Guideline for the use of Antenatal Magnesium Sulphate for Neuroprotection of the Preterm Infant

The survival of infants born preterm have substantially improved with interventions such as antenatal corticosteroids and surfactant, however this survival has been associated with a substantial risk of neurodevelopmental impairment. Cerebral palsy and cognitive dysfunction are the most frequently occurring neurologic impairments associated with preterm birth.

Cerebral palsy is a non-progressive disorder of movement and posture related to injury to developing brain. Overall incidence of cerebral palsy is 1.6/1000 and the risk is highest at early gestational ages. There is a 40-60 fold increase in cerebral palsy rate in extreme preterm babies (<28 weeks). At present there is no cure for cerebral palsy, which makes preventative interventions of paramount importance.

Role of Magnesium Sulphate in Neuroprotection

In humans, Magnesium Sulphate is essential for key cellular processes and has neuroprotective effect (McDonald 1990) in preventing post-hypoxic brain injury. It acts by blocking the cascade of calcium influx and neuronal cell death in damaged neurons.

There is evidence from observational studies, randomised controlled trials and meta-analyses that there is significant reduction in cerebral palsy and severe motor dysfunction with the use of magnesium sulphate without any difference in stillbirth or infant death rates. There were no significant differences in the maternal outcomes like death, cardiac or respiratory arrest with the use of magnesium sulphate for fetal neuroprotection.

Women at high risk of imminent spontaneous preterm birth (i.e. delivery within 24 hours) between 24 and 29 +6 weeks gestation should be administered magnesium sulphate for fetal neuroprotection.

There is controversy about upper gestation age limit for administration of this medication for fetal neuroprotection. The outcome of cerebral palsy was significantly reduced at all gestational ages, as CP is highest at earlier gestational ages, consensus was reached to recommend an upper gestation age cut-off of <30 weeks in our unit.

'Imminent preterm birth' is defined as high likelihood of birth due to active preterm labour with more than or equal to 4cm cervical dilation with or without PPROM or planned preterm birth for fetal or maternal indications.

Magnesium Sulphate for neuroprotection should be administered regardless of single or multiple gestation.

Timing of administration

- Imminent spontaneous preterm birth – commence when cervical dilation more than 4 cm with or without PPROM.
- Magnesium sulphate should be discontinued if delivery is no longer imminent or a maximum of 24 hours of therapy has been administered. There is evidence of neurodevelopmental harm if total dose exceeds 48g.
- Retreatment with antenatal magnesium sulphate is not recommended as there is insufficient data to support the benefit.
- Planned preterm birth, including Caesarean section, magnesium sulphate should be started ideally 4 hours before birth and maintenance dose administered until birth.
- Delivery should not be delayed for administration of magnesium sulphate for fetal neuroprotection if there are maternal and or fetal indication for emergency delivery.
- If IOL is likely to take longer than 24 hours it is reasonable to delay the start of the magnesium sulphate until cervical ripening is achieved.
- Magnesium sulphate should be discontinued after the delivery.

Ensure normal FBC, U&E and LFTs prior to commencing infusion

Dosage and administration

(Same regime as for pre-eclampsia / eclampsia)

Magnesium sulphate for fetal neuroprotection should be administration as 4 gram IV loading dose over 10 minutes via syringe driver followed by 1 gram per hour infusion until birth or when 24 hours of infusion has been administered, whichever is earlier.

Loading dose:

- Each vial of magnesium sulphate (50%) contains 5 grams in 10 mls of water;
- Dilute one vial of magnesium sulphate to 50 mls with normal saline, then discard 10 mls leaving 40 mls (4 grams MgSO4) in the syringe;
- Infuse via syringe driver at a rate of 240 mls/hour (10 minutes).

IV infusion

- Dilute 1 vial of magnesium sulphate to 50 mls with normal saline and infuse at 10 mls /hour via syringe driver;
- Once prescribed by a doctor this can be made up and further infusion continued by any competent health care professional.

This dosage regimen resembles current clinical practice and hospital protocol for magnesium sulphate for eclampsia treatment and prophylaxis and also minimise concerns about maternal safety.

Common side effects include flushing, sweating, headache, nausea and vomiting. Serious side effects are uncommon and include maternal hypotension and tachycardia.

Monitoring of women on magnesium sulphate should be similar to those being administered in the medication for pre-eclampsia and eclampsia.

- Measure respiratory rate and oxygen saturation every 15 minutes with routine pulse rate and blood pressure recordings. Maintain oxygen saturation above 94% and respiratory rate should be above 12 per minute.
- Urine output should be at least 100mls in 4 hours.
- Monitor reflexes every 4 hours. Loss of patellar reflex is the first manifestation of hypermagnesemia. This has been found to be poorly done and often medical staff are busy. The membership has (as with eclamptic guideline) excluded this unless trained staff are able to perform it.
- Routine monitoring of serum magnesium sulphate levels is not required but this should be done if there is a compromise of renal function or suspicion of toxicity.
- **If respiratory rate is <12 breaths per minute –**
    i. Stop the infusion
    ii. Call the Anaesthetist on page 134
- **If respiratory arrest occurs**
    i. Call 2222 – Obstetric Emergency
    ii. Ventilate with an Ambu bag until intubation possible by experienced individual
    iii. Stop the magnesium sulphate infusion
    iv. Give calcium gluconate 1 gram intravenously over 5 minutes (10 mls of 10% calcium gluconate (1 gram) IV over 5 minutes)

Continuous fetal surveillance should be provided while women are on magnesium sulphate for fetal neuroprotection

- This should be by continuous EFM after 26 weeks gestation and by intermittent auscultation every 15 minutes in the first stage and every 5 minutes in the second stage at earlier gestations.

As magnesium sulphate crosses the placenta, slight decrease in the baseline heart rate and variability, which are not clinically significant may be observed.

Tocolysis

Tocolysis is not indicated in advance labour >4 cms.

Magnesium sulphate use is for fetal neuroprotection and not as a tocolytic agent.

Tocolysis should be discontinued before commencing antenatal magnesium sulphate for fetal neuroprotection.

Magnesium sulphate can be immediately commenced after stopping tocolytic medications.

Antenatal corticosteroids should be administered appropriately if not already given and there is no known interaction between corticosteroids and magnesium sulphate.

Contraindications

Magnesium sulphate for fetal neuroprotection is contraindicated in known hypersensitivity, patients with myasthenia gravis and hepatic coma. It should also be avoided in those with significant cardiac conduction defects and myocardial compromise.

Magnesium sulphate is to be used with caution in renal impairment. Monitoring of serum magnesium levels is required if this is the case.

Other considerations

When maternal transport is being considered, magnesium administration should be decided in consultation with the receiving centre on a case by case basis.

The paediatric team attending delivery should be made aware of antenatal magnesium sulphate exposure.

Neonates may present with potentially altered neuro-evaluation due to magnesium sulphate causing hypotonia or apnoea. Therefore, healthcare providers caring for the neonate should have an increased awareness of this effect.

Magnesium sulphate for fetal neuroprotection in imminent preterm birth – Quick Reference

Woman between 24 and 29 +6 weeks gestation with imminent preterm birth.

Active labour with more than or equal to 4 cm cervical dilatation.

PPROM with active labour.

Planned delivery for maternal or fetal indications.

Administer Magnesium Sulphate 4 gram loading dose IV over 10 minutes

Follow with maintenance infusion 1 gram/hour IV or until birth or until 24 hours of therapy has been completed

Administer corticosteroids for fetal lung maturation if not already given

Aim to achieve 4 hours of magnesium sulphate therapy before delivery, but delivery should not be delayed for this purpose if there is maternal/fetal indications for emergency delivery

Monitoring of women on this therapy should be as per existing guidelines on magnesium sulphate for pre-eclampsia/eclampsia

Provide continuous fetal surveillance

Tocolysis should be discontinued before commencing magnesium sulphate for fetal neuroprotection

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