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ROLE OF MAGNESIUM SULPHATE (MgSO4) AS A NEUROPROTECTIVE AGENT ON NEONATAL OUTCOME IN PRETERM DELIVERIES

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Prematurity is the leading cause of perinatal mortality both in developing and developed countries. Among 135 million neonates born each year worldwide, almost 14.9 million are preterm representing a preterm birth rate of 11.1%.Approximately 70% of neonatal deaths and neurodevelopmental impairment in 50% of cases. ACTOMgSO4, MagNET, PREMAG, BEAM were the large studies of MgSO4 for neuroprotection in prematurity previously. Antenatal MgSO4 can prevent neonatal seizures and neonatal deaths in preterms. **Aims and objective of the study:** To evaluate the perinatal outcome of preterm deliveries in women receiving MgS04 **Material and methods-** This was a prospective observational comparative study for one year, from December 2022 to November 2023, conducted in department of Obstetrics and Gynaecology in ASRAM Medical College. A total of 100 pregnant women who gave preterm births were studied. Fifty infants each were born to mothers who were either not given MgSO4 (Group 1) or given 20% 4gm intravenous loading dose MgSO4, followed by maintenance dose of 1gm/hr over a period of 24 hrs before delivery or upto delivery (Group 2), preferably 4 h prior to preterm birth. All the preterm neonates born to the100 women were followed up for 1year for neonatal seizures, deaths and gross motor dysfunction. **Results:** Total 20% neonatal deaths in group A and 10% neonatal deaths in group B Total 18% neonatal seizures in group A and 10% neonatal seizures in group B Total 8% gross motor dysfunction in group A and 6% gross motor dysfunction in group B Antenatal MGSO4 has better role when given at 28-32 weeks of gestation **Conclusion:** MgS04 is a safe drug to use in antenatal women at risk for impending preterm. Antenatal magnesium sulphate given to women in established preterm labour conferred significant neuroprotective advantage to the neonate. It is time for us to start using MgS04 in clinical practice for neuroprotective intent in all our extreme preterm births.

KEYWORDS

INTRODUCTION:
Prematurity is the leading cause of perinatal mortality both in developing and developed countries. Among 135 million neonates born each year worldwide, almost 14.9 million are preterm representing a preterm birth rate of 11.1%. Approximately 70% of neonatal deaths and neuro developmental impairment in 50% of cases.

ACTOMgSO4, MagNET, PREMAG, BEAM were the large studies of MgSO4 for neuroprotection in prematurity previously. Antenatal MgSO4 can prevent neonatal seizures and neonatal deaths in preterms.

AIM AND OBJECTIVE:
To investigate the effectiveness of antenatal magnesium sulphate for neuroprotection in preterm deliveries .

METHODOLOGY:
This was a prospective observational comparative study for one Year, from December 2022 to November 2023, conducted in department of Obstetrics and Gynaecology in ASRAM Medical College.

A total of 100 pregnant women who gave preterm births were studied. Fifty infants each were born to mothers who were either not given MgSO4 (Group 1) or given 20% 4gm intravenous loading dose MgSO4, followed by maintenance dose of 1gm/hr over a period of 24 hrs before delivery or up to delivery (Group 2), preferably 4 h prior to preterm birth. All the preterm neonates born to the 100 women were followed up for 1 yearfor neonatal seizures, deaths and gross motor dysfunction.

Inclusion Criteria:
Pregnant women with preterm labour at 28-32 weeks of gestation, with no associated complications were included in this study.

Exclusion Criteria:
Pregnant women less than 28 weeks of gestation
Pregnant women greater than 32weeks of gestation.
Second stage of labour
Already received magnesium sulphate during present pregnancy
Allergy to drug
Any contraindication to drug

Dosage Of Antenatal MgSO4:
A total 50 pregnant women between 28-32 weeks gestation presenting to the emergency department at risk of preterm delivery / established preterm were given 4gm intravenous loading dose slowly over 20 minutes followed by maintenance dose of 1gm/hour infusion for 24 hours or till delivery.

RESULTS:
TABLE 1: Comparing perinatal outcome showing neonatal death without MgSO4 coverage (Group 1) and with MgSO4 coverage (Group 2)

GESTATIONAL AGE	PERINATAL OUTCOME SHOWING NEONATAL DEATH (GROUP 1)	PERINATAL OUTCOME SHOWING NEONATAL DEATH (GROUP 2)
28-30 weeks	5 neonates	4 neonates
30-32 weeks	3 neonates	1 neonates
32-34 weeks	2 neonates	0 neonate
	10/50 (20%)	5/50 (10%)

According to our study neonatal deaths are comparatively more at the gestational age of 28-30 weeks. Total of 10 neonatal deaths (20% of preterm) in group A and 5 neonatal deaths (10% of preterm) in group B were seen. Fetal lung maturity might be an aiding factor for the neonatal deaths.

TABLE 2: Comparing perinatal outcome showing neonatal seizures without MgSO4 coverage (Group 1) and with MgSO4 coverage (Group 2)

GESTATIONAL AGE	PERINATAL OUTCOME SHOWING NEONATAL SEIZURES (GROUP 1)	PERINATAL OUTCOME SHOWING NEONATAL SEIZURES (GROUP 2)
28-30 weeks	3 neonates	3 neonates
30-32 weeks	4 neonates	1 neonates

32-34 weeks	2 neonates	1 neonate
	9/50 (18%)	5/50 (10%)

At the end of our study, total of 9 neonatal seizures (18% of preterm) in group A and 5 neonatal seizures (10% of preterm) in group B were seen.

TABLE 3: Comparing perinatal outcome showing gross motor dysfunction without MgSO4 coverage (Group 1) and with MgSO4 coverage (Group 2)

GESTATIONAL AGE	PERINATAL OUTCOME SHOWING GROSS MOTOR DYSFUNCTION (GROUP 1)	PERINATAL OUTCOME SHOWING GROSS MOTOR DYSFUNCTION (GROUP 2)
28-30 weeks	1 neonates	2 neonates
30-32 weeks	2 neonates	1 neonates
32-34 weeks	1 neonates	0 neonates
	4/50 (8%)	3/50 (6%)

Gross Motor dysfunction developed in total of 4 neonates (8% of preterm) in group A and 3neonates (6% of preterm) in group B were seen.

At our study among the preterm neonates 37 cases (74%) shows better outcome, 5 cases (10%) of neonatal seizures, 5 cases (10%) shows neonatal deaths and 3 cases (6%) of Gross Motor dysfunction noticed.

DISCUSSION:

Preterm labour resulting into preterm birth is often associated with a number of developmental abnormalities owing to shorter gestational period as well as various perinatal events. Preterm labour is often characterised by a higher risk of neuronal injuries such as intraventricularhaemorrhage and paraventricular haemorrhage which eventually is responsible for different neurological disorders like cerebral palsy or mental retardation.

Currently, infants born at less than 34 weeks of gestation constitute about 25% of all new cases of cerebral palsy. Multiple pregnancy is associated with an increased risk of cerebral palsy, attributed partly to preterm birth.

Prevalence of cerebral palsy worldwide has shown a modest increase secondary to increased survival of very low-birth weight infants. The prevalence of cerebral palsy reported in recent population-based studies ranges between 1.5 cases and 3.6 cases per 1,000 live births. White matter injury and intraventricular hemorrhage are the main developmental stage-specifc brain disease responsible for these neuro-disabilities. Risk of IVH increases inversely with the gestational age at birth. Early intervention is essential in the prevention of the secondary phase of neuronal injury. The immature brain is particularly prone to excitotoxicity, and inflammation has been strongly implicated in the pathogenesis of cerebral palsy.

Magnesium is an ionized mineral essential to hundreds of enzymatic processes, including hormone receptor binding, energy metabolism, muscle contractility as well as neuronal and neurotransmitter function Magnesium has an inhibitory effect at neuronal synapses, leading to its use as an anticonvulsant, particularly in eclamptic seizures. Antenatal MgSO4 administration has demonstrated the neuroprotective effects for preterm births before 32 weeks of gestation. Owing to its biological properties, including its action as an N-methyl-d-aspartate receptor blocker and its anti-inflammatory effects, magnesium is a good candidate for neuroprotection.

The presumed mechanism of action of MgSO4 for neuroprotection is dependent on adequate fetal levels of magnesium at the time of delivery. Animal studies evaluating placental transfer of magnesium sulfate have shown that it crosses fetal blood brain barrier within 2 h of sustained maternal infusion but its concentrations increase in the forebrain only after 4 h of treatment. All neonatal outcomes that is 5 min Apgar score, need for resuscitation, hypotension, sepsis, seizures, IVH, NEC and number of days in NICU were better when time interval between MgSO4 and delivery was more than 4 h in our study. With this evidence, one should aim to commence MgSO4 at least 4 h prior to delivery. However, where it is not possible to achieve the 4-h window period, MgSO4 should still be administered, as it is likely to show some benefit.

Definitive mechanism of action of antenatal MgSO4 in fetal neuroprotection remains unclear.

MgSO4 freely crosses placenta and takes part in many intracellular processes

- cerebral vasodilatation, inhibition of calcium influx into cells.
- preventing early abnormal neuronal cells apoptosis.
- preventing inflammatory and cytotoxic agents release.
- decreasing neuro-inflammation and increasing seizures threshold
- decreasing cerebellar hemorrhage
- MgSO4 also improves vascular tone and maintain good oxygen perfusion to organs which helps the CVS to counter balance when faced with hypoxia for providing cell life protection.

Antenatal MgSO4 causes the promotion of neurogenesis in premature brain cells by stimulating neurotrophic factors like Brain Derived Neurotrophic Factor(BDNF).

BDNF is protective against neonatal hypoxic ischemic brain injury in vivo.

BDNF production correlates with fetal brain maturity, more mature the brain more BDNF production.

Antenatal MgSO4 increases BDNF secretion in premature fetal brain to equal levels seen in term pregnancy thus decreasing destructive processes in fetal brain.

BDNF block N-Methyl D-Aspartate (NMDA) receptors to prevent glutamate.BDNF INHIBITS Damage to the fetal brain first occurs in periventricular region called peri-ventricular leukomalacia (PVL) which may lead to cerebral palsy.

Side effects like nausea, vomiting, respiratory depression, hyporeflexia, oliguria, pulmonary edema , cardiac arrest, atonic post partum hemorrhage are strictly monitored in the mother during MgSO4 infusion.

Calcium gluconate is an antidote if MgSO4 toxicity suspected. Injection BETAMETHASONE 12 grams 2 Intramuscular doses 24 hours apart, also given to mothers for fetal lung maturity.

Previous studies like PREMAG and ACTOMgSO4 has good perinatal outcome with better neuroprotection involving lower neurological disability, less number of neonatal seizures, deaths, Gross neuromotor dysfunction.

CONCLUSION:

When antenatal MgSO4 administered at an appropriate dose with proper monitoring, there is no evidence of harm to the fetus, neonate or mother and it helps in neuroprotection of the preterms by preventing neonatal seizures, neonatal deaths, and gross motor dysfunction in preterms.

REFERENCES:

1. Ginsberg Y, Gutzeit O, Khatib N, Weiner Z, Bang S, Beloosesky R, et al. Magnesium sulphate doses for neuroprotection: low is better. Am J Obstet Gynecol. 2021; 224(2):s294.
2. Moradi Y, Khateri R, Haghighi L, Dehghani S, Hanis SM, Valipour M, et al. The effect of antenatal magnesium sulfate on intraventricular hemorrhage in premature infants: a systematic review and meta-analysis. ObstetGynecol Sci. 2020;63:395–406
3. Muhammad AdrianesBachnas, Muhammad IlhamAldika Akbar, ErryGumilar Dachlan &Gustaaf Dekker (2019): The role of magnesium sulfate (MgSO4) in fetal neuroprotection,The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/ 14767058.2019.1619688
4. Usman S,FooL,TayJ,BennettPR,LeesC.Use of magnesium sulphate in preterm deliveries for neuroprotection of the neonate.The Obstetrician and gynaecologist 2017;19:21-8
5. Williams obstetrics 25th Edition.
6. Manijeh K, Erin ASC, Bradley AY, et al. Antenatal magnesium sulfate, Necrotizing Enterocolitis and Death among neonates < 28 weeks gestation. AJP Rep. 2016; 6(1): 148–54
7. Kamyar M Manuck TA, Stoddard GJ, Varner MW, Clark EAS: Magnesium sulfate, chorioamnionitis, and neurodevelopment after preterm birth. BJOG 2016;123:1161-1166.,
8. RCOG. Magnesium sulphate to prevent cerebral palsy following preterm birth. Scientific impact paper no 29.August,2011
9. Magee L, Sawchuck D, Synnes A, et al. SOGC Clinical Practice Guideline: magnesium sulfate for fetal neuroprotection. J ObstetGynecol Can. 2011;33:516–29.
10. Crowther CA, Hiller JE, Doyle LW, Haslam RR. Australasian Collaborative Trial of Magnesium Sulphate (ACTO MgSO4) Collaborative Group. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. JAMA 2003;290:2669– 2676. DOI: 10.1001/jama.290.20.2669.