

Magnesium Sulphate for Neuroprotection of the Fetus in Women at Risk of Preterm Birth

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Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:

The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.



Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

This guideline provides information on the use of magnesium sulphate for neuroprotection of the fetus in women at risk of preterm birth. It includes medication information, clinical care during magnesium sulphate infusion and infusion regimens.

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Summary of Practice Recommendations

Calcium gluconate should be available where magnesium sulphate is used.

Neuroprotection should be considered for the fetus of women at risk of preterm birth who are between 24⁺⁰ and 30⁺⁰ weeks of gestation.

When early preterm birth is definitely expected or planned within 24 hours, commence magnesium sulphate as close to four hours before expected delivery time.

In situations where urgent birth is necessary because of maternal or fetal compromise, the birth should not be delayed to administer magnesium sulphate.

Nifedipine increases the effects of magnesium sulphate and risk of hypotension.

Magnesium sulphate is best administered intravenously.

Use dedicated intravenous line is to be used for magnesium sulphate.

Continuous fetal monitoring during the infusion is recommended from 26⁺⁰ weeks gestation.

If signs of toxicity occur (hypoventilation, arrhythmia, hypotonia), cease infusion, initiate treatment and call for medical assistance.

Abbreviations

et al.	And others
ECG	Electrocardiogram
g	Gram(s)
IV	Intravenous
<	Less than
L	Litre(s)
mmol/L	Millimoles per litre
mL	Millilitre(s)
%	Percentage
SpO ₂	Pulse Oximetry Oxygen Saturation
URL	Uniform resource locator

Definitions

Cerebral Palsy	Abnormality of tone with motor dysfunction
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Magnesium Sulphate for Neuroprotection of the Fetus in Women at Risk of Preterm Birth

Literature review

A Cochrane systematic review has confirmed that fetal exposure to magnesium sulphate given before preterm birth has a neuroprotective role.¹

- The number of women needed to treat to avoid cerebral palsy in one baby is 63¹
- This review also showed a significant reduction in the rate of gross motor dysfunction in early childhood¹
- Cerebral palsy and cognitive dysfunction are the most frequent neurological impairments in preterm babies (< 37⁺⁰ weeks of gestation). Very preterm birth (< 34⁺⁰ weeks) and very low birthweight (< 1,500 g) are the principal risk factors for cerebral palsy¹

Multiple pregnancy accounts for over 10% of preterm births and has a higher incidence of cerebral palsy than singleton pregnancy (twins have 7 times and triplets 47 times the risk of cerebral palsy compared with singletons).²

Obstetric contributors to cerebral palsy include chorioamnionitis, antepartum haemorrhage, multiple pregnancy, placental insufficiency and less commonly perinatal asphyxia³

Magnesium sulphate

The exact mechanism of action for magnesium sulphate is unknown; however, it is thought that magnesium may reduce vascular instability, prevent hypoxic damage, and mitigate cytokine or excitatory amino acid damage, all of which threaten the vulnerable preterm brain.⁴

Magnesium sulphate readily crosses the placenta and is readily antagonised by IV calcium gluconate in the event of magnesium toxicity (calcium gluconate should be available where magnesium sulphate is used).

Indications

Neuroprotection should be considered for the fetus of women at risk of preterm birth who are between 24⁺⁰ and 30⁺⁰ weeks of gestation.

When early preterm birth is definitely expected within 24 hours or planned (e.g. caesarean section), commence magnesium sulphate as close to four hours before expected delivery time as possible) and regardless of:

- plurality or parity
- reason for the risks of preterm birth
- anticipated mode of birth
- whether antenatal corticosteroids have been given or not

Relative contraindications

- Hypersensitivity to magnesium

Note: In situations where urgent birth is necessary because of maternal or fetal compromise, the birth should not be delayed to administer magnesium sulphate

Drug interactions

Nifedipine increases the effects of magnesium sulphate and risk of hypotension; use cautiously, consider reducing magnesium sulphate dosage; monitor blood pressure, deep tendon reflexes and respiratory function.⁵

Adverse effects

Common adverse effects include:

- Feeling of warmth
- Flushing
- Nausea and vomiting.

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More serious adverse effects which indicate hypermagnesaemia are:

- Loss of deep tendon reflexes
- Respiratory depression or arrest
- Cardiac arrest

Other adverse effects may include:

- Thirst
- Muscle weakness
- Headache
- Dizziness
- Hypotension
- Bradycardia

Levels of magnesium sulphate at which adverse effects occur ⁸	
Symptoms	MgSO ₄ levels (mmol/L)
Feeling of warmth, flushing, double vision, slurred speech	3.8 to 5.0
Loss of tendon reflexes	Greater than 5.0
Respiratory depression	Greater than 6.0
Respiratory arrest	6.3 to 7.0
Cardiac arrest	Greater than 12.0

Dosage and administration

- Magnesium sulphate is best administered intravenously
- In Australia, each ampoule of magnesium sulphate contains a 50% solution (i.e. either 2.5 g in each 5 mL or 5 g in each 10 mL)
- The product guidelines recommend that magnesium sulphate for intravenous use should be diluted with sodium chloride 0.9% to a concentration of 20% magnesium or less, which implies that further dilution is necessary
- Intravenous administration of magnesium sulphate may be via a syringe driver or a volumetric infusion pump, [see appendices for infusion regimens](#)
- If birth has not occurred after 24 hours or is not considered imminent, discontinue magnesium sulphate infusion and resume when in active preterm labour.
 - If at least 6 hours has transpired, recommence with another loading dose, followed by the maintenance dose
- In situations where an infusion pump is not available, an intravenous bolus dose of magnesium sulphate 20 % in combination with intramuscular magnesium sulphate 50 % may be preferable for treating women in actual preterm labour before transferring to a tertiary Centre, [see appendices for Intramuscular dose \(suitable for retrieval and transfer\)](#)

Administration precautions

- Administration of the magnesium may cause pain and phlebitis.
- **Use dedicated intravenous line is to be used for magnesium sulphate.**
- The dedicated magnesium line should be labelled clearly.
- **Never inject other drugs into the dedicated magnesium line.**



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Care during intravenous infusion

- Collect baseline observations (maternal pulse, blood pressure, respiratory rate, SpO₂ and [deep tendon] patellar reflexes)
- Ensure the woman is aware that a feeling of warm flushing may occur during the loading dose
- Recheck observations including patellar reflexes ten minutes after the loading dose was started and at the end of the loading dose (20 minutes)
- Continuous fetal monitoring from 26⁺⁰ weeks gestation until clinical review / discussion by medical staff. Between 24 to 26 weeks gestation, individualised management with regard to fetal monitoring will be considered

Maintenance

- Monitor blood pressure, respiratory rate, pulse oximeter (SpO₂), patellar reflexes and urine output 4 hourly (insert urine catheter).
 - If the urine output is less than 100 mL over 4 hours check magnesium levels and consider reducing magnesium sulphate infusion to 0.5 g / hour.
- Patellar reflexes should be documented as one of the following:
 - A = Absent
 - N = Normal
 - B = Brisk

NB: Patellar reflexes are always suppressed before respiratory depression occurs

- Monitoring magnesium levels is usually not necessary.
 - Where serum creatinine is > 100 mmol / L or urine output is < 100 mL over 4 hours, check serum magnesium levels and adjust infusion levels. In these circumstances check serum magnesium levels every 6 hours after commencing infusion.
 - Blood for magnesium estimation must NOT be taken from the arm receiving the infusion.
 - Levels will vary according to serum albumin concentrations

Symptoms of overdose

Stop the infusion and seek medical review if:

- patellar reflexes are absent
- the respiratory rate is less than 12 per minute
- the diastolic BP drops more than 15 mm Hg below baseline
- the urine output drops below 100 mL in 4 hours

Magnesium sulphate toxicity

If signs of toxicity occur (hypoventilation, arrhythmia, hypotonia):

- Call for medical assistance
- Administer oxygen at 8-12 litres
- Stop infusion
- Monitor vital signs
- Administer calcium gluconate (10 % solution), 10 mL, slowly intravenously
- Commence electrocardiogram (ECG) to identify heart block
- Check electrolytes, creatinine, magnesium sulphate levels



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Neonatal considerations

For the neonate, hypermagnesaemia can lead to hyporeflexia, poor sucking and rarely, respiratory depression needing mechanical ventilation.



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Appendices

Appendix 1: Magnesium sulphate syringe driver infusion regimen

Magnesium sulphate syringe driver infusion regimen	
<ul style="list-style-type: none"> The total adult daily dose should not exceed 30 to 40 g of magnesium sulphate The undiluted syringe driver infusion may be connected into a mainline of sodium chloride 0.9 % or Hartmann's 1,000 mL; however, no other drugs may be administered into this line No more than 8 g of magnesium sulphate should be administered over 1 hour Continue for up to 24 hours or until birth, whichever comes first 	
Magnesium sulphate undiluted 50 %	
<p>Loading dose set up</p> <ul style="list-style-type: none"> Draw up 5 g (10 mL) magnesium sulphate Discard 2 mL magnesium sulphate to give 4 g in 8 mL Using medication added label write "magnesium sulphate 4 g in 8 mL" and attach label to syringe 	<p>Maintenance dose set up</p> <ul style="list-style-type: none"> NB: To avoid mixing up the syringes, do not draw up the maintenance dose until after the loading dose has been commenced Draw up 10 g (20 mL) magnesium sulphate Using medication added label write "magnesium sulphate 10 g in 20 mL" and attach label to syringe
<p>Loading dose administration</p> <p>Set syringe driver at 24 mL / hour to infuse 4 g (8 mL) over 20 minutes</p>	<p>Maintenance administration</p> <p>Set syringe driver at 2 mL / hour to infuse a maintenance dose of 1 g / hour</p>
<p>Ensure calcium gluconate is available if needed.</p>	



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Appendix 2: Magnesium sulphate volumetric infusion pump regimen

Magnesium sulphate syringe driver infusion regimen	
<p>A volumetric infusion pump should only be utilised for the administration of magnesium sulphate where there is no access to a syringe driver.</p> <ul style="list-style-type: none"> • The total adult daily dose should not exceed 30 to 40 g of magnesium sulphate • No more than 8 g of magnesium sulphate should be administered over 1 hour • Continue for up to 24 hours or until birth, whichever comes first 	
Magnesium sulphate diluted	
<p style="text-align: center;">Loading dose set up</p> <ul style="list-style-type: none"> • Draw up 5 g (10 mL) magnesium sulphate • Discard 2 mL magnesium sulphate to give 4 g in 8 mL • Withdraw 8 mL from a 100 mL bag of sodium chloride 0.9 % and discard • Add the 8 mL magnesium sulphate (4 g) to the remaining 92 mL bag of sodium chloride 0.9 % to make 100 mL • Using medication added label write “magnesium sulphate 4 g (8 mL) in sodium chloride 0.9 % to a total volume of 100 mL” and attach label to bag 	<p style="text-align: center;">Maintenance dose set up</p> <ul style="list-style-type: none"> • NB: To avoid mixing up the infusion bags, do not draw up the maintenance dose until after the loading dose infusion has been commenced • Draw up 20 g (40 mL) magnesium sulphate • Withdraw 40 mL from a 100 mL bag of sodium chloride 0.9 % and discard • Add the 40 mL magnesium sulphate (20 g) to the remaining 60 mL bag of sodium chloride 0.9 % to make 100 mL • Using medication added label write “magnesium sulphate 20 g (40 mL) in sodium chloride 0.9 % to a total volume of 100 mL” and attach label to bag
<p style="text-align: center;">Loading dose infusion</p> <p>4 g (set at 300 mL / hour) over 20 minutes. Set volume to be infused at 100 mL.</p>	<p style="text-align: center;">Maintenance infusion</p> <p>Set volumetric infusion pump to 1 g / hour (5 mL / hour)</p>
Ensure calcium gluconate is available if needed	



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Appendix 3: Intramuscular dose (suitable for retrieval and transfer)

In situations where an infusion pump is not available, an intravenous bolus dose of magnesium sulphate 20 % in combination with intramuscular magnesium sulphate 50 % may be preferable for treating women in actual preterm labour before transferring to a tertiary centre

The preferred regimen in such circumstances is:

- Magnesium sulphate 20 % solution, 4 g by slow intravenous injection over a period of 5 minutes, followed by
- Two deep intramuscular injections of 4 to 5 g magnesium sulphate 50 % solution into each buttock (the total dose of up to 10 g injected into one site is highly irritating)
- If no infusion pumps are available, maintenance treatment is 5 g magnesium sulphate 50 %, given by deep intramuscular injection, every 4 hours. Alternate the buttocks in which the injection is administered⁷
- A maintenance infusion (see above) can be commenced at any time after the initial bolus dose.



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Acknowledgements

The South Australian Perinatal Practice Guidelines gratefully acknowledge the contribution of clinicians and other stakeholders who participated throughout the guideline development process particularly:

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Document Ownership & History

Developed by:	SA Maternal, Neonatal & Gynaecology Community of Practice
Contact:	HealthCYWHSPerinatalProtocol@sa.gov.au
Endorsed by:	SA Health Safety and Quality Strategic Governance Committee
Next review due:	19/04/2021
ISBN number:	978-1-74243-295-3
PDS reference:	CG237
Policy history:	Is this a new policy (V1)? N Does this policy amend or update an existing policy? Y If so, which version? 4.0 Does this policy replace another policy with a different title? N If so, which policy (title)?

Approval Date	Version	Who approved New/Revised Version	Reason for Change
14/05/20	V4.1	Chair, SA Maternal, Neonatal & Gynaecology Community of Practice	Re-templated, risk-assessed and extended for 2 years.
19/04/16	V4	SA Health Safety and Quality Strategic Governance Committee	Reviewed.
19/06/12	V3	SA Maternal and Neonatal Clinical Network	Reviewed
17/01/12	V2	SA Maternal and Neonatal Clinical Network	Reviewed
21/08/10	V1	SA Maternal and Neonatal Clinical Network	Original version

