

## ORIGINAL ARTICLE

# Efficacy of Intravenous Magnesium Sulphate in Neonates Suffering from Birth Asphyxia in a Resource Limited Country

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### ABSTRACT

**Objective:** To determine the efficacy of magnesium sulphate in reducing short-term morbidity and mortality among neonates suffering from birth asphyxia.

**Study Design:** Randomized Control trial.

**Place and Period of Study:** Neonatology Unit of Allama Iqbal Memorial Teaching Hospital, Sialkot from November 2022 to July 2023.

**Material and Methods:** Neonates with perinatal asphyxia, meeting the inclusion criteria were enrolled in study (total of 128 with 64 in each Group). Asphyxia was classified according to criteria laid by Sarnat. After taking informed consent case group received magnesium sulphate at the dose of 250 mg/kg at 6 hour, 24 hour and at 48 hour of life. Rest of the management was similar for both groups. Data was collected on predesigned proforma. Distribution of perinatal factors and neonatal baseline characteristics were noted. Data was analyzed by using SPSS version 27, chi-square test applied with p-value <0.05 taken significant.

**Results:** This study showed statistically significant difference (p-value <0.05) in short term outcomes in the form of decrease frequency and early control of seizures along with shorter duration of hospital stay. However, the difference in establishment of sucking reflex and neurological status at discharge was insignificant (p-value >0.05).

**Conclusion:** Magnesium sulphate is an effective drug for reducing the short term morbidities in asphyxia especially in resource limited institutes.

**Key Words:** Birth asphyxia, Magnesium sulphate, Morbidity, Mortality, Neonate, Outcome, Resource limited country, Term

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### INTRODUCTION

According to World Health Organization about 16,000 children die every day below the age of five year. The most common etiologies of

childhood deaths are infectious diseases, preterm birth, and birth related complications.<sup>1</sup> According to WHO, Globally neonatal asphyxia leads to 23 percent of newborn mortality.<sup>2</sup> The incidence of birth asphyxia is 1-2 per 1000 live births in well

developed countries and up to 5 per 1000 live births in under developed countries.<sup>3</sup> The Neonatal mortality rate (NMR) in Pakistan is 41 per 1,000 live births, among them 20.9% of neonatal deaths are due to birth asphyxia.<sup>4</sup> Perinatal asphyxia is a well-known cause of neuro-motor disability and one third to one half develops cerebral palsy and mental retardation.<sup>5</sup>

In neonatal asphyxia, inflow of calcium mainly lead to cellular damage by activating different enzymes. This influx is mainly due to neurotransmitter glutamate which works by acting on N-methyl-D-aspartate (NMDA) receptor. Magnesium sulphate is NMDA receptor antagonist thus it stops calcium influx in the neurons. Moreover, magnesium sulphate has following properties i.e. anti-apoptotic, anti-inflammatory, antioxidant and anticonvulsant due to which it is neuro protective.<sup>3</sup>

Although therapeutic body cooling along with supportive treatment is the recommended treatment of birth asphyxia but in our NICU unit where there are poor resources and lack of trained staff we have difficulties in applying therapeutic body cooling.<sup>6</sup> As magnesium sulphate is less costly, with very few side effects, readily available, easy to administer so it can be a good treatment option along with supportive treatment in our NICU unit. So the goal of this study was to determine whether postnatal magnesium sulfate therapy can improve short-term neurological outcomes in term neonates with birth asphyxia.

### MATERIAL AND METHODS

The study was conducted at Neonatal Unit of Allama Iqbal Memorial Teaching Hospital, Sialkot from November 2022 to July 2023. Birth asphyxia was defined as failure to establish spontaneous breathing at birth as per WHO definition. Sarnat criteria was used to assess the severity of birth asphyxia. Mortality was defined as death while morbidity was assessed by comparing, frequency and duration of seizures, grade of birth asphyxia, ability to take feed and neurological issues such as decreased neonatal reflexes, hypotonia/hypertonia, at the time of discharge from hospital.<sup>7</sup> Term neonates, arriving within six hours of delivery to neonatology unit of Allama Iqbal Memorial Teaching Hospital, Sialkot and meeting the operational definition of birth asphyxia were

included. Neonates with dysmorphic features, prematurity and others co-morbidities (sepsis, gross congenital anomalies and intracranial haemorrhage), were excluded. The “Open Epi Software” sample size determination was used to calculate the sample size.<sup>6</sup> Total of 128 neonates were enrolled in the study (64 in each Group). Sample size was calculated by using 90% power of test and 5% level of significance. After the approval of Ethical Review Committee data was collected. It was a single-blind randomized control trial study. The staff and on duty doctors were unaware which baby has received placebo or magnesium sulphate. Lottery method was used for randomization. After taking informed consent neonates of group one were given magnesium sulphate at dose of 250 mg/kg diluted in 20 ml 10% Dextrose water over forty five minutes at admission then at 24 hours and 48 hours, along with recommended supportive measures. Vitals signs (PR, RR, BP, oxygen saturation, CRT, and temperature) were monitored during (after every 10 minutes) and after administration of magnesium sulphate. Baseline serum magnesium, serum calcium, serum phosphorus and serum potassium level were taken before first dose then at day two, day three, and day four. Group two received only supportive measures along with standard monitoring. Data was collected on pre-designed proforma, data was analyzed by using SPSS version 27. The data was shown as percentages and frequencies. Chi-square test applied, taking p value (< 0.05) as significant.

### RESULTS

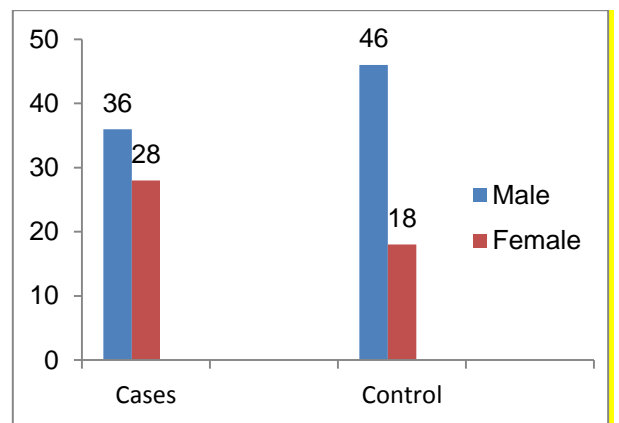


Fig 1: Distribution of gender among case and control group.

Total 128 neonates who met the inclusion criteria were enrolled in the study. Sixty four neonates were randomly assigned to treatment group and sixty four in control group. The distribution of male/female (bar graph), weight for gestation, mode of delivery, and resuscitation were similar in both groups as p-value was found to be insignificant (>0.05).

However, there were significant difference (p-value <0.005) in risk factors of birth asphyxia in both groups as in case group 44 (64.7%) babies had a history of meconium stained liquor whereas in control group 28 (70%) babies had a history of prolonged labor (table 1). Majority of the babies in case group were inborn 36 (60%) while in control group only 24 (40%) were inborn.

**TABLE 1: Baseline Characteristics of study participants**

Parameter	Parameter Category	Cases (%)	Control (%)	p-value
Risk factor	MAS	44 (64.7)	24 (35.3)	0.001
	PROM*	08 (40.0)	12 (60.0)	
	Prolonged labor	12 (30.0)	28 (70.0)	
	Others	00 (0)	00 (0)	
Weight for gestation	AGA*	56 (50.9)	54 (49.1)	0.060
	SGA*	06 (75.0)	02 (25.0)	
	LGA*	02 (20.0)	08 (80.0)	
HIE* Grade	I	15 (36.6)	26 (63.4)	0.106
	II	45 (57.0)	34 (43.0)	
	III	04 (50.0)	04 (50.0)	

MAS: Meconium stained liquor, AGA: Appropriate for Gestational age, SGA: PROM: Prolonged Rupture of Membrane, LGA: Large for Gestational age, HIE: Hypoxic ischemic encephalopathy Small for Gestational age

In case group 45 (57.0%) babies were with grade II asphyxia while in control group only 34 (43.0%) were with grade II. The numbers of babies with severe birth asphyxia grade III were similar (50%) in both groups. However there was no statistically significant (p-value >0.05) difference in severity of birth asphyxia among both groups (table 1). The presence of seizure in both groups were statistically insignificant (table 2). By comparing outcomes in both groups we have found that rate of seizure was much lower in magnesium sulphate group as compare to the control group

and fits were controlled earlier in magnesium sulphate group (cases) as p-value found to be <0.05 (table 2).

In magnesium sulphate group almost 60% babies had presence of sucking and normal neurological status at the time of discharge as compare to 50% babies in control group. However this difference was statistically insignificant (p-value >0.05) table 2. The duration of hospital was shorter in case group as compare to control group and it was statistically significant (p-value <0.05) table 2.

**TABLE 2: outcome variables of case group vs control group.**

Parameter	Parameter Category	Cases (%)	Control (%)	p-value
Seizures	Present	35(47.9.)	38(52.1)	0.592
	Absent	29(52.7)	26(47.3)	
Frequency of seizures	Single	18(81.8)	04(18.2)	0.001
	Multiple	17(33.3)	34(66.7)	
Duration of seizures	Less than 48 Hours	25(71.4)	10(28.6)	0.001
	More than 48 Hours	10(26.3)	28(73.7)	
Suck feed at discharge	Present	56(50.9)	54(49.1)	0.611
	Absent	08(44.4)	10(56.6)	
Neurological status	Normal	56(50.9)	54(49.9)	0.611
	Abnormal	08(44.4)	10(55.6)	
Outcome	Survived	64 (50.0)	64(50.0)	...
	Expired	00	00	
Duration of hospital stay	Less than 60 hours	44 (61.1)	28(38.9)	0.004
	More than 60 hours	20(35.7)	36(64.3)	

## DISCUSSION

Perinatal asphyxia is one of the major causes of morbidity, mortality and long term neurological sequelae in less than 28 days old babies. Different factors effects the severity of asphyxia including amount of insult, metabolic disturbances and developmental state of organs that is affected.<sup>7</sup> Although to understand the pathophysiological mechanism of asphyxia significant advancement has been made, therapeutic interventions are still under progress.<sup>8,9</sup> Unfortunately Pakistan is among the countries with higher neonatal mortality and neonatal asphyxia is among major cause.<sup>9</sup>

In our study frequency of seizures was much lower in magnesium sulphate group as compared to control group with p-value ( $<0.05$ ) which was similar to study done by Siddiqui.<sup>6</sup>

Whereas one study conducted in Japan by Ichiba has showed no difference in duration of seizures among both groups.<sup>10</sup>

Regarding frequency of fits in our study they were significantly lower in case group as compared to control group with p value  $<0.001$ ; however study done by Siddiqui showed no statistically significant difference.<sup>6</sup> A study done in Bangladesh also favored towards our results with p value 0.04.<sup>3</sup>

In our study neurological improvement in group one was 50.9% and in group two it was 49.9% with p-value of 0.611. However study done by Siddiqui showed statistically significant improvement in neurological status in 65 % vs. 37.5% (p value 0.007).<sup>6</sup> Similarly study done by Sajid neurological findings at discharge were improved in 75.8% vs. 45.4% in group-A and group- B respectively with p value ( $p=0.011$ ).<sup>11</sup>

Early establishment of sucking reflex and feeding at discharge was present in 50.9% of case group as compared to 49.1% of control group (p value 0.611). However study done by Sajid showed statistically significant difference in early establishment of feeding with p value of 0.002.<sup>11</sup> A study done by Siddiqui was also in favor of Sajid.<sup>6</sup> Similarly according to study done by Rahman in moderate HIE p value was 0.04 which was significant; however in severe HIE p value was insignificant (0.09).<sup>3</sup> A study done in Nigeria also

showed significant improvement with p value of 0.002.<sup>5</sup> Few other studies also showed similar results.<sup>10,12,13</sup>

Although we included only those newborns who presented within 6 hours of birth there are studies that showed beneficial effects between 6 and 24 hours.<sup>5,14</sup>

All the babies included in our study survived the reason behind this could be the less no of babies with grade III birth asphyxia in our study. Whereas previous studies showed there were fewer deaths in those babies who had received magnesium sulphate.<sup>12-14,5,15,16</sup> Some studies in the past showed no statistically significant difference in the mortality among magnesium sulphate and placebo group.<sup>14,6</sup>

In our study there was statistically significant difference (p-value  $<0.005$ ) in the duration of hospital in both groups. Those babies who had received magnesium sulphate had shorter duration of hospital stay. This was similar to previous studies conducted in the past.<sup>3,4</sup>

Although hypothermia is a standard treatment modality, due to lack of equipment's and trained staff it could not be possible to give this modality in our patients.

However there are certain limitations in our study including failure of long-term follow-up for neurological and developmental assessment and smaller sample size.

## CONCLUSION

Magnesium sulphate is helpful in reducing duration, frequency of seizures and hospital stay. We concluded that magnesium sulphate is a good therapeutic alternative for body cooling in institutes where it is not available

**Conflict of interest:** none to declare.

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