Aneurin Bevan University Health Board

Guideline for the use of antenatal Magnesium Sulphate prior to preterm Birth for neuroprotection of the fetus, infant and Child

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Contents:

1. Introduction

Cerebral palsy and link with preterm birth

Cerebral palsy and cognitive dysfunction are the most frequently occurring neurological impairments associated with preterm birth (before 37 weeks gestation), and any therapy that can reduce their prevalence would substantially reduce overall neurological impairments and disabilities among surviving preterm infants.[1]

Cerebral palsy is a term which includes a number of different diseases or conditions that can arise at any time during brain development. Cerebral palsy can involve a disorder of movement or posture, or both, and a disorder of motor function which is permanent but may change over time.[1] Approximately 42% of all cases of cerebral palsy are associated with preterm birth with the rate of cerebral palsy amongst neonatal survivors born at less than 28 weeks gestation up to 30 times higher compared with infants born at term.[1] The incidence of cerebral palsy decreases significantly with increasing gestational age: 14.6% at 22–27 weeks of gestation, 6.2% at 28–31weeks, 0.7% at 32–36 weeks and 0.1% in term infants.[4] Twenty-five percent of all cases of cerebral palsy are in infants born at less than 34 weeks of gestation.[5] At present there is no cure for cerebral palsy, which makes effective preventive interventions of paramount importance. Strategies to reduce cerebral palsy should be considered and implemented if shown to be effective in order to reduce the effects of this disabling condition on individuals, families, health care and society.

Preterm birth and neurological outcome

Babies born preterm have a higher chance of dying in their first few weeks of life. Preterm infants who survive have greater risk of neurological impairments, such as cerebral palsy, blindness, deafness, or cognitive dysfunction (either intellectual impairment or developmental delay), and a greater risk of substantial disability as a result of these neurological impairments (Doyle 2001; Saigal & Doyle 2008). Intraventricular haemorrhage (IVH) is a known risk factor for the later development of cerebral palsy (Kuban 1992). The risk of IVH and periventricular leukomalacia increases the earlier the gestational age at birth (Vermeulen 2001). The rate of preterm birth is increasing in many countries, with a corresponding increase in the number of babies at risk of death or an adverse neurological outcome.

Biological plausibility for use of magnesium sulphate for fetal and infant neuroprotection

In humans, magnesium is essential for health through key cellular processes, including glycolysis, oxidative phosphorylation, protein synthesis, DNA and RNA aggregation and maintenance of plasma membrane integrity (Mildvan 1987;McIntosh et al 1989). Animal studies have shown that magnesium sulphate

can provide a neuroprotective effect (McDonald 1990) preventing post-hypoxic brain injury by blocking the excess release of glutamate in calcium channels. The fetal and newborn brain seems more susceptible to damage from glutamate release. Consequently, blocking glutamate receptors through agents, such as magnesium sulphate, may reduce the risk of injury in the perinatal period (Espinoza 1991).

Possible role of magnesium sulphate for neuroprotection of the fetus, infant and child

In the late 1990s studies of infants born to mothers given magnesium sulphate to prevent eclamptic seizures or as tocolysis showed a reduction in rates of cystic periventricular leucomalacia (PVL) and cerebral palsy. In those babies born preterm and expsed to magnesium sulphate the odds ratio for cerebral palsy was 0.14 (95% CI 0.05–0.51). Five randomised controlled trials[4,5-9] three subsequent meta-analyses3,10,11 and a Cochrane review[12] followed. The updated Cochrane review concludes that antenatal magnesium sulphate therapy given to women at risk of preterm birth substantially reduced the risk of cerebral palsy in their child (risk ratio (RR) 0.68 95% confidence interval (CI) 0.54 to 0.87; five trials, 6145 infants). On the basis of these studies, the University of Adelaide issued, in March 2010, a guideline on best practice for clinical care in the use of antenatal magnesium sulphate prior to preterm birth for the neuroprotection of the fetus, infant and child, which has been largely adopted in this guideline.[1]

2. Objectives

To provide guidance on the administration of magnesium sulphate antenatally to women less than 30 weeks gestation where early preterm birth is planned or definitely expected within 24 hours, to reduce the risk of cerebral palsy following preterm birth.

3. Policy Scope

This guideline deals with the administration of magnesium sulphate antenatally to women less than 30 weeks gestation where early preterm birth is planned or definitely expected within 24 hours, and maternal monitoring during magnesium sulphate administration in this situation. For information with regards to management of prelabour rupture of membranes in pregnancy, preterm labour, use of antenatal corticosteroids and tocolysis, please see relevant related guidelines.

4. Definitions

The following definitions are for the purpose of this guideline only.

4.1 Early Preterm Labour

Painful contractions > 1 in 10 between 24 and 30 completed weeks gestation with or without cervical dilatation (but with +ve fibronectin)

4.2 Early Preterm Birth

Birth between 24-30 weeks gestation

5. Duties and Responsibilities

5.1 Midwives

Provide ongoing care to women on magnesium sulphate.
To work as part of the multi-disciplinary team to provide the highest quality of care and monitoring of the condition of woman and fetus.
Inform medical staff of any concerns/ changes in condition of woman/fetus.

To maintain accurate records woman's hospital notes.

To reassure woman and family.
To undertake investigations as instructed.
Inform neonatal unit

5.2 Obstetric Medical Staff

The junior medical staff should discuss the intervention either with the ST6-7 on call or consultant on call for delivery suiteThe decision of timing and administration of magnesium sulphate to prevent cerebral palsy in preterm births should be made by the consultant on call
It is the duty of the medical staff to provide full information about use of magnesium sulphate in the prevention of cerebral palsy in preterm births, its benefits, side effects and any long term implications on mother and baby

The patient's verbal consent should be taken

6. Guidance on Use of Magnesium Sulphate

6.1 Indications

Magnesium sulphate should be considered in women who are at risk of early preterm imminent birth[15](<30 weeks) is planned or definitely expected within 24 hours, regardless of the reason, parity, mode of delivery, number of fetuses or administration of antenatal corticosteroids.

6.2 Place of Administration

Magnesium sulphate must be administered on Delivery Suite with one to one midwifery care.
This does NOT need to be in HDU

6.3 Timing of Administration

In the case of planned delivery before 30 weeks gestation, the bolus should be given four hours prior to delivery and the maintenance infusion continued until birth
In spontaneous preterm labour, if delivery is expected within 24 hours (ie in established labour), commence magnesium sulphate and continue maintenance infusion until delivery or 24 hours, whichever is sooner
If birth before 30 weeks is expected to occur sooner than four hours (e.g. Category 2 or 3 caesarean section or late presentation to hospital with >4 cm dilatation), administer magnesium sulphate as there is still advantage likely from administration within this time
Where urgent delivery is necessary because of maternal or fetal compromise (e.g. severe fetal distress or antepartum haemorrhage) then birth should not be delayed to administer magnesium sulphate.
Magnesium sulphate infusions should not be used during antenatal transfer. If a clinical decision is made to transfer a woman who is receiving magnesium sulphate for neuroprotection, the maintenance infusion should be stopped during the transfer

6.4 Dosage and Administration

Loading dose;

Medical staff to administer a loading dose (bolus) of 4g should be given via the Asena Syringe Driver pump over 30 minutes

Take a 10ml ampoule of magnesium sulphate (50%) and draw off 8 mls which equates to 4grams of magnesium. Dilute in 12mls of sodium chloride 0.9% which equates to a 4grams in 20ml solution.

Administer via a syringe pump at 40mls per hour which will give the solution slowly over 30 mins.

Maintenance Dose:

Midwife to commence maintenance infusion immediately following loading dose of 1g/hr (10ml/hr) until delivery or for 24 hours, whichever is sooner

(Adding 50mls of magnesium sulphate(50%) to the 200mls of 0.9% sodium chloride will provide a 250mls solution. This will contain 25g magnesium sulphate in the 250ml solution equating to a 10% magnesium solution i.e. 1g in 10mls)

Administer through an Alaris pump at 10mls per hour therefore giving 1g of magnesium per hour.

6.5 Repeat doses

In the event that birth does not occur after giving magnesium sulphate for neuroprotection of the infant, and preterm birth (less than 30 weeks' gestation) again appears imminent (planned or definitely expected within 24 hours), a repeat dose of magnesium sulphate as described above may be considered at the discretion of the lead consultant or consultant on call in their absence.[1]

6.6 Maternal Monitoring

Magnesium toxicity is unlikely with the above regimens and magnesium levels do not need to be routinely measured (see section 6.8 for indications when levels should be monitored)

Loading dose:

Pulse, blood pressure, respiratory rate and patellar reflexes before loading dose, 10 minutes after loading dose infusion has started and at the end of the loading dose infusion (30 minutes)[1]
Observe for adverse effects (see Section 6.7)
Stop infusion and call for medical assessment if respiratory rate decreases more than 4 breaths per minute below baseline, or is less than 12 breaths

per minute; or diastolic blood pressure decreases more than 15 mm Hg below baseline level[1]

Maintenance infusion:

Observe for any adverse effects.
Pulse, blood pressure, respiratory rate, patellar reflexes and urine output **4-hourly[1]**
Stop infusion and call for medical assessment if respiratory rate is less than 12 breaths per minute; if patellar reflexes are absent, if hypotension occurs or if urine output is less than 100ml over 4 hours[1]
If on calcium channel blockers (eg nifedipine) or evidence of renal impairment, observations must be carried out hourly

6.7 Side Effects

Intravenous magnesium sulphate is associated with minor maternal side effects such as facial flushing, warmth, nausea and vomiting and headaches
Very rarely, hypotension, respiratory depression, muscle weakness and paralysis can occur (see Section 6.8)
When given in conjunction with calcium channel antagonists, cardiovascular and neuromuscular effects may be exaggerated.[1] Close monitoring is therefore required if used in conjunction with calcium channel blockers (eg nifedipine).
If hypotension occurs, nifedipine and magnesium sulphate administration should cease and urgent medical review requested.
There is no evidence of an effect on maternal death, cardiac respiratory arrest, pulmonary oedema, respiratory depression, severe postpartum haemorrhage or caesarean section rates.[3]
There is no association with adverse long-term fetal or maternal outcome.[1]

6.8 Toxicity

Magnesium toxicity is unlikely with the regimens recommended in these guidelines and serum magnesium concentrations do not need to be routinely measured (RCOG 2006)
If toxicity is suspected, urgent medical review is required
In women with renal compromise or on calcium channel blockers (eg nifedipine), where the risk of toxicity is increased, closer observation is required (see Section 6.6)
Calcium gluconate 1g (10 ml of 10% solution) slowly via intravenous route over 10 minutes is the antidote for magnesium toxicity

7 Review, Monitoring, and Revision Arrangements

All Trust policies / guidelines will be monitored for compliance in one of three ways:

Review is normally proactive and designed to evaluate the effectiveness of systems and processes;
Audit is a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria;
Continuous Audits are repeated audit cycles to ensure new controls can be identified and tested as they arise.

Where deficiencies have been identified through any of the above, there must be evidence that recommendations and action plans have been developed and changes implemented.

The frequency and detail of the monitoring process is described in the table below:

Monitoring	Method	Frequency	Lead	Action plan review by
The gestational age when magnesium sulphate was administered	Audit	Annual	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group
Clear lines of communication between the consultant obstetrician, paediatrician and delivery suite shift leader	Audit	Annual	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group

Monitoring during magnesium sulphate administration	Audit	Annual	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group
Neonatal outcome	Audit	Annual	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group
Delivery planning	Audit	Annual	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group
Actions resulting from deficiencies identified from any of the above	Audit	Quarterly	Audit Annual Clinical Lead for Delivery suite	Delivery suite Group

8 Associated Documents

Guidelines for the Management of Prelabour Rupture of Membranes (PROM) at Term

9. References

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14. Premature Labour,Tocolytic Drugs (RCOG Green-top guideline 1B)

Appendix 1 Flowchart for the use of Magnesium Sulphate in preterm labour up to 30 weeks