Original Research Article

The Role of Magnesium Sulphate ($MgSO_4$) In Fetal Neuroprotection

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Abstract

Background: Preterm birth is the major cause of perinatal mortality both in developed and developing countries**.** The prevalence of preterm birth is increasing every year and it is nearly more than 15 million preterm births worldwide according to WHO, approximately one million may die and many more may suffer from neurodevelopmental impairment. 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 use of antenatal Mgso4 for neur protection of preterminfants. **Material and Methods**: This study titled "The Role Of Magnesium Sulphate (MgSO4) In Fetal Neuroprotection" was conducted in Department of Obstetrics and gynecology in ASRAM Medical College. A total 20 pregnant women between 28-32 weeks gestation presenting to the emergency department with abdominal pain associated with cervical dilatation (cervical dilatation > 4cm) at risk of imminent preterm delivery(delivery definitely planned within 24 hours) were given Mgso4 4gm iv for about 20-30 min followed by maintenance dose of 1gm/hr for a period of 24 hrs before delivery or up to delivery and all the preterm neonates born to the 20 women were followed up for one year for neonatal seizures, deaths and gross motor dysfunction. **Results:** Antenatal MGSO4 has better role when given at 28-32 weeks of gestation as only 2 neonates (10% of total preterms) born at 32-34 weeks gestation developed neonatal seizures. **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.

Keywords: Preterm, MgSO4, neuroprotection.

Introduction

Preterm birth, defined as birth before 37 weeks of gestation, is the single most important determinant of adverse infant outcomes, in terms of survival and quality of life. Globally, it is the leading cause of perinatal and neonatal mortality and morbidity. Preterm infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection. With the increasing contribution of neonatal deaths to overall child mortality, it is critical to address the determinants of poor outcomes related to preterm birth to achieve further reductions in child mortality.

Infant mortality and morbidity from preterm birth can be reduced through interventions delivered to the mother before or during pregnancy, and to the preterm infant after birth. Interventions can be directed at all women for primary prevention and reduction of the risk of preterm birth (e.g. smoking cessation programme) or aimed at minimizing the risk in women with known risk factors (e.g. progestational agents, cervical cerclage). However, the most beneficial set of maternal interventions are those that are aimed at improving outcomes for preterm infants when preterm birth is inevitable (e.g. antenatal corticosteroids, magnesium sulfate and antibiotic prophylaxis). Special care of the preterm newborn to prevent and treat complications of prematurity is also critical to newborn survival. In high-income countries, reductions in mortality rates in infants that were born preterm have been driven largely by improved care and, more importantly, by appropriate policy changes.

The prevalence of preterm birth is increasing every year and it is nearly more than 15 million preterm births worldwide according to WHO, approximately one million may die and many more may suffer from neuro developmental impairment. 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 pre terms.

Aim and Objective

To evaluate the use of antenatal MgSO4 for fetal neuroprotection of preterm infants.

Methodology

Study Area: Department of Obstetrics and gynecology in ASRAM Medical College, Eluru
Study Design: Observational study
Study Period: August 2020 to August 2021
Sample Size: 20 women attending to emergency department at our institute who met inclusion criteria

Inclusion Criteria

20 women between 28-32 weeks gestation presenting to the emergency department with abdominal pain associated with cervical dilatation (cervical dilatation > 4cm) at risk of imminent preterm delivery(delivery definitely planned within 24 hours) during a period of one year were included.

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Exclusion Criteria

All the pregnant women who were less than 28 weeks of gestation and who were greater than 32weeks of gestation were excluded.

Dosage of Antenatal MgSO4

Regimens of magnesium sulfate for fetal neuroprotection

The route of administration and dose of magnesium sulfate varied in these trials:

1. IV 4 g over 20 minutes, then 1 g/hour until delivery or for 24 hours, whichever came first;
2. IV 4 g over 10–15 minutes, followed by either IV 1 g/hour for 24 hours, or by IM 5 g every 4 hours for 24 hours;single dose of IV 4 g over 30 minutes;single IV bolus of 4 g; and
3. IV 6 g over 20–30 minutes, followed by maintenance infusion of 2 g/hour for 12 hours, with retreatment permitted whenever birth was imminent.

A total 20 pregnant women between 28-32 weeks gestation presenting to the emergency department with abdominal pain associated with cervical dilatation (cervical dilatation > 4cm) at risk of imminent preterm delivery(delivery definitely planned within 24 hours) were given Mgso4 4gm iv for about 20-30 min followed by maintenance dose of 1gm/hr for a period of 24 hrs before delivery or upto delivery and all the preterm neonates born to the 20 women were followed up for one year for neonatal seizures, deaths and gross motor dysfunction.

Results

Table 1: Antenatal administration of MgSO4 at different gestational age- neonatal seizures

Antenatal MgSO4 given at gestational age	Perinatal outcome showing neonatal seizures
28-30 weeks	0/20 neonates
30-32 weeks	0/20 neonates
32-34 weeks	2/20 neonates (10%)

At the end of our study antenatal MgSO4 has better role when given at 28 - 32 weeks of gestation as only 2 neonates (10% of total preterms) born at 32-34 weeks of gestation developed neonatal seizures.

Table 2: Antenatal MgSO4 at different gestational age –neonatal death

Antenatal MgSO4 given at gestational age	Perinatal outcome showing neonatal death
28-30 weeks	2/20 neonates (10%)
30-32 weeks	0/20 neonates
32-34 weeks	0/20 neonates

According to our study neonatal deaths are comparatively more at the gestational age of 28 - 30 weeks as 2 neonatal deaths(10% of preterms) were seen. fetal lung maturity might be an aiding factor for the neonatal deaths.

Table 3: Antenatal MgSO4 at different gestational age- Neonatal motor dysfunction

Antenatal MgSO4 given at gestational age	Perinatal outcome showing Gross Motor dysfunction
28-30 weeks	0/20
30-32 weeks	0/20
32-34 weeks	1/20 (5%)

Gross Motor dysfunction developed in 1 case (5% of cases) in our study At our study among the preterm neonates 15 cases (75%) shows better outcome, 2 cases(10%) of neonatal seizures, 2 cases (10%) shows neonatal deaths, and 1 case(5%) of Gross Motor dysfunction noticed.

Discussion

Cerebral Palsy and Preterm Birth

Infants born preterm have a higher risk of neurologic impairments, cerebral palsy (CP) and cognitive dysfunction being the most frequent, and of substantial disability as a result of these impairments.

CP describes a group of disorders affecting the development of movement and posture, causing activity limitation, secondary to non progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders are often accompanied by neurodevelopmental or sensory problems, such as seizures, hearing or vision impairments, or behavioral, communicative, and/or cognitive deficits.

The risk of serious medical disabilities such as CP, mental retardation and other developmental and behavioral disorders, as well as of other disabilities, such as blindness, hearing loss and epilepsy increases significantly with decreasing gestational age at birth. The survival rate of very preterm infants who are at higher risk has continued to increase overtime due to advances in perinatal care, and whereas some data suggest that the rate of CP among survivors has declined, other data suggest that the rate is unchanged or even increasing.

MgSO4 has been used in obstetrics for decades as a tocolytic agent and for the prevention or treatment of seizures in women with preeclampsia or eclampsia. Magnesium sulfate (MgSO4) preconditioning decreases the induced lesion's sizes and inflammatory cytokine levels, prevents cell death, and improves long-term behavior. In humans, some observational studies have demonstrated reduced risks of cerebral palsy with antenatal MgSO4 therapy.

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 neuroinflammation and increasing seizures threshold.
- Decreasing cerebellar hemorrhage
- 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 invivo.

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.

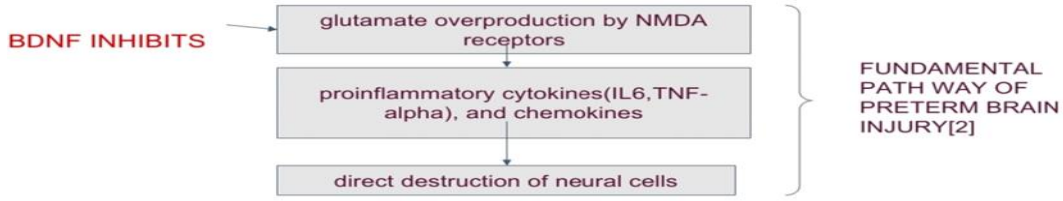

Figure 1: Mechanism of action of MgSO4

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Damage to the fetal brain first occurs in periventricular region called PeriVentricular Leukomalacia (PVL) which may lead to cerebral palsy.

- Side effects like nausea, vomiting, respiratory depression, hyporeflexia, oliguria, pulmonary edema and cardiac arrest 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.
- In our study 75% of neonates has good perinatal outcome.
- Previous studies like PREMAG and ACTOMgSO4. has good perinatal outcome with better neuroprotection involving lower neurological disability, less number of neonatal seizures, deaths, Gross Motor 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, Gross Motor dysfunction in preterms.

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