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ORIGINAL ARTICLE

Comparison of Phenobarbital versus Magnesium Sulphate for Management of Neonate with Birth Asphyxia

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ABSTRACT

Background: Poor breathing effort results in decrease oxygen supply to brain and other organs that lead to birth asphyxia. Phenobarbital and magnesium sulphate are both neuroprotective to asphyxia! injury to brain.

Objective: To compare the frequency of neonatal mortality with phenobarbital versus magnesium sulphate in the management of birth asphyxia

Study Design: Randomized control trial

Place and Duration of Study: Pediatrics Department, Sheikh Zayed Hospital, from 8th March 2020 to 8th September 2020.

Methodology: One hundred and two neonates were enrolled. After taking informed consent from parents their demographic data was obtained. Then patients were divided in to two groups; group A treated with Phenobarbital and other group B treated with magnesium sulphate.

Results: The mean age of group A neonates was 54.37+14.303 days and in group B 48.40+15.20 days with male to female ratio was 0.7:1. Adverse outcome occurred in 12 (11.54%) patients. Statistically insignificant difference (P=0.122) was found between groups.

Conclusion: There is more adverse effects outcome with magnesium sulphate than phenobarbital however the difference was statistically insignificant for management of neonates with birth asphyxia.

Keywords: Birth asphyxia, Neonates, Magnesium sulphate (MgS04), Phenobarbital

INTRODUCTION

Ineffective breathing effort leads to poor blood supply to brain and vital organs cause birth asphyxia. According to WHO, birth asphyxia causes 23% neonatal death world wide.[1] It is fifth largest cause of death under 5 years of age. Advance in medical care, leads to increase morbidity of these neonates.[2,3]

Hypothermia, phenobarbitone and magnesium sulphate (MgSO4) are under investigation modalities to prevent birth asphyxia. Controlled trials showed maternal MgSO4 decreased risk of cerebral palsy. There are controversies regarding role of magnesium sulphate as neuroprotective agent in hypoxic ischemic encephalopathy.[4] Research suggest that the influx of intracellular calcium is the main culprit of cellular damage through the activation of lipases, proteases and endonucleases. Neurotransmitter glutamate causes this excessive calcium influx. Glutamate by its action on N-methyl-D-aspartate (NMDA) receptors results in calcium influx.[5] Cell damage that occurs after reperfusion is caused by release of oxygen free radicals.[6] Magnesium sulphate is a NMDA antagonist that blocks Calcium entry within the neurons. Magnesium sulphate also has antiapoptotic, antioxidant, anti-inflammatory and anticonvulsant properties, which also help in preventing neuronal damage.[7] Phenobarbital decreases the blood supply which decreases the chances of cerebral edema thus decreases cerebral metabolic rate, scavenging free radicals, and depressing glutamate response within the brain.[8] Barbiturates decrease the rate of the cascade of damaging processes and reduce secondary neuronal injury.[9] Cerebral cooling of the head also abort these processes by decreasing the metabolic rate of brain injury and decreases the chances of hypoxic ischemic encephalopathy (HIE).[10]

The rationale of this study is to compare the frequency of neonatal mortality of neonates with phenobarbital versus magnesium sulphate for management of birth asphyxia. There is no comparative local study available in literature.

MATERIALS AND METHODS

This randomized controlled trial done in Department of Pediatrics, Sheikh Zayed Hospital Lahore from 1st November 2020 to 31st April 2021. One hundred and four neonates with age 1-3 days of life, either gender presenting with birth asphyxia were included. Neonates with major birth defects or congenital deformities, unstable vital signs (Apgar<5 after 5 minutes of birth) and very low birth weight <1000 grams (on clinical examination) were excluded from study. Demographic variables (name, age, gestational age at birth, gender, contact) were also obtained. Then neonates were randomly allocated into two groups, each group comprised 52 neonates. In group A, 3 doses of intravenous $MgSO_4$ infusion at 250 mg/kg/dose (0.5 mL/Kg/dose of inj. $MgSO_4$ (50% w/v) diluted in 5 mL/Kg of 5% dextrose infused slowly @25 mg/minute) 24 hours apart. In group B, injection of intravenous phenobarbital (20 mg/kg over 15 min) titrated to response; further loading doses of 5 mg/kg were planned if seizures recurred, until a maximal dosage of 40 mg/kg was given. Then neonates were discharged from the ward and followed-up in OPD for 28 days and parents advised to bring neonates in case of complications. The data was entered and analyzed through SPSS version 20. Both groups were compared for adverse outcome by using chi-square test.p≤0.05 was considered as significant. Data was stratified for expected percentage

of neonatal mortality i.e. 13.8% with $MgSO_4$ and 0%.

RESULTS

There were 20 males and 32 females in phenobarbital group while in magnesium sulphate, 23 males and 29 females respectively (Table 1). According to adverse outcome, 3 in phenobarbital group and 9 in magnesium sulpahte groups were found, statistically insignificant (P>0.05) difference between the groups (Table 2).

There is no significant (P>0.05) difference between age, in males no significant (P>0.05) difference and in females significant (P<0.05) difference, no significant (P>0.05) between 34-48 of gestational age and significant (P<0.05) between 39-41 gestational age and also insignificant (P>0.05) birth weight ≤2500 grams and significant (P>0.05) birth weight >2500 in Phenobarbital and magnesium sulphage groups respectively (Table 3).

Table 1: Descriptive statistics of gender, age, gestational age at birth and birth weight in both groups (n=104)

Variable	Phenobarbital	Magnesium sulphate
Gender		
Male	20	23
Female	32	29
Age (hours)	54.37±14.30	48.40±15.20
Gestational age (weeks)	37.15±2.39	37.87±2.29
Birth weight (gms)	2317.25±629.39	2.00±603.07

Table 2: Comparison of adverse outcome in both groups

Averse outcome	Phenobarbital	Magnesium sulphate	P value
Yes	3	9	0.122
No	49	42	

Table 3: Comparison of adverse outcome with age, gender, gestational age and birth weight in both groups

Variable		Phenobarbital		Magnesium sulphate		P value
		Averse outcome				
		Yes	No	Yes	No	
Age (years)	≤50	1	14	5	23	0.423
	>50	2	35	4	20	0.202
Gender	Male	2	18	3	20	1.000
	Female	1	31	6	23	0.045
Gestational age (weeks)	34-38	3	33	2	24	1.000
	39-41	9	16	7	19	0.033
Birth weight (grams)	≤2500	3	30	3	26	1.000
	>2500	0	19	6	17	0.024

DISCUSSION

Birth asphyxia resulting from decrease maternal blood pressure or interference to blood supply to infant's brain during delivery cause serious harm to the brain.[7] This leads to intracellular energy failure. In hypoxic ischemic encephalopathy there are two types of neuronal injury, first is primary that occurs immediately due to hypoxia and secondary occurs in days due to release of calcium having influx in neurons. Magnesium ions act via NMDA antagonist decreasing NMDA receptor mediated injury.[11]

In our study the adverse outcome occurred in 12 (11.54%) patients in 3 were from phenobarbital group and 9 were from group MgSO4, statistically both groups are equally effective but more number of adverse outcome occurred in MgSO4 group than to phenobarbital group (p=0.122). Randomized placebo controlled trials have found that with $MgSO_4$, the frequency of neonatal mortality was ranged from 13.8-16%.[5,6]

Some randomized placebo controlled trials have found that with phenobarbital, the frequency of neonatal mortality ranged from 0-20%.[7, 8] which is 13.8% that is comparable with our study.

In a study done by Meyn and colleagues[12] showed prophylactic use of phenobarbital to asphyxiated infants having head cooling decreases the adverse effect of asphyxia. It is also noted in our study that prophylactic use of phenobarbital has beneficial effect even without cooling of head.

There was 67% reduction in neonatal fits by administration of phenobarbital within 60 minutes of birth of child having hypoxia as represented by Svenningsen et al study.[13]

In another trial conducted in very small number of neonates done by Singh et al[14] showed on 45 infants induction of prophylactic phenobarbital within 30 minutes of birth of asphyxiated neonates reduced fits to 80%.

Gathwala et al[15] study showed on 22 neonates with severe birth asphyxia showed that magnesium is well tolerated and had benefits on these infants. Same is the case in our study that it is well tolerated but less as compared to phenobarbital group.

Whereas in another double-blind, randomized, controlled trial on 22 asphyxiated full-term neonates, eight babies were given $MgSO_4$, it has no positive effect on the EEG patterns.[16]

Meta-analyses showed maternal MgSO4 decreased the risk of cerebral palsy and its comorbidities[5] but it has no role after the birth as represented in our study that phenobarbital has better effect.

CONCLUSION

There is more number of adverse outcome occurred in MgSO4 group than to phenobarbital group however the difference was statistically insignificant for management of neonates with birth asphyxia.

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