Guideline

Magnesium Sulphate - Neuroprotection of Preterm Infants

1. Purpose

Cerebral palsy is a term which includes a number of different diseases or condition that can arise any time during brain development. Approximately 45% of all cases of cerebral palsy are associated with preterm birth (Australian Cerebral Palsy Register Report December 2009) 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.

Theoretically magnesium sulphate (MgSO4) might be neuroprotective due to effects on cellular metabolism, cell death or injury or blood flow to the brain. The first case control study was published fifteen years ago and the evidence has been growing ever since (Nelson et al, 1995). The current Cochrane review concludes that antenatal MgSO4 given to women at risk of preterm birth substantially reduces the risk of cerebral palsy in their child (RR 0.68 95% confidence interval 0.54 to 0.87; five trials, 6145 infants). This Cochrane review contains five trials: Mittendorf et al, 2002; The Magpie Trial 2002; Crowther et al, 2003; Marret et al, 2007; Rouse et al, 2008. Two meta-analysis were published recently (Costantine et al; Doyle et al). National Clinical Practice Guidelines were released in March 2010.

This clinical guideline outlines the requirement for the use of Magnesium Sulphate to a woman at risk of preterm birth to prevent cerebral palsy in their child at the Women's.

2. Definitions

Not applicable.

3. Responsibilities

Staff caring for a woman at risk of preterm birth should be aware about this guideline.

4. Guideline

4.1 Recommendations for use

The use of MgSO4 is recommended for neuroprotection of the fetus/infant/child:

- when women are at risk of imminent preterm birth before 30 weeks gestation
- when preterm birth before 30 weeks gestation is planned or definitely expected within 24 hours.

The use of MgSO4 is recommended:

- regardless of the number of babies in utero
- regardless of the anticipated mode of birth
- whether or not antenatal corticosteroids have been given.

4.2 Dose

When birth is planned commence $MgSO_4$ as close to four hours before birth as possible.

Note: Ensure magnesium sulphate is administered concurrently via a Y-site with a compatible IV fluid.

Loading dose: using a 10ml vial of $MgSO_4$ prepare 4gram (i.e. 8ml) of magnesium sulphate 50% in a 10mL syringe, configure pump to accept the 10mL syringe and set the pump to 32mL an hour for 15 minutes.

Maintenance: once the loading dose has been completed, using the 50mL vial of magnesium sulphate, magnesium sulphate 50% in a 50mL syringe, re-set the pump to accept 50mL syringe and set the pump to administer the maintenance rate of 1g/hr (2mL/hour) or as ordered.

Continue the regime until birth or 24 hours, whichever comes first.

Urgent delivery: In situations where urgent delivery is necessary because of actual or imminent maternal or fetal compromise then delivery should not be delayed to administer $MgSO_4$.

Repeat doses: In the event that birth does not occur after giving $MgSO_4$ 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 $MgSO_4$ may be considered.

4.3 Monitoring

Magnesium level monitoring

Measurement of magnesium levels will facilitate management where there are signs of toxicity or in the presence of renal impairment.

Serum magnesium concentrations should be checked every 6 hours in the antepartum and intrapartum phase (therapeutic level of magnesium: 1.7 to 3.5 mmol/L).

Magnesium is excreted by the kidneys and regular monitoring of serum levels should be conducted in women with oliguria (urine output <100mL over 4 hours) or urea >10mmol/L and those with renal impairment.

Mg conc (mmol/L)	Effects
0.8 - 1.0	Normal plasma level
1.7 - 3.5	Therapeutic range
2.5 - 5.0	ECG changes (P-Q interval prolongation, widen QRS complex)
4.0 – 5.0	Reduction in deep tendon reflexes
> 5.0	Loss of deep tendon reflexes
> 7.5	Sinoatrial and atrioventricular blockade. Respiratory paralysis and CNS depression
> 12	Cardiac arrest

Note: If serum magnesium level is >3.5mmol/L, cease infusion and consult with obstetrician.

Clinical observations

During administration of the loading or bolus dose:

- 5 minutely blood pressure and pulse (x 4 readings)
- observe for the development of side effects
- check patellar reflexes after administration.

During administration of the maintenance infusion:

- ½ hourly blood pressure, pulse, and respiratory rate (pre-treatment respiratory rate should be ≥ 16per minute). These may be undertaken hourly post-birth.
- 1 hourly patellar reflexes
- 1 hourly urine measures, 4 hourly testing of urinary protein
- 2 hourly temperature
- continuous electronic fetal monitoring from 26 weeks gestation until clinical review/discussion by medical staff. Between 24- 26 weeks gestation, individualised management with regard to fetal monitoring will be considered
- maintain strict fluid balance chart.

Record patellar reflexes as:

- A = Absent

- N = Normal
- B = Brisk.

Request magnesium level and review management if:

- respiratory rate < 12 breaths/minute
- urine output < 100mLs in 4 hours
- loss of patellar reflexes
- further seizures occur.

Response to magnesium toxicity:

The following clinical signs of magnesium toxicity must be reviewed by a consultant obstetrician/anaesthetist:

- urine output <100mL in 4 hours
- absent patellar reflexes
- respiratory depression.

The antidote for magnesium toxicity is: 10mL calcium gluconate available as 2.2 mmol calcium in 10mL vial (formerly known as 10% solution) over 10 minutes by slow intravenous injection. The patient requires ECG monitoring during and after administration because of the potential for cardiac arrhythmias.

Resuscitation and ventilator support should be available during and after dose administration of both magnesium sulphate and calcium gluconate.

CEASE Magnesium infusion in the following emergencies:

- respiratory arrest: call: Code Blue - Adult and Child (intranet)
- cardiac arrest: call: Code Blue - Adult and Child (intranet).

4.4 Potential interactions

There is a potential theoretical interaction between $MgSO_4$ and nifedipine resulting in hypotension and neuromuscular blockade effects. This is seldom reported in clinical practice (Snyder & Cardwell, 1989; Ben-Ami et al, 1994). If hypotension occurs, nifedipine and $MgSO_4$ administration should be ceased.

5. Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be monitored by review of incidents reported through VHIMS.

6. References

See Evidence Table over the page.

Magnesium Sulphate - Neuroprotection of Preterm Infants

Evidence Table

Author/s	Title	Source	Level of Evidence	Comments
Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J et al.	Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial.	Lancet 2002;359:1877-1890.	II	RCT n =10, 141
The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel	Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child. National Clinical Practice Guidelines.	The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. March 2010.		Review and summary
Ben-Ami M, Giladi Y, Shalev E.	The combination of magnesium sulphate and nifedipine: a cause of neuromuscular blockade.	BJOG 1994;101:262-263.	IV	Case report
Constantine MM, Weiner SJ.	Effects of antenatal exposure to magnesium sulphate on neuroprotection and mortality in preterm infants.	Obstet Gynecol 2009;114:354-364.	I	Meta-analysis (5 RCT)
Crowther CA, Hiller JE, Doyle LW, Haslam RR for the Australasian Collaborative Trial of Magnesium sulphate (ACTO $MgSO_4$) Collaborative Group.	Effect of magnesium sulphate given for neuroprotection before preterm birth a randomised controlled trial.	JAMA 2003;290:2669-2676.	II	RCT n =1,064
Doyle LW, Crowther CA, Middleton P, Marret S.	Antenatal magnesium sulphate and neurologic outcome in preterm infants.	Obste Gynecol 2009;113:1327-1333.	I	Meta-analysis (5 RCT)
Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D.	Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus.	Cochrane Database of Systematic Reviews 2009, Issue 1.	I	Cochrane review (5 RCT)
Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Leveque Hellot MF for PREMAG trial group.	Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial.	BJOG 2007;114:310-318.	II	RCT n = 573
Mercer BM & Merlino AA.	Magnesium sulphate for preterm labor and preterm birth.	Obstet Gynecol 2009;114:650-667.		Review - commentary

Author/s	Title	Source	Level of Evidence	Comments
Mittendorf R, Dambrosia J, Pryde PG, Lee KS, Gianopoulos JG, Besinger RE et al.	Association between the use of antenatal magnesium sulphate in preterm labor and adverse health outcomes in infants.	Am J Obstet Gynecol 2002;186:1111-1118.	II	RCT n =149
Nelson KB, Grether JK.	Can magnesium sulphate reduce the risk of cerebral palsy in very low birthweight infants?	Pediatrics 1995;95:263-269.	III-2	Case control n =117
Rouse DJ, Hirtz DG, Thom E, Varner MW, Alexander J, Spong CY, Mercer BM et al.	Magnesium sulfate for the prevention of cerebral palsy.	N Engl J Med 2008;359:895-905.	III	RCT n = 2,241
Snyder SW, Cardwell MS.	Neuromuscular blockade with magnesium sulphate and nifedipine.	Am J Obstet Gynecol 1989;161:35-36.	IV	Case report

7. Legislation/Regulations related to this guideline

Not applicable.

8. Appendices

Not applicable.