MAGNESIUM SULPHATE FOR NEUROPROTECTION IN PRETERM BIRTHS < 30 WEEKS OF GESTATION AT CHRISTCHURCH WOMEN'S HOSPITAL

DEFINITION

The prevalence of preterm birth is increasing[1] and while the survival of infants born preterm has improved[2], the prevalence of cerebral palsy has risen[3].

Magnesium sulphate given to women within a minimum of four hours before birth reduces the risk of cerebral palsy and protects gross motor function in those infants born preterm. The effect may be greatest at early gestations and is not associated with adverse long-term fetal or maternal outcome4.

The incidence of cerebral palsy decreases significantly with increasing gestational age:

14.6%	22 – 27 weeks
6.2%	28 – 31 weeks
0.7%	32 – 36 weeks
0.1%	Term infants

Twenty-five percent of all cases of cerebral palsy are in infants born at less than 34 weeks of gestation[6]. In children born preterm the proportion whose cerebral palsy is considered to have a perinatal origin (49%) is greater than those born at term (35%)[7,8]. Strategies to reduce cerebral palsy in these infants should be considered and implemented if shown to be effective in order to reduce the effects of this disabling condition on individuals, family/whanau, health care systems and society.

Studies in the late 1990s of mothers given magnesium sulphates showed a reduction in cerebral palsy rates[9]. Although the exact mechanism of magnesium sulphate as a neuroprotective is unknown, it contributes effectively to protecting the preterm neonatal brain.

Five randomised controlled trials[4,10,11,14] showed that magnesium sulphate administered to women prior to preterm birth can reduce the risk of cerebral palsy and death in newborn infants, 63 mothers need to be treated with antenatal magnesium sulphate for one baby to avoid cerebral palsy. Three subsequent meta-analyses,[6,15,16] and a Cochrane review[17] followed. 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[18]. This guideline was developed according to the requirements of the Australian National Health and Medical Research Council and the New Zealand Guideline Groups.

The authors concluded that in women at risk of early preterm imminent birth, magnesium sulphate should be used for neuroprotection of the fetus.[18]

BACKGROUND

GESTATION AT ADMINISTRATION

In the clinical practice guidelines by the University of Adelaide the panel conclude that magnesium sulphate should be considered in women at less than 30 weeks gestation[18]. In the discussion they argue that while benefit has been observed at more advanced gestations, the magnitude of effect is likely to be largest at earliest gestations and limitation of resources makes an upper limit of 30 weeks a pragmatic choice.

SIDE EFFECTS

Common

50% of women may experience some side effects during the therapy such as:

- Facial Flushing
- Flushing
- Nausea and vomiting
- Headaches
- Sweating
- Injection site issues[19]

More unusually

- Hypotension and tachycardia

Rarely

Women with neuro- muscular disorders may experience,

- Muscle weakness
- Paralysis

POTENTIAL INTERACTIONS

There is a potential theoretical interaction between magnesium sulphate and nifedipine of hypotension and neuromuscular blockade effects, although this is seldom reported in clinical practice. This does not preclude its use in this situation; refer to maternity guideline Preterm Labour GLM0027.

Regular monitoring of the mother is recommended as detailed in individual obstetric unit protocols. If hypotension occurs, nifedipine and magnesium sulphate administration should cease and the woman be reviewed by a medical practitioner.

MANAGEMENT

All necessary equipment is located in the 'Magnesium Sulphate for Neuroprotection Trolley'.

Cardiac monitoring is not required for the indication of neuroprotection for the preterm infant ALONE.

BLOOD PRESSURE

BP is measured:

- Prior to commencement of the protocol
- Ten minutes after the protocol has commenced
- Hourly thereafter, unless otherwise indicated

FLUID BALANCE

- Fluid balance must be maintained with monitoring and recording of input and output
- Urine output should be greater than 100 mLs over four hours
- If a woman cannot pass urine consider catheterisation. However a urinary catheter is seldom indicated

RESPIRATORY RATE

- Recorded hourly whilst on magnesium sulphate regime
- Must be greater than 12 breaths per minute
- If less than 12 breaths per minute an oxygen saturation monitor should be used and infusion STOPPED

DEEP TENDON REFLEXES

- Recorded hourly whilst on magnesium sulphate

MAGNESIUM TOXICITY

- This is unlikely with the above regime, therefore blood levels are not routinely required.
- Magnesium toxicity is identified clinically by loss of deep tendon reflexes followed by respiratory depression (< 12 breaths/min). Symptomatic hypertension
- If concerned stop magnesium sulphate
- If there are major concerns over respiratory depression, consider calcium gluconate 10% (1 g/10 mL). Give 10 mL over 10 minutes

CONTRAINDICATIONS

Cardiac disease or acute renal failure

Loading Dose 4 g Magnesium Sulphate over 20 minutes

PREMIXED (or reconstituted) 40 mmol magnesium sulphate in 128 mL (equals 10 g magnesium sulphate).

Run at 153 mL per hour for 20 minutes

Volume to be infused (VTBI) must be set at 51 mL.

Maintenance Dose 1 g Magnesium Sulphate per hour

PREMIXED (or reconstituted) 40 mmol magnesium sulphate in 128 mL (equals 10 g magnesium Sulphate

Run at 13 mL/hr

If premixed magnesium sulphate is NOT available

Add four 5 mL vials of 2.5 g magnesium sulphate (total ~ 10 g) to standard 100 mL bag normal saline.

This will give the same strength solution as the premixed bag. All 100 mL bags of normal saline actually contain an average of 108 mL so total solution is now 128 mL, the same volume as premixed bags.

DOCUMENTATION

The Modified Early Obstetric Warning Observation chart (MEOWS) Ref.6962 should be used for all measures and results. This should be reviewed at every handover.

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APPENDIX 1

Canterbury District Health Board
Te Poari Hauora o Waitaha

Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child

When to give magnesium sulphate?

☑ Gestational age < 30 weeks
☑ Birth planned or definitely expected within 24 hours

Give $MgSO_4$ regardless of:
☑ plurality ☑ reason at risk of preterm birth ☑ anticipated mode of birth
☑ parity ☑ whether antenatal corticosteroids have been given or not

What/When to administer?

Magnesium sulphate intravenously using a **dedicated** intravenous line:
☑ Commence magnesium sulphate as close to four hours before birth as possible
☑ Loading: 4g dose (slowly over 20-30 minutes)
☑ Maintenance: 1g/hour for up to 24 hours or until birth, whichever comes first

When urgent delivery/birth needed

☒ Do not delay delivery to administer magnesium sulphate

What if birth does not occur within 24 hours?

☑ Once 6 hours has transpired following the cessation of the 24 hour maintenance dose, a further loading and maintenance infusion may be considered

How to monitor women?

☑ Monitoring is essential for both loading and maintenance doses.
☑ Monitoring **pulse, blood pressure, oxygen saturation, respiratory rate** and **deep tendon reflexes**:
a) before loading infusion
b) 10 minutes after starting infusion
c) after loading infusion is complete
d) every 1 hour during the maintenance infusion
☑ Maintain fluid balance chart and inform medical staff if urine output < 100 mL in 4 hours
☑ Resuscitation and ventilator support should be available during and after administration of both magnesium sulphate and calcium gluconate

When to stop magnesium sulphate administration?

- Absent deep tendon reflexes
- Respiratory depression (< 12 breaths/min)
- Symptomatic hypotension

→ **If magnesium toxicity occurs:** STOP magnesium sulphate infusion and administer antidote of calcium gluconate 10% (1 g/10 mL). 10 mL of 10% solution slowly intravenously over approximately 10 minutes.

Potential interactions between magnesium sulphate and nifedipine may result in hypotension and neuromuscular blockade effects. If such interactions are evident, cease nifedipine and magnesium sulphate infusion and seek medical review.

Refer: http://www.adelaide.edu.au/arch/research/translational_health/wish/A4_Implementation_Poster.pdf

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