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

Implementing the guidelines
What this presentation covers

- Background
- Scope of guidelines
- Definitions
- Recommendations for use, dose, monitoring, potential interactions
- Implementation outcomes & significance
- WISH Project – implementation & audit

Babies born very early
- high risk of dying in their first few weeks of life
- if they survive, may have damage to their brain, manifesting as cerebral palsy, blindness, deafness or cognitive dysfunction

In Australia
- over 600 children are diagnosed with cerebral palsy each year
- about 40% of all cases are associated with preterm birth
- the rate of cerebral palsy amongst neonatal survivors born at less than 28 weeks’ gestation is up to 30 times higher compared with infants born at term
- the cost of cerebral palsy is AUD$3.87 billion per annum
Background

- Updated Cochrane review ‘Magnesium sulphate for women at risk of preterm birth for the neuroprotection of the fetus’

- 5 RCTs

- 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 1 baby to avoid cerebral palsy

- number needed to treat to prevent combined death and cerebral palsy is 42
Magnesium plays a role in essential cellular processes\textsuperscript{7}

Magnesium has been found in animal studies to have a neuroprotective effect\textsuperscript{8,9}

$\text{MgSO}_4$ may reduce post-hypoxic brain injury in the perinatal period by blocking excess release of glutamate\textsuperscript{10}
Scope of guidelines

- The NHMRC approved guidelines provide evidence-based guidance on the best practice for the use of magnesium sulphate prior to preterm birth for neuroprotection.

- These guidelines are relevant for:
  - health professionals who care for women at risk of preterm birth and their babies
  - pregnant women and their partners and families
  - policy makers in maternity care
# Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Presentation</th>
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<tbody>
<tr>
<td>Early preterm birth</td>
<td>When gestational age is less than 30 weeks</td>
</tr>
<tr>
<td>Imminent birth</td>
<td>When early preterm birth is planned or definitely expected within 24 hours</td>
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Who to give MgSO\textsubscript{4} to and when?

Indications for magnesium sulphate therapy

- Neuroprotection of the fetus for women at risk of imminent early preterm birth before 30 weeks’ gestation

- When birth is anticipated within 24 hours or in cases of expected planned delivery as close to four hours before expected delivery time and regardless of:
  - plurality
  - reason why the woman is at risk of preterm birth
  - parity
  - anticipated mode of birth
  - whether antenatal corticosteroids have been given or not
What to give?

Dosage for magnesium sulphate therapy

When birth is planned, commence MgSO₄ as close to four hours before birth as possible

- Intravenously with a 4 gram loading dose (slowly over 20-30 minutes) and 1 gram per hour maintenance dose via IV route, with no immediate repeat doses

- Continue regimen until birth or for 24 hours, whichever comes first

***Urgent delivery/birth:*** In situations where urgent delivery is necessary because of actual or imminent maternal or fetal compromise then delivery should not be delayed to administer MgSO₄
If birth does not occur ≤ 24 hours?

- If birth does not occur after giving MgSO₄ for neuroprotection of the infant, and preterm birth (less than 30 weeks’ gestation) again appears imminent (planned or definitely expected with 24 hours), a repeat dose of MgSO₄ may be considered at the discretion of the attending health professional.
**Monitoring**

Monitor as per your individual obstetric unit protocols. The clinical practice guidelines suggest:

<table>
<thead>
<tr>
<th>Administration Phase</th>
<th>Clinical Observation</th>
<th>Notes</th>
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<tbody>
<tr>
<td><strong>LOADING</strong></td>
<td></td>
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<tr>
<td>• Before infusion</td>
<td>• Pulse</td>
<td>Stop infusion if:</td>
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<td></td>
<td>• Blood Pressure</td>
<td>• respiratory rate decreases more than 4 breaths per minute below baseline or is less than 12 breaths per minute</td>
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<tr>
<td></td>
<td>• Respiratory Rate</td>
<td>• patellar reflexes are absent</td>
</tr>
<tr>
<td></td>
<td>• Patellar Reflexes</td>
<td>• diastolic blood pressure decreases more than 15 mm Hg below baseline level.</td>
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<tr>
<td>• 10 minutes after beginning infusion</td>
<td>• Pulse</td>
<td></td>
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<tr>
<td></td>
<td>• Blood Pressure</td>
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<td></td>
<td>• Respiratory Rate</td>
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<td></td>
<td>• Patellar Reflexes</td>
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<tr>
<td>• At conclusion of loading infusion</td>
<td>• Urine Output</td>
<td></td>
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<td></td>
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<tr>
<td><strong>MAINTENANCE</strong></td>
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<tr>
<td>• During maintenance infusion</td>
<td>• Pulse</td>
<td>Stop infusion if:</td>
</tr>
<tr>
<td>• 4 hourly thereafter</td>
<td>• Blood Pressure</td>
<td>• respiratory rate is less than 12 breaths per minute</td>
</tr>
<tr>
<td></td>
<td>• Respiratory Rate</td>
<td>• patellar reflexes are absent</td>
</tr>
<tr>
<td></td>
<td>• Patellar Reflexes</td>
<td>• hypotension occurs</td>
</tr>
<tr>
<td></td>
<td>• Urine Output</td>
<td>• urine output is less than 100 mL over 4 hours.</td>
</tr>
</tbody>
</table>
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 1g of calcium gluconate (10mL of 10% solution over 10 minutes) by slow intravenous injection

***Resuscitation and ventilator support should be available during and after administration of both magnesium sulphate and calcium gluconate***
Potential interactions with MgSO$_4$

- 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$^{11,12}$

- If hypotension occurs, nifedipine and MgSO$_4$ administration should be ceased and the woman reviewed by a medical practitioner.
Active guideline implementation strategies will lead to a significant increase in the appropriate use of antenatal magnesium sulphate for mothers prior to early preterm birth.

Successful adoption of this research into clinical practice in Australia is estimated to lead to 40 per 1000 fewer babies who are born early, dying or suffering the long term consequences of cerebral palsy.
Information for health professionals

- 3 fold information sheet for health professionals
- For all clinicians involved in the care of women at risk of very preterm birth
Information for women

- 3 fold information sheet for women
- For women at risk of very preterm birth at < 30 weeks gestation

Antenatal magnesium sulphate therapy for improving the health of preterm babies

*Information for Women*
Magnesium sulphate (MgSO₄) implementation poster

Antenatal magnesium sulphate (MgSO₄) prior to preterm birth for neuroprotection of the fetus, infant and child

When to give MgSO₄?

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

Give MgSO₄ regardless of:
- Plurality
- Parity
- Reason at risk of preterm birth
- Anticipated mode of birth
- Whether antenatal corticosteroids have been given or not

What/When to administer?
MgSO₄ intravenously using a dedicated intravenous line:
- Commence MgSO₄ 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 MgSO₄

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.
- Monitor pulse, blood pressure, respiratory rate and patellar reflexes: (a) before loading infusion (b) 10 mins after starting infusion (c) after loading infusion is complete (d) every 4 hours during the maintenance infusion.
- Resuscitation and ventilator support should be available during and after administration of both magnesium sulphate and calcium gluconate.

When to stop MgSO₄ administration?
- Urine output <100ml in 4 hours • Absent patellar reflexes • Respiratory depression (< 12 breaths/min) • Hypotension (diastolic BP < 15 mm Hg below baseline).
- If Magnesium toxicity occurs: Stop MgSO₄ infusion and administer antidote of calcium gluconate (10mL of 10% solution slowly intravenously over approx. 10 minutes).

Potential interactions between MgSO₄ and nifedipine may result in hypotension and neuromuscular blockade effects. If such interactions are evident, cease nifedipine and MgSO₄ infusion and seek medical review.
Is this woman eligible for magnesium sulphate for neuroprotection of her fetus?

- < 30 weeks’ gestation
- Birth planned or definitely expected within the next 24 hours
- Regardless of
  - Plurality
  - Parity
  - Reason for preterm birth
  - Anticipated mode of birth
  - Whether antenatal corticosteroids have been given or not

Please see the poster overleaf “Antenatal magnesium sulphate (MgSO₄) prior to preterm birth for neuroprotection of the fetus, infant and child” for a quick reference on magnesium sulphate dosage, timing, monitoring and potential interactions.
WISH Project

Implementation and Audit Project

- Implementation of the “MgSO₄ for Neuroprotection Clinical Practice Guidelines” to increase uptake

AIMS

- To optimise the care of women at risk of early preterm birth, improving the chance of survival and long term good health for their preterm babies
- Specifically, to nationally monitor and improve uptake of the antenatal MgSO₄ for neuroprotection guidelines
- Explore the barriers and enablers to implementation of the guidelines

- To reduce the risk of the baby dying or having cerebral palsy

Website:
More information

- For the complete National Clinical Practice Guidelines, visit:
  - www.adelaide.edu.au/arch

- For implementation advice, email:
  - wish@adelaide.edu.au


