Section : Obstetrics and Gynaecology

Original Research Article

ROLE OF ANTENATAL MAGNESIUM SULPHATE AS A FETAL NEUROPROTECTION IN PRETERM LABOUR

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Abstract

Background: Preterm birth is one that occurs at <37 weeks of gestation or less than 258 days of gestation. WHO classifies premature infants into three categories, Extremely preterm(<28weeks), Very preterm(<32 weeks), Moderate to late preterm (32 - <37 weeks),Preterm infants born before the 30th week of pregnancy are especially at risk of prenatal mortality and morbidity . Damage to the immature brain is one of the central concerns. Typical lesions include peri-/intraventricular hemorrhages (PIVH) and periventricular leukomalacia (PVL). **Aim:** To understand the risk of neurological disability in preterm babies. To understand the role of MgSO4for neuroprotection in preterm deliveries and its effect in preventing neurological outcomes. To evaluate the feasibility of its application in all mothers with preterm labour in future. **Materials and Methods:** All pregnant women who attended the labour ward in the Department of Obstetrics and Gynaecology in Dharmapuri medical college hospital based on inclusion and exclusion criteria will be enrolled in the study. We selected 100 antenatal mothers and all of them were given magnesium sulphate and the outcome of the neonates regarding neurological abnormalities were studied**. Results**: Among 100 patients with preterm labour who was given magnesium sulphate, only 14 % shows features of cerebral palsy and 20 % babies shows neurological abnormalities at 6 months compared to groups who has not given magnesium sulphate where > 30 % of babies at 6 months shows neurological abnormalities. Finally neuroprotection was better in mothers without PPROM, those who got magnesium sulphate infusion > 6 hours and in babies whose weight > 1.5 kg**. Conclusion**.Antenatal magnesium sulphate given prior to preterm birth for fetal neuroprotection prevents CP and reduces the combined risk of fetal/infant death or CP. Benefit is seen regardless of the reason for preterm birth, with similar effects across a range of preterm gestational ages and different treatment regimens. Widespread adoption worldwide of this relatively inexpensive, easy-to-administer treatment would lead to important global health benefits for infants born preterm.

INTRODUCTION

The prevention of preterm birth represents one of the most significant challenges to the field of obstetrics in the 21st century. Damage to the immature brain is one of the central concerns, Typical lesions include peri/intraventricular hemorrhages [PIVH] and periventricular leukomalacia [PVL]. Both of these complications specifically affect the pyramidal tracts of the lower extremities. The resulting damage leads to spastic cerebral palsy of the legs.[1-3]

PIVH originates in the vascular bed of the germinal matrix, an area of the brain that almost completely disappears as the fetus matures. Blood vessels in this area of the brain burst very easily. Pre- and postpartal fluctuations of the cerebral blood flow can thus lead to the rupture of these blood vessels and induce PIVH. The extent of the hemorrhage can be increased by an alteration in the thrombocyte aggregation and the coagulation system. Such hemorrhages have been shown to lead to the destruction of the germinal

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matrix, periventricular hemorrhagic infarction of the white brain matter, and hydrocephalus.[4-6]

PVL most commonly leads to damage of the radiatio occipitalis on the trigonum of the lateral cerebral ventricles and the white matter around the foramen of Monroe. This involves axons and oligodendrocytes, especially those that are in the early stage of development. Activated microglia then enter the lesion and strip away the necrotic tissue. Subsequently, small cysts form, which can then be identified sonographically. The lack of myelinisation as a result of damaged oligodendrocytes and an expansion of the lateral cerebral ventricle are then the consequence.[7,8]

PVL can be caused by both cerebral ischemia and infection. During the genesis and the development of the cerebral vascular bed, vascular watersheds develop in the radiatio occipitalis on the trigonum of the lateral cerebral ventricles and the white matter around the foramen of Monroe. The vasodilatation capacity and thus the ability to increase blood circulation during and after arterial hypotension appear to be very restricted in these areas of the brain. After the 32nd week of pregnancy, the vascularisation of these predilection sites increases significantly and the likelihood of PVL decreases.[9]

Ascending intrauterine infections can also induce PVL. An ascending infection causes a so-called "fetal inflammatory response syndrome". The release of endotoxins associated with this syndrome leads to serious impediment of the fetal cardiovascular system regulation, resulting in a reduction in cerebral blood circulation and thus in ischemic lesions in the white brain matter. Cytokines, glutamate, and free radicals are also able to directly damage oligodendrocytes in the early stages of development and thus also disrupt the subsequent myelinisation process, which can significantly affect the development of an infant's motor skills.[10]

Cerebral palsy is a syndrome which includes neuro developemental disabilities such as permanent defects in movements, postural maintainence and function.

It is caused by a single damage in developing brain in the area of motoric regulation. The 36brain is most commonly damaged during fetal period, either during 1st trimester or during 26 -34 weeks gestation when the matter sourrounding the ventricles is more vulnerable. Another known cause of cerebral palsy is hypoxic ischemic encephalopathy.

It is suggested that 14.5% of children with cerebral palsy would have been damaged by ischemia or hypoxia during labour at term. Additionally gastrointestinal and nutritional problems, orthopaedic problems, sensory disabilities, intellectual disabilities, trouble in cognition and behaviour, limited life expectancy and epilepsy occurs in some cases.

Aim of study

- To understand the risk of neurological disability in preterm babies.
- To understand the role of MgSO4for neuroprotection in preterm deliveries and its effect in preventing neurological outcomes.
- To evaluate the feasibility of its application in all mothers with preterm labour in future.

MATERIALS AND METHODS

All women with singleton, twin, or triplet pregnancies were eligible for the protocol if they were admitted with a viable fetus at less than 33 weeks of gestation. Gestational age was the best estimate of completed weeks of gestation based on early ultrasound and menstrual history, as recommended by the French College of Gynecologists and Obstetricians guidelines. For women with imminent preterm birth between 24 and 33 weeks of gestation, antenatal magnesium sulfate is to be administered as a 4-g IV loading dose, over 30 minutes, followed by a 1 g/hour maintenance infusion until birth (for a maximum of 12 hours)[8].

Imminent preterm birth is defined as high likelihood of birth due to either active labor with cervical dilatation ≥4 cm, with or without preterm premature rupture of membranes (PPROM), or planned preterm birth for fetal or maternal indications or other situations such as significant vaginal bleeding.

In our protocol, the relative contraindications for magnesium sulfate are: electrolyte disorders, renal failure, defined as rapidly progressive loss of renal function characterized by oliguria (quantified as less than 400 mL per day), maternal cardiac arrhythmia during this pregnancy, myasthenia, ingestion of calcium channel blockers during the previous 2 hours, and "urgent delivery" (i.e., sulfate administration is allowed in this type of indication as long as it does not delay cesarean delivery).

We considered "urgent delivery" any maternal or fetal emergency that required delivery in the shortest time such as abnormal fetal heart rate tracing, severe antepartum hemorrhage or abruptio placenta.

Our study included all women who were admitted for preterm labor and induced preterm birth (fetal or maternal indications) for delivery between 24 and 33 weeks of gestation,.Exclusion criteria were major fetal abnormalities, intrauterine fetal death between 24 and 33 weeks and incomplete medical records.

All babies were followed up until 6 months of age .fetal outcome was studied in terms of occurrence of cerebral palsy and achievement of milestones at 2,4 and 6 months.

RESULTS

In our study, the outcome of the babies at 2,4 and 6months were analysed, among the 100 patients with preterm labour who received neuroprotective magnesium sulphate.There was no significant difference between the two groups of gestational age [28-30 wks and 30-32 wks].As the duration of magnesium sulphate infusion increases >6 hrs,it had

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a significant outcomes in babies at 6mths. Outcome was better in mothers without PPROM.

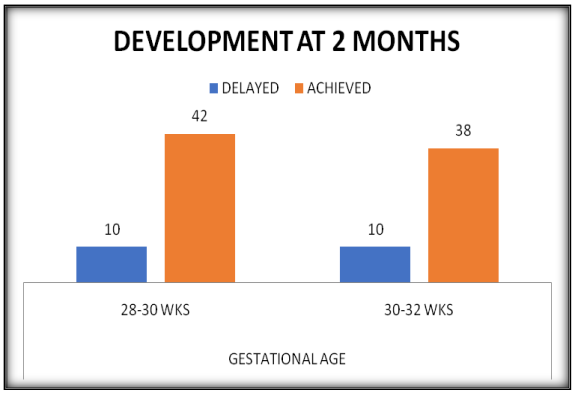

Figure 1: Gestational age vs Outcome at 2 months

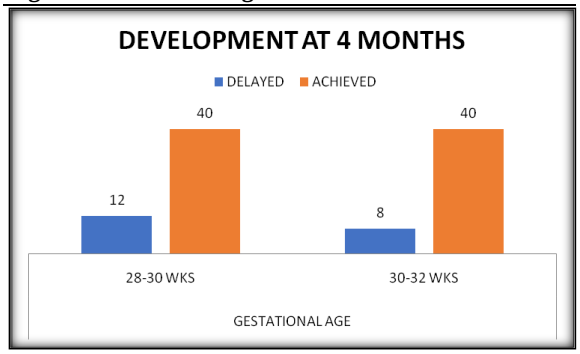

Figure 2: Gestational age vs Outcome at 4 months

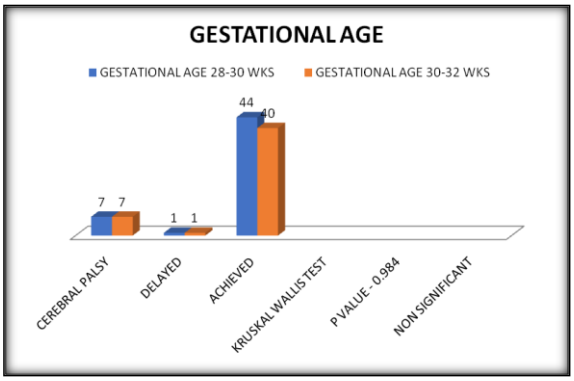

Figure 3: Gestational age vs Outcome at 6 months

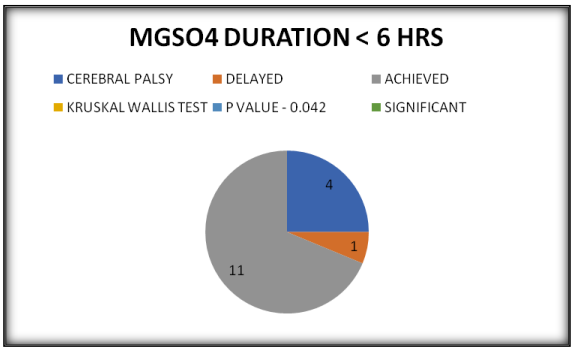

Figure 4: MGSO4 duration of infusion vs Outcome at 6 months

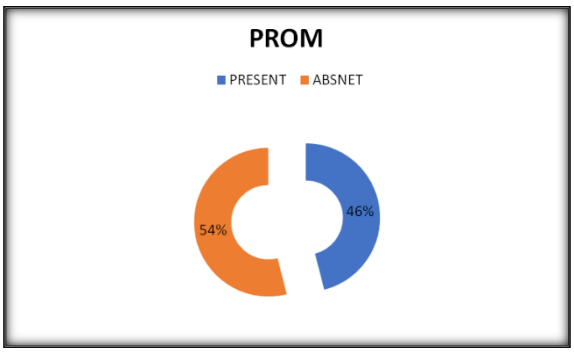

Figure 5: Prom

Table 1: Gestational age vs Outcome at 2 months

Outcome at 2 months	Gestational age	
	28-30 wks	30-32 wks
Delayed	10	10
Achieved	42	38
Fishers exact test		
P value - 0.841		
Non-significant		

Table 2: Gestational Age Vs Outcome At 4 Months

Outcome at 4 months	Gestational age	
	28-30 wks	30-32 wks
Delayed	12	8
Achieved	40	40
Fishers exact test		
P value - 0.423		
Non-significant		

Table 3: Gestational age vs Outcome at 6 months

Outcome at 6 months	Gestational age	
	28-30 wks	30-32 wks
Cerebral palsy	7	7

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Delayed	1	1
Achieved	44	40
Kruskal wallis test		
P value - 0.984		
Non-significant		

Table 4: MGSO4 duration of infusion vs outcome at 6 months

Outcome at 6 months	MGSO4 duration	
	< 6 hrs	> 6 hrs
Cerebral palsy	4	10
Delayed	1	1
Achieved	11	73
Kruskal wallis test		
P value - 0.042		
Significant		

Table 5: Prom

Prom	No of patients	Percentage
Present	46	46%
Absent	54	54%

Table 6: prom vs outcome at 6 months

Outcome at 6 months	Prom	
	Present	Absent
Cerebral palsy	11	3
Delayed	2	0
Achieved	33	51
Kruskal wallis test		
P value - 0.018		
Significant		

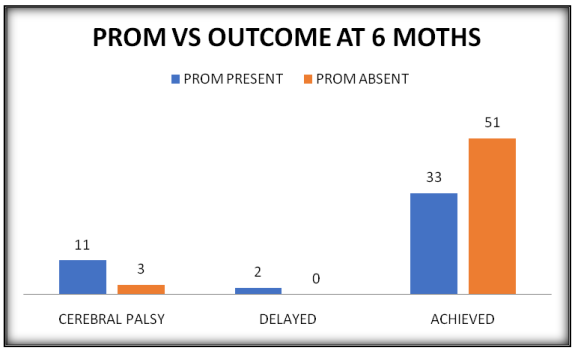

Figure 6: prom vs outcome at 6 months

DISCUSSION & CONCLUSION

This study demonstrates the feasibility of implementing a protocol to use magnesium sulphate among gravidas at imminent risk of delivery before 33 weeks of gestation to prevent cerebral palsy. Appropriate selection of women at high risk of imminent preterm birth is feasible, We first organized a multidisciplinary meeting (midwives, obstetricians, anaesthesiologists, and paediatricians) to discuss the recently issued guidelines, and the level of evidence for the use of magnesium sulphate for neuroprotection in preterm infants and its possible side effects.

The maternal-fatal medicine department and the labour room quickly adopted the use of magnesium sulphate to prevent cerebral palsy.

The significant differences between the groups with and without magnesium sulphate treatment for maternal and neonatal characteristics (i.e., abnormal fatal heart rate, general anaesthesia, neonatal cord pH < 7.10 at birth, Apgar score at 5 minutes < 7, neonatal external cardiac massage, use of epinephrine, and antenatal corticoid administration) strongly suggest that "urgent delivery" for fatal indication was much more frequent in the untreated group.

To our knowledge, only three studies[11] have assessed the feasibility and maternal safety of implementing the use of magnesium sulphate for neuroprotection. Ow et al, reported a 40% rate in the first 12 months after implementation of their guideline. The only information available in that study related to potentially magnesium-attributable maternal complications was that infusion was discontinued as result of side effects in 2% of women, mostly for hypotension.

Antenatal magnesium sulphate given prior to preterm birth for fetal neuroprotection prevents CP and reduces the combined risk of fetal/infant death or CP. Benefit is seen regardless of the reason for preterm birth, with similar effects across a range of preterm gestational ages and different treatment regimens. Widespread adoption worldwide of this relatively inexpensive, easy-to-administer treatment would lead to important global health benefits for infants born preterm.

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