Magnesium Sulfate for Pre-eclampsia and for Neuroprotection in Pre-term Births

Unique Identifier	NMP200/SSM/085 - v05.00
Document Type	Clinical Guideline
Risk of non-compliance	may result in significant harm to the patient/DHB
Function	Clinical Practice, Patient Care
User Group(s)	Auckland DHB only
• Organisation(s)	Auckland District Health Board
• Directorate(s)	Women's Health
• Department(s)	Maternity
• Used for which patients?	All women in maternity
• Used by which staff?	All clinicians in maternity including access holder Lead Maternity Carers (LMC)
• Excluded	
Keywords	Magnesium sulfate ($MgSO_4$), preterm labour, cerebral palsy, prematurity, pre-eclampsia, hypertension
Author	MFM Consultant - Women's Health
Authorisation	
• Owner	Service Clinical Director - Secondary Maternity Services
• Delegate / Issuer	Service Clinical Director - Secondary Maternity Services
Edited by	Document Control
First issued	March 2012
This version issued	22 December 2020 - updated
Review frequency	3 yearly

Contents

Back to Contents

1. Purpose of guideline

This guideline establishes the use of magnesium sulfate for women accessing maternity services within Auckland District Health Board (Auckland DHB). Magnesium sulfate is of proven benefit for the prevention and treatment of eclampsia at any gestation and for neuroprotection in infants born < 30 weeks gestation. This guideline covers the indications for its use and a protocol for its administration. For women with severe pre-eclampsia/eclampsia, this guideline should be used alongside the Women's Health Clinical guideline Hypertension - Antenatal, Intrapartum and Postpartum Management (see Associated documents).

2. Guideline management principles and goals

2.1 Eclamptic fit (antenatal, intrapartum or postnatal)

Magnesium sulfate is of proven benefit in the management of eclampsia, reducing the risk of recurrent seizures when compared to other anticonvulsants (Duley, 2010a, b). It is the anticonvulsant of choice and should be administered as soon as possible once venous access is obtained (or by intramuscular injection if venous access is not possible). It should not be delayed awaiting transfer to higher level care unit (external transfers, or internal within Auckland City Hospital (ACH) to the Maternity Complex Care Unit (MCCU) – Level 9).

2.2 Severe pre-eclampsia/imminent eclampsia (antenatal, intrapartum or postnatal)

Magnesium sulfate has also been shown to reduce the risk of eclamptic convulsions in women with severe pre-eclampsia (Altman, 2002) more than halving the risk of seizure (risk ratio 0.41, 95% CI 0.29 to 0.58; 6 trials, 11 444 women) (Duley, 2010c). Prophylactic therapy during and after birth should be considered in women with severe pre-eclampsia, especially if neurological symptoms or signs are present. The decision to give magnesium for women with severe pre-eclampsia should be made on an individual basis and involve discussion with the on call obstetric senior medical officer (SMO) or maternal fetal medicine (MFM)/obstetric physician.

2.3 Imminent preterm delivery < 30 weeks gestation

Over 120 children are diagnosed with cerebral palsy each year in New Zealand and approximately 45% of all cases of cerebral palsy are related to preterm birth. The most recent Cochrane review (Doyle, 2009) concludes that antenatal magnesium sulfate therapy given to women at risk of preterm birth substantially reduced the risk of cerebral palsy in their child (risk ratio 0.68, 95%CI 0.54-0.87; 5 trials, 6145 infants). Australian and New Zealand National Clinical Practice Guidelines were published in March 2010 (The Antenatal Magnesium Sulfate for Neuroprotection Guideline Development Panel, 2010). These guidelines are supported by senior medical staff members at National Women's Health and recommend consideration of the antenatal use of magnesium sulfate in women at risk of imminent* preterm birth < 30 weeks regardless of plurality (number of babies in utero), parity, reason for early delivery, anticipated mode of delivery and whether or not antenatal corticosteroids have been used. The decision to give magnesium for women at risk of imminent* preterm birth should be made on an individual basis and involve discussion with the on call obstetric SMO or MFM SMO.

*** Imminent delivery is defined** as when early delivery is planned or definitely expected within 24 hours (if birth is planned commence magnesium sulfate as close to four hours before birth as possible). Do not delay starting magnesium sulfate in eligible women who may deliver within a few hours - the sooner the better and there is benefit even if a full four hours is not given.
If urgent delivery is necessary because of actual or imminent maternal or fetal compromise (e.g. severe fetal distress or antepartum haemorrhage), birth should NOT be delayed to administer magnesium sulfate.

3. Indications for magnesium sulfate in obstetrics

Eclamptic fit (antenatal, intrapartum or postnatal); severe pre-eclampsia/imminent eclampsia (antenatal, intrapartum or postnatal)

Signs and/or symptoms of imminent fitting:

- Visual or auditory aura
- Severe headache
- Restlessness and confusion
- Hyper reflexia with clonus

Signs and/or symptoms of severe pre-eclampsia:

- Persistent severe hypertension (systolic blood pressure ≥ 160 or, diastolic blood pressure ≥ 110)
- Oliguria less than 80 mL/4 hours
- Progressive renal insufficiency (serum creatinine > 90 µmol/L or doubling of serum creatinine concentration in the absence of other renal disease, urine output of 80mL/4hrs)
- Pulmonary oedema
- Impaired liver dysfunction not responding to treatment and not accounted for by alternative diagnosis – elevated liver transaminases (AST and ALT_ - at least twice the upper limit of normal +/- right upper quadrant or epigastric abdominal pain (may be referred to upper back).
- Thrombocytopenia < 100 or falling platelets, DIC)
- HELLP syndrome: A variant of severe pre-eclampsia (elements include Haemolysis, Elevated Liver enzymes and Low Platelet count). In a woman with pre-eclampsia, the presence of any of the following is an indicator of HELLP:
  - Maternal platelet count of less than 100x 10^9/L
  - Elevated transaminases (elevated blood concentrations of liver enzymes to twice normal concentration)
  - Microangiopathic haemolytic anaemia with red cell fragments on blood film
  - Eclampsia

Imminent preterm delivery < 30 weeks gestation

This includes planned delivery due to maternal or fetal compromise (when delay will not further compromise mother or fetus) e.g. fetal growth restriction, pre-eclampsia, severe maternal cardiac or respiratory disease. Imminent delivery also includes women in progressive preterm labour i.e. advanced cervical dilatation (> 3cm), NOT simply threatened preterm labour with a positive fetal fibronectin or PPROM with no contractions or cervical dilatation.

Back to Contents

4. Counselling and patient information

Women's Health is using the information provided by the WISH Project (see Supporting evidence) which is looking at ways to improve uptake of magnesium sulfate in eligible women. Practitioners should be aware that counselling about neonatal prognosis in an emergency situation is often difficult.

5. Precautions with magnesium sulfate

Special precautions must be taken with the following conditions:

- Myasthenia Gravis or other neuromuscular disorder
- Cardiac disease - arrhythmia or cardiomyopathy
- Current drug therapy such as aminoglycoside (Gentamicin)
- Paralysing anaesthetic agents
- Renal impairment (with urine output < 30 mL/hr and/or creatinine > 80 µmol/L) or renal failure. In these patients, toxicity is a major risk. Give loading dose as usual. Maintenance dose should be discussed with obstetric physician on call, who may recommend reducing the infusion rate to 0.5 g/hr (SOMANZ, 2018). In these cases magnesium levels should be taken four hours after starting infusion, to monitor for toxicity. An alternative anticonvulsant (e.g. phenytoin) may be more appropriate.

6. Administration of magnesium sulfate

6.1 Intravenous (IV) magnesium sulfate

Presentation: 50 mL premixed bag 5 of magnesium sulfate 5 g

Administer: 4 g of magnesium sulfate by intravenous infusion via an Alaris pump over 20 minutes:

Loading dose

1. Use the first bag to run through the alaris pump giving set & insert cassette into pump.
2. Choose 'Magnesium **LOAD**' from the Women's Health Guardrails profile.
3. Concentration is still 5 g/50 mL.
4. Set Volume to be infused to **40 mL** and then **STOP.**
5. Set Rate to **120 mL/hr**. This will deliver a 4 g loading dose over 20 minutes.
6. Connect to woman and press 'start'.

Maintenance dose

1. Change the nearly empty 5 g/50 mL magnesium sulfate bag for a new one (no need to change the giving set).
2. Choose 'Magnesium **MAINT**' from the Women's Health Guardrails profile.

3. Concentration will read **25 g/250 mL** (to be updated in the future but is the same as the 5 g/50 mL bags).
4. Set Volume to be infused to **50 mL** and then **STOP.**
5. Set Rate to **1 g/hr**. This will run at 10 mL/hr.
6. Press 'start'.

You will need to change the magnesium bag every 5 hours.

Severe pre-eclampsia/eclampsia:
Continue for at least 24 - 48 hours after delivery (stopping maintenance infusion should be discussed with on call obstetric SMO or MFM SMO).

Neuroprotection:
Continue until delivery or 24 hours (whichever is sooner). Timing of administration should aim to be as close as possible to total duration of use of four hours. On going infusion is NOT required post-natally when administered for neuroprotection only.
If after 24 hours, delivery does not appear likely within the next six hours then the infusion should be stopped.

6.2 Intramuscular (IM) magnesium sulfate

If intravenous (IV) access is not available, treatment may be started with an intramuscular injection.

Note: For settings where infusion pumps are also not available, this is a useful way to administer prior to transferring to a higher-level unit. In this context, ideally the 4 g loading dose should be given intravenously followed by intramuscular maintenance dosage

A total dose of 10 g can be given. Onset of effect is slower and administration can be painful.

Loading dose
Administer 5 g (2 ampoules) of magnesium sulfate (2.47 g/5 mL) intramuscularly, unless a loading dose has been given intravenously.

Maintenance dose
Administer 5 g (2 ampoules) of magnesium sulfate (2.47 g/5 mL) intramuscularly every four hours in alternating buttocks (starting from the time of the loading dose) until IV administration is possible.

6.3 Magnesium sulfate for recurrent seizures

Further seizures should be discussed with the on call obstetric SMO/MFM SMO/obstetric physician and anaesthetist/Critical Care SMOs as appropriate (see associated documents for Hypertension - Antenatal, Intrapartum and Postpartum Management for indications for transfer to critical care).

- A further 2 g bolus of magnesium sulfate should be given intravenous infusion via an Alaris pump over 20 minutes, using the 5 g/50mL premixed bags of magnesium sulfate:

1. Choose 'Magnesium **LOAD**' from the Women's Health Guardrails profile.
2. Concentration is still 5 g/50 mL.
3. Set Volume to be infused to 2**0 mL** and then **STOP.**
4. Set Rate to **120 mL/hr**. This will deliver a 2 g loading dose over 10 minutes.
5. Connect to woman and press 'start'.

- Once the additional bolus of 2 g has been given, return to the previous magnesium maintenance infusion regime.
- Consideration could be given to increasing the infusion level to 1.5 – 2 g/hour with appropriate monitoring for toxicity including magnesium levels, after discussion with the on call obstetric SMO/MFM SMO/obstetric physician.

7. Observation and management whilst on magnesium sulfate

Magnesium sulfate is excreted by the kidneys and is a smooth muscle relaxant. With normal renal function, the recommended loading and maintenance doses should not cause toxicity and so routine serum magnesium levels are not required. However, close maternal observation is necessary.

7.1 Observations and management required

- Take a set of baseline recordings; blood pressure (BP), Maternal pulse, respiration, temperature, current reflexes (so you can denote changes)
- Instigate a cardiotocography (CTG) if not already commenced
- Blood pressure every 5 minutes during loading dose, hourly thereafter
- Fluid restriction 80-85 mL/hour for severe pre-eclampsia
- Urine output >100 mL over four hours
- Fluid Balance – hourly
- Reflexes (patella or bicep) – hourly (if you are unable to do this you should enlist a practitioner who can)
- Respiratory rate/SpO_2 – hourly [respiratory rate should be above 12 breaths per minute]
- Continuous CTG.

Infusion can be continued at standard rate provided that:

- Reflexes (patella or bicep) are present
- Urine output remains > 100 mL/4hrs
- Respiratory rate does not fall below 12 per minute.

Note: in cases of severe pre-eclampsia additional observations and management are required (see Hypertension - Antenatal, Intrapartum and Postpartum Management guidelines in Associated documents).

Continuous electronic fetal monitoring is strongly recommended during magnesium infusion. Interpretation of the cardiotocography (CTG) should take into account the reduced variability that may be seen with magnesium infusions.

Hourly formal assessment through use of the prescribed CTG sticker in the clinical notes should be employed. If the woman is labouring two hourly 'fresh eyes' with another competent practitioner is recommended.

7.2 Place of administration

The administration of magnesium sulfate, particularly in the case of eclampsia or imminent eclampsia, should not be delayed awaiting transfer to a high dependency unit (HDU) or maternity complex care unit setting. The loading dose should be given as soon as possible.

Ongoing management of women with severe pre-eclampsia receiving magnesium sulfate for seizure prevention/treatment should be in the Maternity Complex Care Area (MCCA) on level 9, ACH.

In cases of planned administration of magnesium sulfate for neuroprotection of the infant < 30 weeks gestation, this should be performed in a setting where appropriate monitoring can occur. In women with severe pre-eclampsia, this should be level 9 Maternity Complex Care Area (MCCA) as above. For all other women where administration is for neuroprotection of the infant < 30 weeks gestation only, this should ideally be in the delivery suite with one-to-one midwifery care (this includes women receiving magnesium sulfate prior to a pre labour caesarean section).
If a non-Auckland DHB midwife wishes to continue labour care for a woman on magnesium sulfate for neuroprotection, this should be discussed with the clinical charge midwife of Labour and Birthing. Continuity of midwifery care is recommended wherever possible.

7.3 Documentation

- Record the indication in the clinical record
- Use the National Medication chart to prescribe
- Use a fluid balance chart or if in MCCA use the appropriate fluid balance chart
- Always record observations on the Maternity Early Warning Score (MEWS)
- The CTG will need hourly review in the clinical notes along with blood results and any other relevant clinical observations.

8. Magnesium sulfate levels

Magnesium levels do not require to be measured routinely. If measured (Lu, 2000):

Therapeutic levels	1.8 – 3.0 mmol/
Loss of tendon reflexes	3.5 – 5.0 mmol/
Respiratory paralysis	5.0 – 6.5 mmol/
Cardiac arrest	> 12.5 mmol/

Back to Contents

Indications for measuring magnesium levels include:

- Altered renal function (urine output < 25 mL/hour, creatinine > 90); take levels 4 hours after starting infusion
- Signs of toxicity such as drowsiness, loss of deep tendon reflexes, respiratory depression RR < 12 breaths/min
- Unexplained clinical symptoms or signs
- Further seizures.

9. Magnesium antidote

If loss of deep tendon reflexes and/or respiratory depression is observed:

- STOP magnesium infusion
- Call obstetric and anaesthetic registrar
- Send blood for urgent magnesium levels
- After receiving medical instruction: Administer 1 g of calcium gluconate intravenously
- (10 mL of calcium gluconate 10% solution) over 5 - 10 minutes. Rate should not exceed 2mL/min of undiluted solution.

10. Repeat doses of magnesium sulfate

For the vast majority of women receiving magnesium sulfate for the management of severe pre-eclampsia/eclampsia delivery should be planned within 24 hours of commencing the infusion. Continue magnesium sulfate for 24 hours following birth or 24 hours after the last seizure, whichever is later.

Stopping maintenance infusion should be discussed with the on call obstetric SMO or MFM SMO. For women receiving magnesium sulfate for neuroprotection of the infant, in the event that birth does not occur and preterm birth at < 30 weeks gestation again appears imminent (planned or definitely expected within 24 hours), a repeat dose of magnesium sulfate (loading and maintenance) may be considered but must be discussed with the on call obstetric SMO or MFM SMO.

11. Supporting evidence

- Group, T. M. T. C. (2002). Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *The Lancet, 359*(9321), 1877-1890.
- Crowther, C. A., Middleton, P. F., Bain, E., Ashwood, P., Bubner, T., Flenady, V., ... & McIntyre, S. (2013). Working to improve survival and health for babies born very preterm: the WISH project protocol. *BMC pregnancy and childbirth, 13*(1), 239.
- Doyle, L. W., Crowther, C. A., Middleton, P., Marret, S., & Rouse, D. (2009). Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database of Systematic Reviews, (1)*.

- Duley, L., Henderson-Smart, D. J., & Chou, D. (2010). Magnesium sulphate versus phenytoin for eclampsia. *Cochrane Database of Systematic Reviews*, (10).
- Duley, L., Henderson-Smart, D. J., Walker, G. J., & Chou, D. (2010). Magnesium sulphate versus diazepam for eclampsia. *Cochrane Database of Systematic Reviews*, (12). (b)
- Duley, L., Gülmezoglu, A. M., Henderson-Smart, D. J., & Chou, D. (2010). Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. *Cochrane database of systematic reviews*, (11).
- Lu, J. F., & Nightingale, C. H. (2000). Magnesium sulfate in eclampsia and pre-eclampsia. *Clinical pharmacokinetics, 38*(4), 305-314.
- Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. (2010). *Antenatal Magnesium Sulphate Prior to Preterm Birth for Neuroprotection of the Fetus, Infant, and Child 2010: National Clinical Practice Guidelines*. Australian Research Centre for Health of Women and Babies, the University of Adelaide.
- The Society of Obstetric Medicine of Australian and New Zealand. Guideline for the management of hypertensive disorders if pregnancy 2014. Accessed 28 December 2018. Available at https://www.somanz.org/documents/HTPregnancyGuidelineJuly2014.pdf
- New Zealand Formulary (NZF). Magnesium sulfate, NZF v79 Jan 2019. Available from: www.nzf.org.nz (Accessed December 2018)

12. Associated documents

- Magnesium Guardrail Loading Dose
- Magnesium Guardrail Maintenance Dose
- Hypertension - Antenatal, Intrapartum and Postpartum Management
- Medications - Administration
- Medications – Prescribing
- Preterm Labour (PTL) – Management of Threatened and Active PTL
- Rupture of Membranes in Pregnancy

13. Disclaimer

No guideline can cover all variations required for specific circumstances. It is the responsibility of the health care practitioners using this Auckland DHB guideline to adapt it for safe use within their own institution, recognise the need for specialist help, and call for it without delay, when an individual patient falls outside of the boundaries of this guideline.

14. Corrections and amendments

The next scheduled review of this document is as per the document classification table (page 1). However, if the reader notices any errors or believes that the document should be reviewed ***before*** the scheduled date, they should contact the owner or Document Control without delay.