





in Greater Manchester

Greater Manchester and Eastern Cheshire Strategic Clinical Networks

Greater Manchester and Eastern Cheshire SCN

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 MgSO4 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 MgSO4 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 15 minutes prior to delivery. Delivery should not be delayed to allow magnesium sulphate to be administered, however if delivery is anticipated MgS02 and Steroids should be given.

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 can act quickly and why it may need to be repeated if delivery does not occur but is anticipated later – each admission should be assessed individually to evaluate whether magnesium sulphate should be considered.

The woman needs to have the intravenous magnesium sulphate between 20 minutes and four hours before delivery as magnesium sulphate reaches the foetus within minutes, but the level of magnesium sulphate decreases sharply after four hours.

Maternal adverse events increase with higher total dose of magnesium sulphate. The decision when to start to administer magnesium sulphate to women in established labour, whether induced or not, needs to balance the need to cover the period immediately before delivery whilst minimising adverse events.

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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 Greater Manchester and East Cheshire (GMEC) 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 GMEC Guideline: 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 when delivery is anticipated within 24 hours (birth should not be delayed administering MgSO4).

4.2 30-33+6 weeks gestation

Magnesium sulphate should be offered 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.

Magnesium sulphate should be offered 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

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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.

6. Administration

Patients should be in a one-to-one care maternity setting ideally in a delivery suite or theatre due to their preterm labour diagnosis. However, administration of MgS04 should not be delayed for transfer if sufficient and safe care can be given in another maternity care setting e.g. Triage or Antenatal ward.

Administer 4g IV loading dose –to give over 10 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 an infusion device to increase safety and reduce task time for clinicians.

* 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 MgSO4 should be discussed with Consultant/Senior Registrar

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

Continue until birth or for a maximum of 24 hours. If there is no evidence of progression of preterm labour by cervical dilatation after 12 hours, then the infusion should be ended and the clinical picture reviewed by Consultant Obstetrician.

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

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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)

Elective or Planned Preterm Delivery

Women undergoing induction of labour should have the loading dose (as above) when labour is established and a maintenance dose until delivery.

For women who are having a planned caesarean section, who have not been started on magnesium sulphate, a 4g intravenous bolus 2 hours before the section should be administered and if an unexpected delay occurs beyond 4 hours a further extra dose may be required.

7. Monitoring and side effects

Maternal observations (including oxygen saturations) should be commenced and documented on a MEOWS chart prior to administration and hourly thereafter. In addition, deep tendon reflexes (patellar or biceps reflexes in the presence of an epidural anaesthesia) should be undertaken and documented 4 hourly.

The patient should be closely observed for adverse reactions.

7.1 Loading dose

Hourly MEOWS should be recorded.

Formal clinical review must occur at least every 4 hours with the following additional observation of deep tendon reflexes.

Fetal monitoring should be undertaken from 26+0 weeks gestation and performed as per GMEC CTG Guideline.

7.2 Maintenance dose

Observations (excluding temperature) Urine output should be measured 4 hourly (catheterisation is not required if good urine output) and deep tendon reflexes should be documented 4 hourly.

*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 oliguric or anuric patients there is a real danger.

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7.3 Concerns

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)
- Concerns with Cannulae patency

7.4 Side effects

7.4.1 Maternal

Common side effects and less serious side effects include:

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

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

7.4.2 Fetal

Serious side effects are very rare but babies with hypermagnesemia can experience hypotonia and apnoea. MgSO4 given to mothers in labour for fetal neuroprotection is safe, in the doses recommended by NICE. In the rare event that mothers have been given repeated courses of MgSO4 (exceeding 5-7 days cumulatively) it would make sense to check a serum bone profile in the baby and it would be prudent for the maternity team to inform the neonatal team if exposure has been this extensive. The majority of very preterm babies on NICUs will have bone profiles measured regularly in any event, as very preterm babies with compromised nutrition may have bone problems (including fractures) related to phosphate deficiency.

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
- Sleepy/drowsy/confusion/altered mental state
- Respiratory depression
- Paralysis
- Cardiac arrest

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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 (bicep if epidural in place)
 - 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

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 to be repeated after 24 hours.

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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+0– 30+0 weeks gestation, offer for babies up to 33+6 weeks



Stop magnesium sulphate following delivery /no evidence of imminent delivery after 24 hours

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

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

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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 magnesium sulphate should be considered. Decision to give magnesium sulphate should not be made on the basis of fetal fibronectin result alone.

2. Bleeding

Tocolysis would not usually be used in the event of an abruption or significant APH as this may delay delivery, and & there is a risk of (in the event of an abruption) increased bleeding. If bleeding is due to other causes – e.g. Placenta previa, reducing uterine activity may reduce blood loss. If there has been significant bleeding or an acute abruption with maternal or fetal compromise delaying delivery to administer magnesium sulphate should not be considered. 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 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

Pulmonary oedema except as a complication of PET is rarely seen magnesium sulphate is recommended for seizure prevention for women with severe PET therefore it is not contraindicated.

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

Thank you for accepting this transfer.

Patient ID)		
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Gestation

Steroids given (dates/times)
Magnesium sulphate given:
Loading dose
Maintenance dose

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

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Reason for transfer

Parental concerns/wishes/understanding
Safeguarding concerns
Yours sincerely,

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