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PReCePT Guideline

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1. Introduction

Babies born prematurely are at an increased risk of dying in the first few weeks of life, and those who survive may suffer from varying degrees of cerebral palsy (CP), blindness, deafness or physical disabilities.

Meta-analyses of RCTs looking at the role of $MgSO_4$ for neuroprotection conclude that antenatal magnesium sulphate reduces cerebral palsy and motor deficits in preterm infants, irrespective of the reasons for preterm birth.

The risk of cerebral palsy is related to the degree of prematurity decreasing significantly with increasing gestational age:

- 14.6% at 22-27 weeks of gestation,
- 6.2% at 28-31 weeks,
- 0.7% at 32-36 weeks and
- 0.1% in term infants.

The number of women needed to treat with $MgSO_4$ at <30 weeks' gestation to prevent one child from having cerebral palsy is 37.

NICE guidelines recommend giving magnesium sulphate at less than 30 weeks gestation, with consideration being given to use up to 33+6 weeks gestation.

Unlike antenatal steroid administration which is ideally given at least 24 hours prior to delivery, magnesium sulphate confers some neuroprotective benefit if given as close as 20 minutes prior to delivery. Treatment is most effective when commenced 4 hours prior to delivery but benefits have been shown at less than 4 hours. **Delivery should not be delayed to allow magnesium sulphate to be administered.**

Mode of action – magnesium sulphate works almost immediately by rapidly crossing the placenta and entering the fetal brain within minutes. The magnesium ions block glutamate receptors on the surface of the brain preventing the uptake of calcium ions into the brain thus preventing cell death.

The loading dose of magnesium sulphate quickly raises the concentration of magnesium ions needed to block these receptors. The maintenance dose then keeps this level constant for up to 24 hours. The levels of magnesium in the blood return to normal rapidly once the infusion is stopped. This explains why it is able to act quickly and why it may need to be repeated if delivery does not occur but is anticipated at a later time – each admission should be assessed individually to evaluate whether magnesium sulphate should be considered.

2. Purpose

This guideline is to provide evidence-based information and to promote and ensure good quality maternity care for all women in preterm labour across the Northern England Maternity Clinical Network.

This guideline is aimed at all healthcare staff caring for women and their babies in preterm labour and delivery.

The aim is that all eligible women are offered magnesium sulphate antenatally for neuroprotection, that women and families receive accurate information, staff are fully informed about the treatment and that treatment is accurately recorded and transferred into the neonatal care pathway.

3. Diagnosis of preterm labour

The accurate diagnosis of preterm labour is key to determining eligibility of mothers and ensuring appropriate risk assessment and timing for treatment.

This guideline should be read in conjunction with individual Trusts own guidelines for the diagnosis and management of preterm labour, including the regional standards for when to consider intrauterine transfer. All mothers across the region should receive standardised care, information and the opportunity to access magnesium sulphate regardless of where they labour and deliver.

4. Indications for use

4.1. Under 30 weeks gestation

Magnesium sulphate should be offered to all women less than 30 gestation and at risk of early preterm birth, except when there is a Category 1 indication for urgent delivery (birth should not be delayed to administer $MgSO_4$).

4.2. 30-33+6 weeks gestation

Magnesium sulphate should be considered for women from 30+0 to 33+6 weeks gestation. Treatment is still of benefit but the number needed to treat to prevent a case of CP is higher. Treatment in this group should be considered on an individual case basis and discussed with a Consultant Obstetrician. If any woman in this group herself requests magnesium sulphate, this should be administered unless there are any contraindications present.

Magnesium sulphate should be considered regardless of:

- Singleton or multiple pregnancy
- Reason for expected preterm birth
- Expected mode of delivery
- Antenatal steroid administration
- Bleeding
- Intact membranes or not
- Infection
- Tocolytic use

5. Contraindications

There are very few contraindications to magnesium sulphate:

- Myasthenia gravis (this is the only contraindication to magnesium sulphate given in the NICE guidance)*
- Hypersensitivity to magnesium sulphate
- Acute renal failure
- Hepatic coma with risk of renal failure
- Heart block

Caution should be used in patients with renal impairment – urine output should be closely monitored in all women receiving magnesium sulphate.

Steroids, tocolysis and antibiotics should all be considered and administered as per local guidance.

* Caution should be taken if used with nifedipine as the hypotensive effects can be potentiated – consideration should be given to slower administration of the loading dose as this is less likely to result in maternal side effects.

Any concerns regarding suitability of maternal condition including haemorrhage & sepsis – decision to give $MgSO_4$ should be discussed with Consultant

6. Administration

It would be anticipated that these patients would already be in a one-to-one care setting on a labour ward due to their preterm labour diagnosis, however, due to the risk of respiratory depression and hypotension leading to maternal and fetal compromise, magnesium sulphate should be administered where there is access to appropriate staff and resources for adequate maternal and fetal monitoring, on delivery suite or in theatre.

Administration is by the same regime as for pre-eclamptic patients but these patients receiving magnesium sulphate for neuroprotection without underlying pre-eclampsia do not require fluid restriction as per pre-eclampsia guidelines.

Administer 4g IV loading dose – NICE and RCOG guidance is to administer this over 15 minutes, the national PReCePT team suggest to give over 20 minutes –- if a patient is unwell (for example in cases of sepsis), or receiving nifedipine therapy – consideration should be given to slower administration of the loading dose as this is less likely to result in maternal side effects. The loading dose should be given via a syringe driver to increase safety and reduce task time for clinicians.

Commence maintenance dose of 1g per hour (10ml of 10%/hour).

Continue until birth or for a maximum of 24 hours.

A repeat dose of magnesium sulphate (including loading dose) may be considered if the patient still meets the criteria – this should be following discussion with the Consultant Obstetrician.

If undergoing intrauterine transfer:

- Give loading dose prior to transfer if time
- Commence and continue maintenance dose until ambulance arrives
- Stop maintenance dose during transfer
- Reassess on arrival at tertiary unit and recommence maintenance dose if still indicated.
- Ensure complete handover of information given to receiving unit (*complete proforma)

7. Monitoring and side effects

Maternal observations (including oxygen saturations) and patellar reflexes should be documented on a MEOWS chart prior to administration.

The patient should be closely observed for adverse reactions.

When used for seizure prophylaxis for PET/eclampsia then it would be prudent to check renal function. Women with no renal impairment undergoing magnesium therapy should have their urine output monitored but there is no need for routine checking of U&Es, or magnesium serum levels.

7.1. Loading dose

Continuous ECG should be performed

7.2. Maintenance dose

Observations (excluding temperature) should be documented hourly

Urine output should be measured 4 hourly (catheterisation is not required if good urine output)

*normally fit and healthy patients on magnesium sulphate for neuroprotection and not pre-eclampsia do not require an indwelling catheter or hourly urine output monitoring - magnesium sulphate is excreted by the kidneys. Patients with a normal urine output are unlikely to exceed therapeutic levels, but in oligouric or anuric patients there is a real danger.

7.3. Stop the infusion and get prompt review (call obstetrician, anaesthetist and senior midwife) if

- Respiratory rate decreases by more than 4 breaths/minute, or is less than 12
- Hypotension/diastolic BP drops by more than 15mmHg below baseline level
- Patellar reflexes are absent (remember to check elbow reflexes in patients with epidural anaesthesia)
- Urine output is less than 100ml in 4 hours
- Oxygen saturations fall below 90% (start oxygen therapy)

7.4. Side effects

7.4.1. Maternal

Serious side effects are very rare and include hypotension, respiratory depression and tachycardia

Less serious side effects include:

- Flushing
- Sweating
- Nausea and vomiting
- Pain at infusion site
- Headaches

7.4.2. Fetal

Serious side effects are very rare but babies with hypermagnesemia can experience hypotonia and apnoea.

7.4.3. Magnesium toxicity

Magnesium toxicity is unlikely with this regime and serum magnesium concentrations do not need to be routinely measured in women with normal renal function.

In women with renal compromise, serum magnesium monitoring is recommended.

- If this toxicity is suspected, stop the magnesium sulphate infusion
- With magnesium overdose, vital functions are lost in the following sequence:
  - Loss of tendon reflexes
  - Somnolence
  - Respiratory depression
  - Paralysis
  - Cardiac arrest

Symptoms	Mg level (mmol/L)
Therapeutic range	2-4
Loss of tendon reflexes, weakness, feeling of warmth, flushing, drowsiness, double vision, slurred speech	5
Muscle paralysis, respiratory arrest	6-7.5
Cardiac arrest	>12

- Loss of patellar reflex
  - stop magnesium infusion
  - if possible, check magnesium level
  - withhold further magnesium until reflexes return or Mg levels known
- oxygen saturations persistently <92%
  - commence oxygen therapy
  - inform anaesthetist
  - check patellar reflexes
    - if present exclude other causes (opiates, pulmonary oedema)
    - if absent see above
  - In case of overdose warranting immediate reversal (discuss with Consultant/Senior registrar) – the antidote is 10ml calcium gluconate 10% (1g) IV over 3 minutes
  - If cardiac arrest – 2222 and follow Trust protocol

Fetal monitoring

Fetal monitoring should be performed as per Trusts guidelines

8. Repeat doses

In the event that birth does not occur, if preterm delivery is again anticipated, the process for giving repeated doses of magnesium sulphate should be repeated including loading dose again.

Magnesium has a short half life and is renally excreted therefore levels rapidly return to normal once maintenance infusion has been stopped. There is no clear guidance about length of time to leave between repeating doses – Crowther et al noted this as an area where further research is needed. Each case should be considered individually with Consultant Obstetrician guidance – as long as the fetus remains at risk of brain injury due to prematurity, magnesium sulphate could be considered for neuroprotection.

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Flow chart for consideration of magnesium sulphate for neuroprotection in preterm infants

Eligible case identified – all deliveries anticipated within 24 hours (confirmed preterm labour or planned elective delivery) of babies 22+6 – 30+0 weeks gestation, consider for babies up to 33+6 weeks, give if requested by patient up to 33+6 unless contraindicated

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Discuss with Consultant Obstetrician

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Include in care planning for preterm delivery including discussions with families, give patient information leaflet, discuss expected side effects with patients – magnesium sulphate can be given/prepared whilst other preparations for delivery are on-going such as arranging for tertiary transfer, consider alternative to nifedipine if tocolysis is required

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Perform baseline maternal observations to include P, BP, respiratory rate, oxygen saturations, patellar reflexes, fetal monitoring as per unit guidelines, commence ECG

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Loading dose – 4g IV to be given over 15-20 minutes via syringe driver – consider slower administration if maternal condition requires or used with nifedipine – continuous ECG should be performed during loading dose

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Maintenance dose – 1g IV to be given per hour via syringe driver – continue until delivery or for up to 24 hours – stop maintenance dose for ambulance transfer – recommence on arrival at tertiary unit if still indicated

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Hourly observations to be recorded during maintenance infusion including reflexes, 4 hourly urine output

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Stop magnesium sulphate following delivery or after 24 hours

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Ensure that neonatal transfer documentation includes administration of magnesium sulphate and that badgernet is completed correctly

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Audit any cases where eligible babies did not receive magnesium sulphate for neuroprotection

Supporting information

1. Use of fetal fibronectin – units should follow their own guidance for the diagnosis of preterm labour – for maternity units without a NICU facility, if intrauterine transfer is being planned then it would be anticipated that magnesium sulphate would be considered. Decision to give magnesium sulphate should not be made on the basis of fetal fibronectin result.

2. Bleeding - we would not usually use tocolysis in the event of an abruption or significant APH as we would not wish to delay delivery, & there is a risk that if we relax the uterus (in the event of an abruption) this can lead to increased bleeding. If bleeding is due to other causes – eg. Placenta previa, reducing uterine activity may reduce blood loss. We would normally only be planning preterm delivery before 30 weeks in the presence of an acute bleed if there has been significant bleeding or an acute abruption with maternal or fetal compromise in which case we should not be delaying delivery to administer magnesium sulphate. There may be benefit to giving the loading dose in these cases but not the maintenance dose as delivery may be indicated by class 1 or 2 (within 30-75 minutes). There is no absolute contraindication to giving magnesium sulphate in the presence of vaginal bleeding but senior obstetric input should be recommended.

3. Sepsis - birth should not be delayed in urgent circumstances to allow for administration of magnesium sulphate, however, where birth is indicated such as sepsis – concerns about the tocolytic effects of magnesium sulphate should not prevent its administration – in these cases where the decision has been made to allow labour and delivery to progress (eg. Sepsis, fetal concerns – not requiring immediate class 1 delivery), it is of even more importance to protect these vulnerable brains, and therefore any tocolytic effect. If a patient is unwell consideration should be given to slower administration of the loading dose as this is more likely to result in maternal side effects. The NICE guideline does not suggest exclusions for sepsis.

4. Pulmonary oedema – we rarely see pulmonary oedema except as a complication of PET, magnesium sulphate is recommended for seizure prevention for women with severe PET therefore it is not contraindicated. Magnesium sulphate is used as a treatment for severe asthma and respiratory deterioration, while in magnesium toxicity there can be respiratory depression – the guidelines and recommendations for monitoring and administration should follow those in its use for severe PET – for example, if a patient is severely oligouric then reduce infusion rate and monitor magnesium levels.

References

NICE guideline (NG25) Preterm labour and birth; November 2017 www.nice.org.uk/guidance.ng25

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:239
http://www.biomedcentral.com/1471-2393/13/239

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Intrauterine transfer letter SBAR

Dear Dr

Thank you for accepting this transfer.

Patient ID

Gestation

Steroids given (dates/times)

Magnesium sulphate given:

Loading dose

Maintenance dose

Last scan report – weight, doppler, concerns (placental location etc)

Reason for transfer

Parental concerns/wishes/understanding

Safeguarding concerns

Yours sincerely,

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