia was 2.81 (±0.20) mEq/L while in neonates with severe asphyxia, it was 2.89 (±0.61) mEq/L. The moderate asphyxia patients in group-A showed significant statistical improvement in terms of seizure control (hours) (14.11±1.22 vs 18.11±1.56; P=0.01), normal cry appearance (Days) (11.1±0.12 vs 13.11±1.29; p=0.03), normal activity appearance (Days) (11.9±0.02 vs12.00±1.51; p=0.01), full oral feed acceptance by sucking (Days) (13.31±0.99 vs 14.61±1.51; p=0.01) and mean hospital stay duration (Days) (14.99±1.66 vs 16.21±1.11; p 0.02).* ***Conclusion:*** *Our study concludes that in asphyxiated newborns, postnatal magnesium sulphate infusion is safe and likely to enhance the short-term neurological prognosis in cases with moderate-grade encephalopathy.*

Keywords: Efficacy; Magnesium sulfate; Neonates; perinatal asphyxia

Introduction

In Pakistan, neonatal mortality and morbidity are remarkably high. Birth asphyxia (perinatal asphyxia) is one of the main contributors to this, apart from prematurity, sepsis and other causes (1). It is described as the "inability to commence and maintain spontaneous respiration at birth." It may also be characterised as a deficiency in placental or pulmonary gas exchange, resulting in hypoxaemia and hypercarbia, which subsequently causes metabolic acidosis, an Apgar score below 3 at the 10th minute, and aberrant muscle tone (2). It is estimated that seven million perinatal fatalities occur annually, mostly in underdeveloped nations. According to the WHO, from 4 to 9 million neonates experience birth asphyxia annually. It is predicted that among them, 1.2 million individuals die, and approximately an equal number have serious consequences, including epilepsy, cerebral palsy, developmental delays, pneumonia, diarrhoea, newborn infections, and difficulties from premature labour(3). Various factors may predispose an infant to birth asphyxia, with the primary aetiology being reduced cerebral blood supply. These consist of maternal complications (haemorrhage, amniotic fluid embolism, or hypertension), placental complications (acute abruption), uterine complications (rupture), cord complications (tight nuchal chord or cord prolapse/avulsion), intrapartum infection, and protracted or difficult labour(4). Currently, hypothermia is regarded as the most effective therapy for managing hypoxic-ischemic encephalopathy (HIE) in newborns (5). However, in over 30% of the patients, hypothermia was ineffective in preventing mortality or moderate to severe neuro-developmental impairments (6). In hypoxic-ischaemic insult, magnesium has been linked to a potential neuroprotective effect. An antagonist of the N-methyl D-aspartate (NMDA) receptor that occurs naturally is magnesium. It blocks the neuronal inflow of Catt to function inside the ion channels. This voltage-dependent obstruction, which is caused by axonal depolarization, arises during hypoxic ischemia. If the extracellular concentration of magnesium is raised, this barrier may be cleared (7). Rashid et al. (2015) reported that after comparing the two groups, it was found that 71% of the individuals in the treatment group and 23% of the individuals in the control group were discharged using oral feeding. Treatment group mortality was 13%, whereas the control group mortality was 23%.7Another study reported post-intervention Seizures as 69.4% in MgSO4 and 81.8% in the control group.8 Rasheed et al. (2023) reported that mortality (7.8% vs. 23.6%, p-value 0.003) was significantly lower in the MgSo group compared to the control group (9). The rationale for this study lies in the critical need to evaluate the effectiveness of magnesium sulfate in term neonates with perinatal asphyxia. This study will introduce novel insights into the efficacy of magnesium sulfate in term neonates with perinatal asphyxia, potentially uncovering its role in improving neurological outcomes (8). By adding to existing literature, it aims to fill gaps in knowledge,

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providing updated evidence on the effectiveness of magnesium sulfate therapy in this specific population. By investigating its effectiveness, we aim to provide valuable evidence that could lead to improved management strategies for perinatal asphyxia, particularly in low-resource settings like Pakistan. The research was to determine the outcome of magnesium sulfate in term neonates having perinatal asphyxia.

Methodology

Randomized Controlled Trail Department of Pediatrics, Sheikh Zayed Hospital Rahim Yar Khan Sample size of 130 patients (65 patients in each group) is calculated with 80% power of the test and 95% confidence interval while taking the expected frequency of Mortality to be 7.8% in MgSo group and 23.6% in the control group.9 Non-probability consecutive sampling from July 2023 to December 2023. According to the operational definition, newborns of both genders who had a gestational age of more than 37 weeks, an Apgar score of less than five at five minutes after delivery, and a need for active resuscitation were classified as having moderate and severe prenatal asphyxia based on Sarnat staging. Newborns presenting within 6 hours of the birth of both genders. Based on clinical examination & medical records following were excluded Newborns with syndromic characteristics, congenital cardiac conditions (apart from patent ductus arteriosus), and C-reactive protein of more than 6 (neonatal sepsis). Infants born with chromosomal abnormalities and intrauterine growth retardation (birth weight of less than 2.0 kg) Neonates with prematurity, dimorphism After approval from the Hospital's Ethical Review Board and CPSP 130 patients (65patients in each group) patients presenting in the Outpatient Department of Pediatrics, Sheikh Zayed hospital Rahim Yar Khan who fulfil the above criteria were counselled and explained the details of the study. Written informed consent and detailed history were taken from the parents or guardians of each child. These patients were then randomly divided into the following two treatment groups using the lottery method Group-A: MgSO4 infusion (n=65) Group-B: 20 ml normal saline infusion (n=65) Neonates in group A received MgSO through I/V, 3 doses 250mg/kg/dose, 24 hours apart along with standard treatment (oxygen therapy, intravenous (IV) fluids, intensive monitoring, broad-spectrum antibiotic cover for possible role of infection and control of fits if required). Group B was a control group that received 20 ml of normal saline infusion at the same interval with similar supportive and symptomatic treatment with regular monitoring. The outcome in terms of mortality, seizure, early initiation of feed, time to establishment of full oral feeding, duration of seizures and duration of hospital stay was assessed as per operational definition at the time of discharge. When the baby became free of clinical features, it was discharged. Monitoring during the infusion included blood pressure, vital signs, and pulse oximetry. This was sustained for up to 72 hours of life. Both patient groups received identical supportive treatment by NICU policy. The result was assessed based on the initiation of oral feeding at discharge or by 14 days of life, whichever occurred first. Outcome in terms of mortality was measured at 28 days of life and seizure control was assessed up to 28 days of life. Patients who achieved neurological stability early were switched to oral nutrition promptly, resulting in a reduced hospital stay. A neurological examination was conducted by a physician who was unaware of the patients' group assignments at the time of hospitalization and on the 14th day. All the information was collected on a specially designed pro forma (attached) by me. Confounding variables were controlled by exclusion. The data was analyzed by SPSS version 25. Descriptive statistics including mean and standard deviation of quantitative values like age, birth weight and gestational age were calculated. Shapiro rank test was applied to check the normal distribution of data taking a p value of <0.05 as statistically significant. Frequency and percentage were calculated for all qualitative variables like gender, grade of birth asphyxia, mode of delivery, seizures, oral feed and mortality. The chi-square test was applied to compare the outcomes in two groups. Effect modifiers like age, gender, gestational age, grade of birth asphyxia, mode of delivery and birth weight were controlled by stratification. Post-stratification chi-square test was applied taking p-value ≤ 0.05 as significant. If the frequency was found $\leq 5\%$ in any cell then the Fisher Exact test was applied to take a p-value of ≤ 0.05 as statistically significant.

Results

In the current study, a total of 130 neonates were enrolled. They were divided into Group A treated with MgSO4 infusion (n=65) and Group B treated with 20 ml normal saline infusion (n=65). Among them, moderate asphyxia was observed in 90 (69.23%) patients whereas severe perinatal asphyxia was observed in 40(30.77%) patients. (Figure 2) Gender-wise distribution of enrolled neonates is given in Figure 1. The baseline characteristics were similar both in group A and group B. In the current study, the first dose of magnesium sulfate was administered at 121.23 (±52.45) minutes (Table 1). In group A, the mean level of serum magnesium in neonates with moderate asphyxia was 2.81 (±0.20) mEq/L while in neonates with severe asphyxia, it was 2.89 (±0.61) mEq/L. The moderate asphyxia patients in group A showed significant statistical improvement in terms of seizure control (hours) (14.11±1.22 vs 18.11±1.56; P=0.01), normal cry appearance (Days) (11.1±0.12 vs 13.11±1.29; p=0.03), normal activity
Appearance (Days) (11.9±0.02 vs12.00±1.51; p=0.01), full oral feed acceptance by sucking (Days) (13.31±0.99 vs 14.61±1.51; p=0.01) and mean hospital stay duration (Days) (14.99±1.66 vs 16.21±1.11; p 0.02) (Table 2). In infants with severe asphyxia, a greater percentage exhibited recovery across all aforementioned measures; nonetheless, the findings did not achieve statistical significance. In improvement, no significant difference was seen in cranial ultrasonography and electroencephalography at 14 days between the two groups. This finding highlights the significance of clinical assessment in these individuals. No substantial difference in mortality was seen between the two groups.

Table 1: Demographic Data (Age or Gender) frequency

Parameters	Sub-category	Group-A	Group-B	P value
Weight (grams)	mean (± SD)	2712.1(±261.39)	2762.9 (±299.99)	0.49
Starting therapy Time (minutes)	mean (± SD)	121.23 (±52.45)	145.11 (±81.96)	0.26
Gestation age (weeks)	mean (± SD)	40.07(±2.11)	39.61(±1.56)	0.92
Mode of delivery, n (%)	Vaginal	30 (50%)	30 (50%)	1.22
	Caesarean	30 (50%)	30 (50%)	
Meconium stained amniotic fluid,	Frequency (%)	39 (65%)	30 (50%)	0.67
Apgar score (5 minute)	mean (± SD)	4.07(±0.99)	4.03(±1.09)	0.81
values of Arterial blood gas pH	mean (± SD)	7.15(±0.17)	7.17(±0.16)	0.71
Arterial blood gas base excess values	mean (± SD)	17.06(±3.99)	17.04(±4.91)	1.22
Encephalopathy	Moderate	39 (65%)	39 (65%)	1.22
	Severe	18 (30%)	21 (35%)	
Level of Serum magnesium	Baseline	1.51(±0.25)	-	0.09
	24 hour	2.81 (±0.20)	-	0.02
	72 hour	2.89(±0.61)	-	0.02

Table 2: Baseline features of both the groups

Features		Moderate Asphyxia (N=90)			Severe Asphyxia (N=40)		
	Sub-category	Group-A N=45	Group-B N=45	P	Group-A N=20	Group-B N=20	P
seizures Control (hours)	Mean (±SD)	14.11(±1.22)	18.11(±1.56)	0.01	19.21(±2.11)	21.31(±2.79)	0.09
Normal cry appearance (days)	Mean (±SD)	11.1 (±0.12)	13.11(±1.29)	0.03	17.21(±0.51)	18.99(±0.75)	0.07
Normal activity appearance (days)	Mean (±SD)	11.9(±0.02)	12.00(±1.5)	0.02	19.11(±1.87)	22±(1.45)	0.19
Full oral feed acceptance by sucking (days)	Mean (±SD)	13.31(±0.99)	14.61(±1.51)	0.01	19.11(±1.87)	22±(1.45)	0.21
duration of hospital stay (days)	Mean (±SD)	14.99(±1.66)	16.21(±1.11)	0.02	22±(1.45)	24.99 (±1.11)	0.09
Abnormal cranial Sonography (day 14)	Frequency (%)	12(26.67%)	24(53.33%)	0.21	10(50%)	10(50%)	1.75
Abnormal EEG (day 14)	Frequency (%)	14(31.11%)	12(26.67%)	0.11	10(50%)	10(50%)	1.44
Mortality	Frequency (%)	2(4.44%)	8 (17.78%)	1.21	10(50%)	10(50%)	1.09

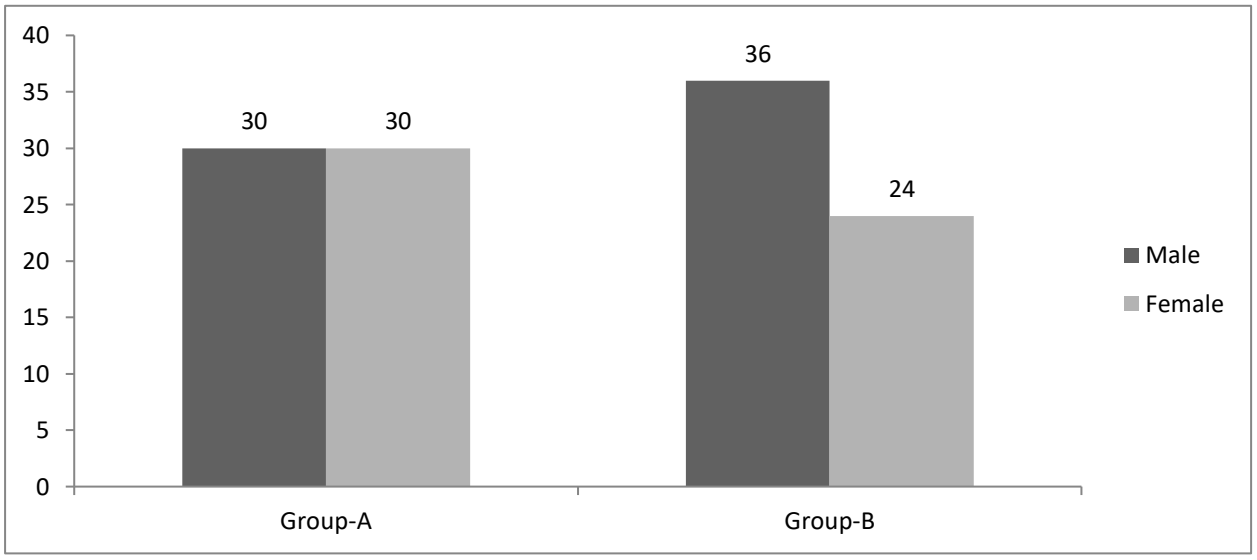

Figure 1: Gender-wise distribution of enrolled neonates

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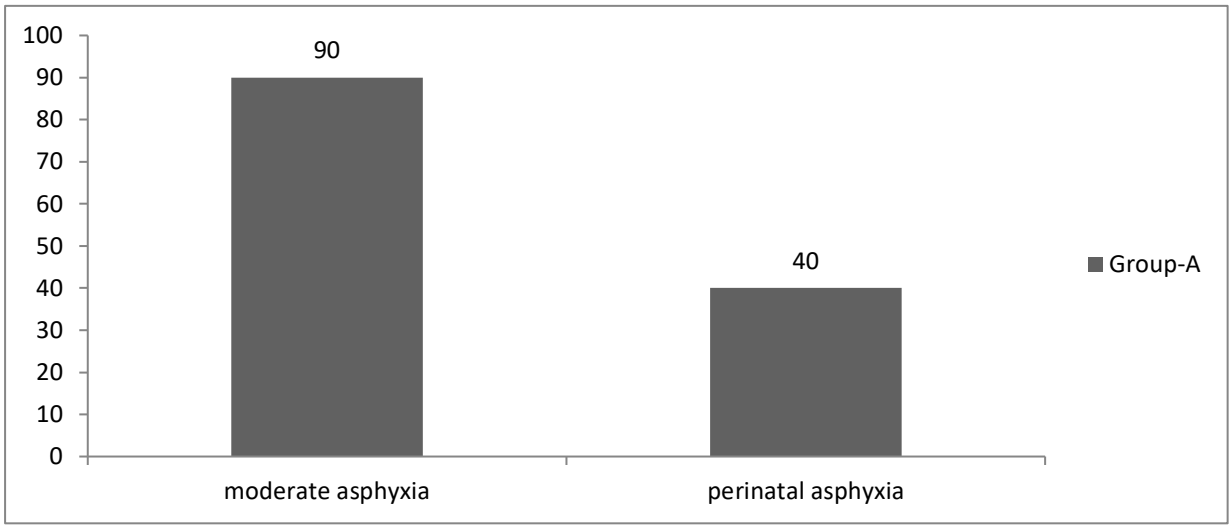

Figure 2: Distribution of patients based on type of asphyxia

Discussion

In the newborn age range, perinatal asphyxia is a leading cause of illness and death. It is also a major contributor to long-term neurological consequences. The extent of the injury, the metabolic disequilibrium during the re-oxygenation phase, and the developmental stage of the impacted organ all influence the severity of perinatal asphyxia (1). Even while our knowledge of the pathophysiologic process has advanced significantly, therapeutic strategies are still in the early stages of research (1-9). NMDA receptor opening-mediated glutamate-induced excitotoxicity is the main cause of neonatal asphyxia. According to perinatal asphyxia 7, magnesium, an NMDA receptor antagonist that occurs naturally, protects the developing brain. This can inhibit pro-inflammatory pathways and has neuroprotective properties (10). When taken as prescribed, magnesium does not worsen any of these individuals' negative effects (7). We assessed the magnesium sulphate infusion's efficacy in treating moderate and severe perinatal asphyxia in the current research. Neonates with mild perinatal asphyxia showed considerably greater neurological recovery than the control group about of presentation of normal activity, presentation of normal cry, mean duration of accepting a complete oral feed, and length of hospital stay. Other studies have reported similar findings (12-13). Similar to the findings of prior research (14,2). Neonates with severe perinatal asphyxia did not demonstrate significant statistical neurological improvement when compared with control. A combination of poor neurological state at birth and unfavourable prenatal and perinatal circumstances may be the cause of this poor outcome in patients with severe perinatal asphyxia. Given the importance of early management in preventing the second phase of damage, the time of magnesium sulphate infusion is a significant predictor of improvement. In comparison to previous research, the average duration of magnesium sulphate infusion for our patients is longer (11, 12, 15) At 14 days, the investigative profiles of both the Moderate and severe groups—cranial ultrasonography and Electroencephalography—exhibited no detectable change. None of the other trials showed significant changes in the Investigative profile (16). While the current research showed a considerable increase in short-term parameters, the mortality advantages are not statistically demonstrated to be the same as those obtained in earlier studies (12). This demonstrates that magnesium treatment helped prevent subsequent insult but was ineffective in preventing initial asphyxia-related death.

Conclusion

Our study concludes that in asphyxiated newborns, postnatal magnesium sulphate infusion is safe and likely to enhance the short-term neurological prognosis in cases with moderate-grade encephalopathy. To confirm the findings, further research with larger sample sizes and multicenter trials is required.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-SZ-0908/23)
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

AHMED AMMAR ALI (Post Graduate Resident Paeds Medicine Unit 1)
Coordination of collaborative efforts.

Study Design, Review of Literature.
SADIA SUBHANI (Medical officer)
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.
Conception of Study, Final approval of manuscript.
TOOBA ALI (Medical officer)
Manuscript revisions, critical input.
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JAMAL ANWER (Professor Paeds Medicine Unit 1)
Data acquisition, and analysis.
Manuscript drafting.
MUHAMMAD ARSHAD (Senior Registrar Paeds Medicine Unit 1)
Data entry and Data analysis, drafting article.
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Data acquisition, and analysis.
Coordination of collaborative efforts.

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