Magnesium sulphate for neuroprotection of the fetus in women at risk of preterm birth

Literature review

- A recent Cochrane systematic review has confirmed that fetal exposure to magnesium sulphate given before preterm birth has a neuroprotective role (Doyle et al. 2009)
- The number of women needed to treat to avoid cerebral palsy in one baby is 63 (Doyle et al. 2009)
- This review also showed a significant reduction in the rate of gross motor dysfunction in early childhood (Doyle et al. 2009)
- Cerebral palsy (abnormality of tone with motor dysfunction) 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 (< 1500 g) are the principal risk factors for cerebral palsy (Doyle et al. 2009)
- 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) (Petterson et al. 1993)
- Obstetric contributors to cerebral palsy include chorioamnionitis, APH, multiple pregnancy, placental insufficiency and less commonly perinatal asphyxia (Walker 2010)

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 (Rouse et al. 2008)
- Magnesium sulphate readily crosses the placenta
- Magnesium 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 of the fetus for women at risk of preterm birth who are at least 24^{+0} weeks of gestation 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
    - why the women is at risk of preterm birth
    - parity
    - anticipated mode of birth
    - whether antenatal corticosteroids have been given or not

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Relative contraindications

- Hypersensitivity to magnesium
- **In situations where urgent delivery 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 (AMH 2004)

Dosage and administration

- Magnesium sulphate is best administered intravenously
- In some countries a pre-diluted magnesium sulphate 20 % solution is available
- 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
- 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

Administration precautions

- Administration may cause pain and phlebitis. Use a dedicated intravenous line for magnesium sulphate
- Never inject other drugs into this line

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Magnesium sulphate syringe driver infusion regimen

- 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 %

Loading dose set up	Maintenance dose set up
> 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	> **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
Loading dose administration	**Maintenance administration**
> Set syringe driver at 24 mL / hour to infuse 4 g (8 mL) over 20 minutes	> Set syringe driver at 2 mL / hour to infuse a maintenance dose of 1 g / hour

Ensure calcium gluconate is available

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Magnesium sulphate for neuroprotection of the fetus in women at risk of preterm birth

Magnesium sulphate volumetric infusion pump regimen

- **A volumetric infusion pump should only be utilised for the administration of magnesium sulphate where there is no access to a syringe driver**
- 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

Loading dose set up

- 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

Maintenance dose set up

- **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

Loading dose infusion

- 4 g (set at 300 mL / hour) over 20 minutes. Set volume to be infused at 100 mL

Maintenance infusion

- Set volumetric infusion pump to 1 g / hour (5 mL / hour)

Ensure calcium gluconate is available if needed

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Care during intravenous infusion

- Collect baseline observations (pulse, BP, RR, SpO_2 and patellar reflexes)
- Ensure the woman is aware that a feeling of warm flushing may be evident during the infusion. Other side effects may include nausea, vomiting and headache
- 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 (SpO_2), patellar reflexes and urine output 4 hourly
- Patellar reflexes should be documented as one of the following:
  - A = Absent
  - N = Normal
  - B = Brisk
- Stop the infusion 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
  - or the urine output drops below 100 mL in 4 hours
- 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 the infusion
  - Blood for magnesium estimation must NOT be taken from the arm receiving the infusion.
  - The therapeutic level is 1.7 - 3.5 mmol / L (4 – 8 mg / 100 mL).
  - Levels will vary according to serum albumin concentrations
- If signs of toxicity occur (e.g. hypoventilation, arrhythmia, hypotonia):
  - Call for medical assistance
  - Administer oxygen at 8-12 litres
  - Stop the infusion
  - Monitor vital signs
  - Administer calcium gluconate (10 % solution), 10 mL, slowly intravenously
  - Check electrolytes, creatinine, magnesium sulphate levels

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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 administered (Duley et al. 2003)
    - A maintenance infusion (see above) can be commenced at any time after the initial bolus dose

Neonatal considerations

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

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Abbreviations

APH	Antepartum haemorrhage
BP	Blood pressure
et al.	And others
g	Gram(s)
IV	Intravenous
<	Less than
L	Litre(s)
mmol/L	Millimoles per litre
mL	Millilitre(s)
%	Percentage
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RR	Respiratory rate
SpO2	Pulse Oximetry Oxygen Saturation
URL	Uniform resource locator

Version control and change history

PDS reference: OCE use only

Version	Date from	Date to	Amendment
1.0	21 Sept 10	17 Jan 12	Original version
2.0	17 Jan 12	19 June 12	Review
3.0	19 June 12	current	

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