Magnesium Sulphate for Neuroprotection of the fetus in women at risk of preterm birth

Originator: Labour ward Forum, maternity Services

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Contents:

Section

1.0 Introduction

Cerebral Palsy (CP) is the most common cause of severe motor disability in childhood with a prevalence rate of approx. 2-3/1000 live births. At present there is no cure for CP which makes effective preventative interventions of paramount importance.

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. There is strong evidence to suggest the giving MgSO4 <24h prior to birth less than 32w reduces the risk of cerebral palsy and death without risk to mother or fetus.

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.

1.1 Abbreviations used within this guideline:

CP - cerebral palsy
PTL - preterm labour
PPROM - preterm pre-labour Rupture of membranes
NNT - number needed to treat
IV - intravenous
CI - confidence interval
RR - relative risk

2.0 Purpose

To provide guidance to obstetric, midwifery, anaesthetic and neonatal staff on indications for and appropriate use of Magnesium Sulphate for neuroprotection of the fetus in women at risk of preterm birth.

3.0 Scope

This guideline applies to all obstetrics, midwifery and neonatal staff. It addresses the management of women who are at risk of delivering between 24+0 and 30+0 weeks gestation, whether as a result of spontaneous preterm labour or by iatrogenic delivery.

4.0 Indications for the use of Magnesium Sulphate for Neuroprotection of the Fetus

At **gestations between 24+0 to 30+0 weeks,** Magnesium Sulphate should be given to women in whom preterm delivery is likely.

Consider intravenous magnesium sulphate for neuroprotection of the baby for women between **30+0 and 33+6** weeks of pregnancy who are:

- in established preterm labour OR
- having a planned preterm birth within 24 hours

5.0 Cautions

Women with **renal impairment** (serum Creatinine >90 umol/L) should receive half the loading dose and half the maintenance dose (see Appendix 1). Check magnesium levels after 4 hours and re-check depending on the initial result. The therapeutic magnesium range is 2-4 mmol/L.

Severe cardiac disease – discuss with Obstetric Consultant before starting Magnesium Sulphate.

6.0 Regimen

The meta-analysis of this topic does not suggest a particular dosing regimen; the loading dose of Magnesium Sulphate used in the five trials ranged from 4 to 6g, followed by either no maintenance dose or between 1 and 3 g/hour. The most recent trial published by Rouse *et al* in 2008 included an empirical protocol for discontinuation of treatment if delivery was not imminent after 12 hours of treatment, with a further loading dose given if contractions recommenced more than 6 hours after treatment had been discontinued.

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6.1 Magnesium Sulphate administration regimen.

Dosage-

Loading dose: **Pre-filled syringe** – 4g of MgSO4 in 20ml of Normal Saline (0.2g in 1ml) given slowly over 5 minutes i.e set pump rate to 240ml/hr

Maintenance dose: **Pre-filled syringe** – 5g of MgSO4 in 50ml of Normal Saline (0.1g in 1ml) to be administered via syringe pump, set pump rate to10ml/hr

Monitoring on Magnesium Sulphate

- 4 hourly MEOWS should be recorded
- Oxygen saturation, respiratory rate, tendon reflexes 4 hourly.
- If Oxygen saturation **<95%**, respiratory rate **< 12/minute,** loss of tendon reflexes a medical review is required and measurement of magnesium levels.
- In conditions where there is risk of oliguria (e.g. PET), monitor hourly urine output.
- Half the loading and maintenance dose if urine output is <25 mls/hr.

In the rare event of severe toxicity leading to cardiorespiratory arrest:

- Stop maintenance infusion; Dial 2222 ‘maternal cardiac arrest call’
- Institute CPR
- Administer 10 ml calcium gluconate IV, (kept on PET trolley)
- Intubate immediately and manage with assisted ventilation until resumption of spontaneous respirations.

6.2 See Appendix 1 for Magnesium Sulphate pharmacokinetics.

6.3 Preterm labour.

The woman should be given the loading dose of Magnesium Sulphate and the maintenance infusion commenced immediately. The maintenance infusion should be continued until delivery but can be stopped immediately after delivery.

6.4 PPROM.

When delivery is indicated, the woman should be given the loading dose of Magnesium Sulphate and the maintenance infusion commenced immediately. The maintenance infusion should be continued until delivery but can be stopped immediately after delivery.

Rarely, a woman in apparent established preterm labour will not progress. In this situation, if delivery is not imminent after 12 hours of treatment, the magnesium infusion should be discontinued. If contractions recommence later, a further loading dose of magnesium may be given if more than 6 hours have elapsed since the treatment has been discontinued.

6.5 Elective preterm delivery

When elective preterm delivery between 24+0 and 30+0 weeks' gestation is planned, the woman should be given only the loading dose of Magnesium Sulphate within 4 hours prior to delivery. Magnesium sulphate should also be considered for neuroprotection of the baby for women between 30+0 and 33+6 weeks of pregnancy who are having a planned preterm delivery within 24hours.

7.0 Anaesthetic considerations for delivery of pre-term infant on magnesium

- Anaesthetist must be informed where magnesium has been given.
- Magnesium can cause significant hypotension in combination with regional anaesthetic so this must be prepared for.
- When giving a general anaesthetic magnesium can reduce or even eliminate fasciculations due to suxamethonium so this must be expected. However, the onset of action is still the same so intubation can be commenced 30-60 seconds after giving suxamethonium.
- Magnesium prolongs neuromuscular blockade so care should be taken with dosing non-depolarising neuromuscular blockers.
- Where there is fetal compromise the anaesthetic MUST NOT delay delivery. The above complications must be expected and dealt with appropriately.
- However, where there is no urgent need for delivery i.e. Cat 3 or 4 delivery it may be beneficial to have a time delay (30 minutes) between the bolus of magnesium and anaesthetic, to minimise the risk of hypotension.

Although birth should not be delayed in situations where urgent delivery is necessary because of actual or imminent maternal or fetal compromise (e.g. severe fetal distress or antepartum haemorrhage), all efforts should be made to administer the loading dose of Magnesium Sulphate from prefilled syringes.

8.0 Side effects and monitoring

Minor side effects include pain at the site of injection, nausea or vomiting, thirst, drowsiness and confusion. These symptoms resolve quickly when treatment is stopped.

Magnesium Sulphate toxicity may cause muscle weakness (due to neuromuscular blockade) which may lead to decreased deep tendon reflexes and respiratory suppression, so monitoring of respiratory rate and oxygen saturation is important.

9.0 Evidence

Several trials and two large systemic reviews suggest that Magnesium Sulphate given to the mother around the time of the delivery reduces the risk of CP in babies delivered preterm. All showed that the risk of death or CP is lower in children at 2 years if the mothers were allocated Magnesium Sulphate rather than placebo. The 2009 Cochrane review included five randomised control trials (involving 6145 babies) of antenatal Magnesium Sulphate in women at risk of preterm delivery (before 37 weeks gestation). This review concluded that Magnesium Sulphate substantially reduced the

risk of CP (RR 0.68; 95%CI 0.54 to 0.87). There was also a significant reduction in gross motor function deficit (RR 0.61; 95%CI 0.44 to
0.85). However, there was no effect on neonatal mortality (RR 1.04; 95% CI 0.92 to 1.17).

The most recent study (which prompted the Cochrane review) was published in 2008 and studied 2241 babies born in 20 centres in the USA between 1997 and 2004. All were born before 32 weeks gestation, 87% were associated with preterm pre-labour rupture of membrane (PPROM), and all were followed up for 24 months. The incidence of moderate or severe CP was lower in the Magnesium Sulphate group (1.9% vs 3.5%; RR 0.55, 95% CI: 0.32 to 0.95). However, the perinatal mortality rate was similar (9.5% vs 8.5%; RR 1.12 CI: 0.85 to 1.47).
The numbers needed to treat (ie the number of women who need to be given Magnesium Sulphate to prevent one case of cerebral palsy) for all gestations under 37 weeks is **63** (95% CI: 43 to 87); NNT for gestation less then 28 weeks is **29**.
The ACOG (American College of Obstetricians and Gynaecologists) and the Society for Maternal-Fetal Medicine published an opinion paper in which they recognize that the available evidence suggests that Magnesium Sulphate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants.

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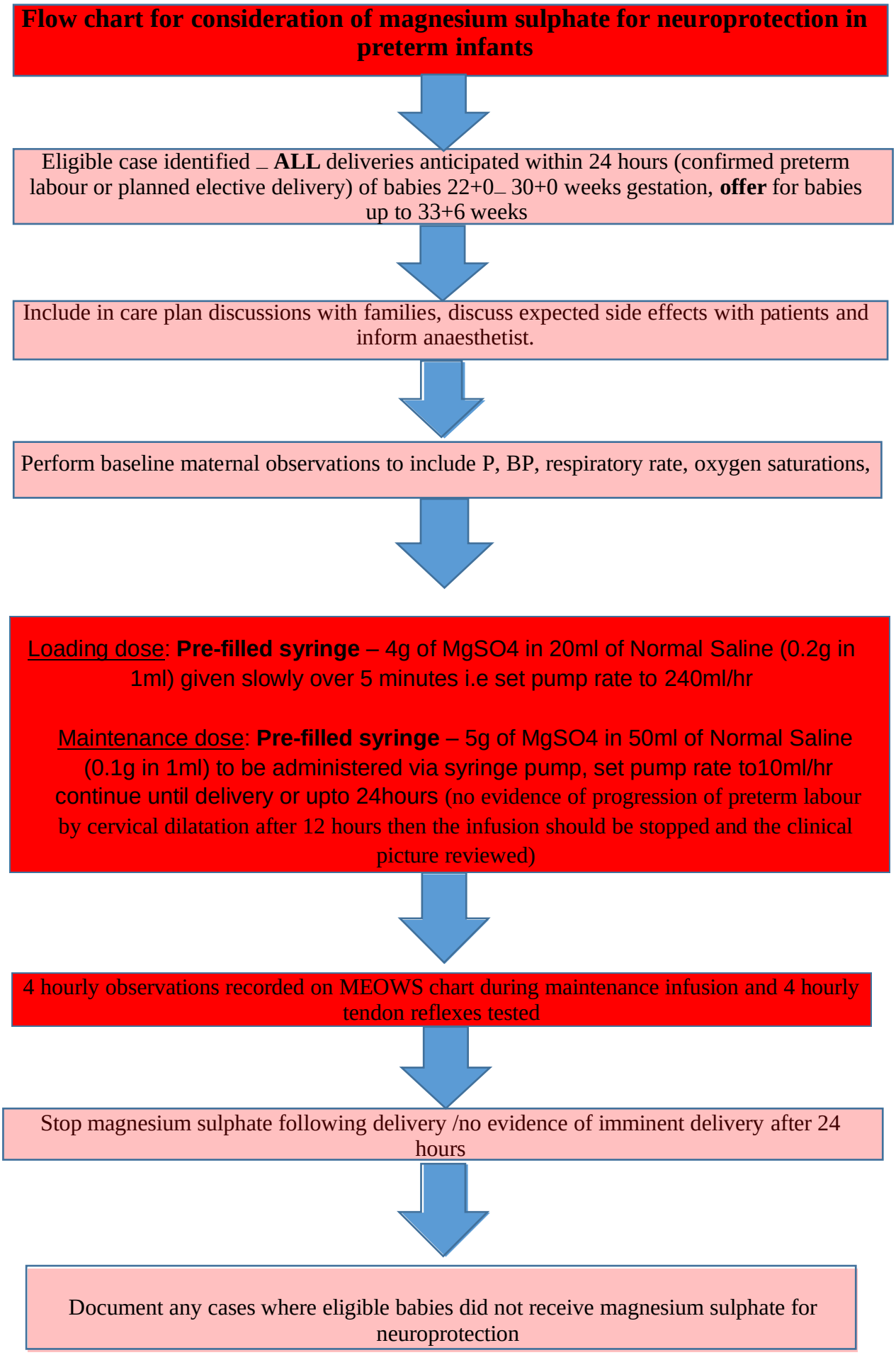
Appendix 1: Pharmacokinetics of Magnesium Sulphate

With intravenous administration, the onset of anticonvulsant action is immediate and lasts around 30 minutes. Peak magnesium levels are reached at around 20 minutes. Magnesium is excreted solely by the kidney at a rate proportional to the plasma concentration and glomerular filtration.
When used as an intravenous infusion in pregnant women, the elimination half-life of ionised magnesium (the active form) is 313 ± 29 minutes.

Appendix 2 flowchart for consideration of magnesium sulphate for neuroprotection in preterm infants



Directorate of Women & Child Health Checklist for Clinical Guidelines being Submitted for Approval by Quality & Safety Group

Title of Guideline:	MAGNESIUM SULPHATE FOR NEUROPROTECTION OF THE FETUS IN WOMEN AT RISK OF PRETERM BIRTH
Name(s) of Author:	*Labour Ward Forum*
Chair of Group or Committee supporting submission:	Labour Ward Forum
Issue / Version No:	*3*
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Details of persons included in consultation process:	Revision of previous guideline. Madhu Dey (Consultant Obstetrician) Najiya Ali (Obstetric registrar) Nigel Jenkins (Consultant Anaesthetist) Labour ward forum members
Brief outline giving reasons for document being submitted for ratification	To provide guidance to obstetric, midwifery and neonatal staff on indications for and appropriate use of Magnesium Sulphate for neuroprotection of the fetus in women at risk of preterm birth.
Name of Pharmacist (mandatory if drugs involved):	n/a
Please list any policies/guidelines this document will supercede:	*Previous guideline*
Please indicate key words you wish to be linked to document	Magnesium, Sulphate, Neuroprotection, Fetus, Preterm
Date approved by Clinical Guideline Group:	12/08/24
File Name: Used to locate where file is stores on hard drive	ABM Group (Z:)\Maternity\policies and guidelines\Obs\2020 onwards