Preterm Labour (PTL), Preterm, Prelabour Rupture of Membranes (PPROM) & Magnesium Sulphate to prevent Cerebral Palsy - Full Clinical Guideline

Reference no.: UHDB/Obst/04:21/L1

Contents

1. Introduction

Prematurity is the leading cause of perinatal death and disability. It contributes significantly to cerebral palsy, respiratory distress, intracranial bleeding, necrotising enterocolitis, infection, jaundice, hypothermia and hypoglycaemia are the main complications to which preterm infants are susceptible. Although preterm birth is defined as delivery below 37^{+0} weeks gestation, the majority of pre-maturity related adverse outcomes relate to birth before 33^{+0} weeks of gestation.

The causes of neonatal death associated with PPROM are prematurity, sepsis and pulmonary hypoplasia. Maternal intrauterine infection is associated with earlier delivery. About $^{1}/_{3}$ of women with PPROM have positive amniotic fluid cultures due to ascending infection from the lower genital tract. Neonates born with sepsis are four times more likely to die than those without.

There is limited evidence of successful intervention to prevent preterm labour so the primary aims of treatment are to optimise fetal pulmonary function in order to improve perinatal outcome. Tocolysis allows administration of corticosteroids to the mother to promote fetal pulmonary maturity, usually requiring 48 hours treatment. It is well recognised that outcome following delivery of a sick, preterm infant is improved if delivery occurs in the same unit providing neonatal intensive care.

2. Purpose and Outcomes

- To ensure staff are aware of the management of women in the case of PTL / PPROM.
- To diagnose and manage suspected chorioamnionitis.
- The guideline also covers the use of steroids in the AN period and Tocolysis
- To ensure correct management in the use of Magnesium sulphate to prevent cerebral palsy following preterm birth.

3. Abbreviations and Definitions

ABW	-	Actual body weight
AFI	-	Amniotic Fluid Index
ANC	-	Antenatal Clinic
APH	-	Antepartum Haemorrhage
BP	-	Blood Pressure
CRP	-	C-ReactiveProtein
CS	-	Caesarean Section
CTG	-	Cardiotocograph
FBC	-	Full Blood Count
fFN	-	fetal Fibronectin
FH	-	Fetal Heart
GA	-	General Anaesthetic
G&S	-	Group & Save
GBS	-	Group B Streptoccocus
HVS	-	High vaginal Swab
IBW	-	Ideal body weight
IA	-	Intermittent Auscultation
ICH	-	Intracranial Haemorrhage
IgF	-	Immunoglobulin F
IM	-	Intramuscular
IV	-	Intravenous
IVH	-	Intra-ventricular Haemorrhage
MSU	-	Mid Stream Urine
PPROM	-	Preterm Prelabour Rupture of Membranes
PTL	-	Preterm Labour
RCOG	-	Royal College of Obstetrics & Gynaecology
RDS	-	Respiratory Distress Syndrome
QDS	-	Four times daily
TDS	-	Three times daily
TPR	-	Temperature / Pulse / Respiration
TTN	-	Transient Tachypnoea of the Newborn
USS	-	Ultrasound Scan
UTI	-	Urinary Tract Infection

Definitions

Preterm labour: labour occurring below 37^{+0} weeks of gestation

Extreme preterm birth: labour occuring below 27 weeks (for guidance related to singleton pregnancy below 27^{+0} weeks, multiple pregnancy below 28^{+0} weeks or anticipated birth weight below 800 gram click here for full guideline)

4. Key Responsibilities and Duties

- All staff caring for women in suspected or diagnosed PTL/PROM have a responsibility to ensure they are aware of the appropriate and timely care and management of these women.
- Assessment of PPROM may be carried out by an experienced midwife or experienced

doctor (St 2 or above) if gestational age is 32 weeks or more only in the absence of any other symptoms such as pain or bleeding
- Assessment of PPROM in case of gestational age below 32 weeks should be carried out by a senior obstetrician (SpR3 or above)
- A decision for intrauterine transfer should be made by a consultant obstetrician
- A decision on timing of delivery with PPROM should be made by a consultant obstetrician
- Decisions regarding outpatient management of PPROM should be decided by senior medical staff / consultant level
- Refer to extreme preterm guideline if singleton <27 weeks, multiple <28 weeks or anticipated birth weight is <800 grams

5. Assessment and diagnosis

Diagnosis of preterm labour accurately is important to reduce unnecessary intervention.

5.1 Baseline assessment and investigations

- Presence of risk factors click here for full overview in preterm prevention guideline
- Complete full antenatal review including:
  - Maternal observations
  - Urinalysis ± MSU
  - Abdominal palpation
  - Assessment of fetal wellbeing:
    - FHR (Pinnard or handheld Doppler for minimum of 60 seconds
    - Followed by CTG if 26^{+0} weeks gestation or over
- Blood tests:
  - FBC
  - CRP
- Sterile speculum examination (do not use lubricant or antiseptic solution):
  - Cervical appearance (length and dilatation)
  - Presence of liquor or blood
  - HVS for culture and sensitivity
- Digital examination should be avoided with suspected PPROM unless there is a strong suspicion of preterm labour with obvious cervical dilation visualised during speculum examination
- Fetal Fibronectin/Actim Partus test only if:
  - Intact membranes
  - No bleeding (or very minor)
  - Placenta location not low lying
  - NO evidence of significant cervical effacement/dilatation at speculum examination
- Amnisure test in case of strong history of PPROM but no liquor visible in posterior fornix
- Ultrasound scan:
  - Presentation
  - Liquor volume and Dopplers
  - Time allowing: biometry (unless carried out less within last 14 days)

5.2 Diagnosis of preterm labour <37 weeks

- Painful uterine contractions 1:10 or more frequent plus one or more of the following:
  - Rupture of membranes
  - Cervical change on vaginal examination
  - Cervical length < 15mm on trans-vaginal ultrasound scan

5.3 Diagnosis of rupture of membranes <37 weeks

- Direct visualisation of liquor in posterior fornix
- In case of a strong history with inconclusive/negative speculum examination:
  - Positive Amnisure

6. Management of Preterm labour and/or PPROM

If <27 weeks gestation singleton pregnancy or <28 weeks multiple pregnancy or anticipated fetal weight below 800 gram: additionally refer to extreme preterm guideline and commence extreme preterm care pathway booklet

	Steroids	Atosiban	MgSO4	Antibiotics	Additional
Basic limits always to adhere to regardless of below investigations	<34+6 In case of diabetes or fetal growth restriction: < 35+6	<34+0 Only < 4cm Or >4cm as consultant decision and *only* consider when intrauterine transport (IUT) required	<27 singleton, <28 multiple or anticipated weight <800g: Refer to extreme preterm guideline Offer up to 29+6 Consider between 30+0-33+6	All preterm <37+0 Labourers require Prophylactic antibiotics to be commenced at the first attendance to labour ward in spontaneous labour or when ARM for induction regardless of status of membranes or GBS status in pregnancy.	**Below 24 weeks consultant decision only**
PPROM	✓	✗ *Unless* IUT required or extreme prematurity (consultant decision)	✗ *unless* delivery <24 hours		• Monitor for infection • Erythromycin if not in labour
Evidence of *significant* cervical effacement/dilatation	✓	✓	✓		
Positive Actim Partus With NO evidence for PPROM or significant cervical effacement/dilatation	✓	✓	✗		
Risk factors present for PTL in absence of all the above	Consultant decision	Consultant decision	✗		Consider Cx length scan in fetal medicine

Click here for guidance on Antibiotics regimes in obstetrics

6.1. Management following diagnosis of preterm labour with/without PPROM

- Deliver if indication for immediate delivery e.g. (abruption, fetal or maternal compromise, chorioamnionitis)
- Treat dehydration and suspected infective aetiology e.g. UTI, chorioamnionitis
- If > 34 weeks gestation, allow to labour if no contraindication, inform the neonatal unit of expected pre term delivery
- If < 34 weeks, discuss with neonatal team and ascertain cot availability (see IUT guideline if transfer needed for no cot availability). If appropriate, a Neonatologist may be available to discuss with parents likely interventions in the neonatal unit
- Steroids and Magnesium Sulphate as table in 6.0 and more in paragraph 9 and 10
- GBS prophylaxis during labour as per Obstetric Infections guideline for all preterm labour regardless of GBS status in pregnancy and regardless of status of membranes
- Senior obstetrician to decide most suitable mode of delivery should labour progress
- Where appropriate the obstetric anaesthetic team to be made aware of patient

6.1.1 Tocolysis (Atosiban SOP: Appendix A)

- Most useful when:
    - Considering in utero transfer
    - Not completed steroid course
    - Very preterm
- Consider tocolysis if <34^{+0} with intact membranes
- Where doubt exists the decision should be made by a consultant obstetrician
- Should not be used where there is a contraindication to prolonging pregnancy
- Agent of choice is Atosiban (Tractocile) (Appendix B for SOP)
- Maternal age <18 is not licensed, however, may be given after adequate counselling

6.2. Management following diagnosis of Preterm, Prelabour Rupture of Membranes (PPROM) (not in labour)

The initial assessment determines subsequent management. Chorioamnionitis, abruption, and preterm labour need to be excluded.
Women should be advised to be admitted to the antenatal ward for 48 hours for observation, but may have to stay in longer depending on clinical signs and symptoms (including colour of liquor, fetal movements, tightenings, previous obstetric history, presentation of fetus, severity of oligohydramnios, home to hospital distance etc).

Observations and assessments during inpatient admission to include:

- Minimum 4-hourly maternal observations documented on MEOWS chart (increased frequency if chorioamnionitis/infection suspected)
- Minimum 12 hourly assessment of fetal wellbeing:
    - CTG if ≥26 weeks
    - Intermittent auscultation if < 26 weeks
    - A rising baseline is an early sign of infection so baseline must be documented
- Document: fetal movements
- Daily documentation of colour of liquor, developing of offensive smell, new uterine tenderness and bleeding
- If any features of chorioamnionitis: for senior/consultant level review
- If delivery considered: for Consultant Obstetrician decision
- For steroids and Mag Sulph see table and more information below
- Oral antibiotics: see obstetric infections guideline click here to open
- Discuss tocolysis with senior obstetrician IF contractions commence in extremely preterm fetus and/or intrauterine transfer is being considered, otherwise tocolysis in women with PPROM is not recommended because it does not significantly improve perinatal outcome, and may increase maternal risk.
- Repeat CRP and FBC prior to discharge review

- Senior review (St3 or above) prior to discharge:
    - only after 48 hours inpatient stay
    - documenting clear outpatient management plan
    - women should be advised of the signs and symptoms of chorioamnionitis and how/when to seek advice

Outpatient management following discharge should include surveillance for chorioamnionitis and the onsetof preterm labour. This should include:

- Follow up appointments in MAU/PAU (typically twice weekly for the first two weeks, either continued after two weeks or changed to once weekly): FBC, CRP, maternal observations, assessment of fetal wellbeing including fetal movements / CTG if 26 weeks or over / IA if below 26 weeks
- Ultrasound scan and ANC appointment at next antenatal clinic and fortnightly after that as a minimum
- Decision regarding possible outpatient management, plan of care and time/ modeof delivery to be decided by at senior medical staff/Consultant level.
- Follow-up HVS not required

6.3 Timing of delivery with PPROM

- Women whose pregnancy is complicated by PPROM after 24+0 weeks' gestation and who have no contraindications to continuing the pregnancy should be offered expectant management until 37+0 weeks; timing of birth should be discussed with each woman on an individual basis with careful consideration of patient preference and ongoing clinical assessment
- Decision on timing of delivery should be made at Consultant level

7. Diagnosis and Management of Chorioamnionitis

Chorioamnionitis can occur in the absence of ruptured membranes.
The diagnosis should be suspected if:

- There is a maternal pyrexia > 37.8C
- A fetal tachycardia > 160 bpm *(one of the best predictors with a low false positive rate)*
- Offensive vaginal discharge
- Uterine tenderness

Leucocytosis and a raised C-reactive protein may be useful clinically where there is doubt.

The differential diagnosis includes infection in another site, particularly in the urinary tract and effects should be made to exclude or aggressively treat UTI in suspected PTL.
Management of chorioamnionitis includes:

- Prompt delivery
- Broad spectrum antibiotics including an agent active against GBS should replace GBS specific antibiotic prophylaxis

As per Antibiotics Guideline: Obstetric Infections: click here to open

Discuss with consultant microbiologist if any concerns, after 48 hours to obtain culture results or if failing to improve. Review need for continuing treatment after 5 days. Continue for one dose post-partum, or until patient has been apyrexial and asymptomatic for 24hrs post delivery.

- Blood Cultures / HVS should be taken before antibiotics are commenced
- Antibiotics should be commenced within one hour from diagnosis
- Senior paediatrician should be present at delivery and made aware of diagnosis

Invasive fetal procedures during labour should be avoided in the presence of chorioamnionitis including FBS as its interpretation is unreliable in the presence ofinfection

7.1 Gentamicin Dosing and monitoring in Pregnancy

Gentamicin treatment dosing now as per Trust guideline for gentamicin dosing in adults rather than divided daily doses. click here for full Trust guideline

8. Mode of Delivery

If presentation is cephalic aim for vaginal delivery with Caesarean Section for normal obstetric indications. The decision to proceed to Caesarean Section at gestations < 28 weeks should only be made at Consultant level.

8.1 Preterm Vaginal Breech Delivery

This should be supervised by an experienced obstetrician.
An effective epidural is recommended to prevent pushing prior to full dilatation and to allow manipulations at time of delivery
Anaesthetist and Paediatrician should be available for second stage Delivery
with intact membranes is advantageous

Forceps are generally not required for after coming head.
To release an entrapped head, it should be flexed abdominally and a finger inserted vaginally into the mouth to flex the head before consideration of cervical incision

8.2 Preterm Caesarean Section

This should be undertaken by an appropriately experienced obstetrician
The De Lee or classical uterine incision appears to confer little benefit to the fetus in terms of reduced trauma from 28 weeks onwards. But may be required with abnormal lie or severe oligohydramnios. If a transverse incision needs extending then a J shape is preferred to an inverted T as the latter leaves a weakness in the scar increasing the chance of rupture in a subsequent pregnancy

9. Antenatal Corticosteroids for preterm birth

Relative contraindications include systemic infection including tuberculosis, sepsis, porphyria, uncontrolled diabetes (may require additional insulin and close monitoring), thyrotoxicosis, cardiomyopathy or aortic stenosis. For guidance on singletons <27 weeks, multiple <28 weeks or anticipated weight <800 gram see extreme preterm birth guideline

- Betamethasone 12mg, IM or Dexamethasone 12mg, IM (one course of two doses with 12 hours apart; for total of 24mg to be administered in 24-48 hours) are the steroids of choice to enhance lung maturation (Optimum effectiveness between 24hours and 7 days thereafter.)
- Clinicians should offer a single course of antenatal corticosteroids to women <34^{+6} weeks of gestation who are at risk of preterm birth
- Pregnancies below 35^{+6} weeks of gestation at risk of delivery, affected by fetal growth restriction or diabetes, should receive a single course of antenatal corticosteroids
- Decision to administer corticosteroids <24^{+0} weeks gestation should be made by a consultant obstetrician
- Refer to Diabetes guideline for management of blood sugar variation related to steroids

10. Antenatal Magnesium Sulphate for Fetal Neuroprotection (Appendix B for SOP)

- Recommended Magnesium sulphate for neuroprotection where a viable outcome is anticipated and women are in established labour or having a planned preterm birth within 24 hours:
    - To be offered to women below 30 weeks gestation
    - To be considered for women between 30^{+0} weeks and 33^{+6} weeks gestation (it would be reasonable to offer to cases where there is evidence of fetal growth restriction and/or conditions that may increase the risk of cerebral palsy)
- Magnesium sulphate should be considered regardless of:
    - Single or multiple pregnancy

- Reason for expected preterm labour
- Expected mode of delivery
- Bleeding
- Ruptured membranes
- Infection
- Tocolytics use (although caution with calcium channel blockers is advised it is not contraindicated)
- Whether antenatal corticosteroids have been administered or not

- If birth is planned or expected to occur sooner than 4 hours, administer Magnesium sulphate as there is still likely benefit from administration within this time.
- In cases where urgent delivery is necessary because of actual or imminent maternal or fetal compromise, then birth should not be delayed to give Magnesium sulphate
- In the event that birth does not occur after giving Magnesium sulphate, and preterm birth (less than 30 weeks or 30-34 considered as above) appears imminent again, a repeat dose of Magnesium sulphate should be administered:
  - When women represent in preterm labour within 24 hours of having the MgSO4 regimen (bolus and maintenance) then it is reasonable to recommence the maintenance infusion
  - When women represent more than 24 hours after completing the MgSO4 regimen then a repeat loading and maintenance dose should be administered.
- In case of intrauterine transfer, women can still benefit from its use as it could be commenced locally ,discontinued for transfer, then recommenced at receiving unit if they are happy with the plan (please check with receiving unit).

11. Monitoring Compliance and Effectiveness

Monitoring requirement	Compliance of this guideline in 1% of health records of women who have presented with PTL/PPROM, to include the appropriate management of women requiring Magnesium sulphate
Monitoring method	Retrospective case note review
Report prepared by	Named individual undertaking audit
Report Sent to:	Labour Ward Forum
Report frequency	3 yearly

12. References

Antenatal corticosteroid to reduce neonatal morbidity and mortality-RCOG green-top guideline No 7.Oct-2010.

Clinical Practice Guidelines on Magnesium Sulphate Prior to Preterm Birth for Neuroprotection of the Fetus, Infant and Child-Australian Research Centre for Health of Women and Babies, The University of Adelaide 2010.

Magnesium Sulphate to Prevent Cerebral Palsy following Preterm Birth-RCOG SAC Opinion Paper 29-August 2011

Atosiban Administration

ATOSIBAN	STEP 1	STEP 2	STEP 3
	LOADING DOSE to be given by medical staff	HIGH DOSE LOADING INFUSION	LOW DOSE SUBSEQUENT INFUSION
Total time	Over 1 minute	For 3 hours	For 25 hours, then reassess
Concentration	6.75 mg/1 minute	18mg/hr = 24ml/hr	6mg/hr = 8ml/hr
Preparation	Draw up 0.9ml of Atosiban 7.5mg/ml solution for injection	Take 0.9% NaCl, 100ml bag and remove 10ml. Add two 5ml vials of 7.5mg/ml Atosiban concentrate for intravenous infusion and add to the bag	Use same solution as step 2 but decrease the infusion rate.

Possible side effects: nausea, hyperglycaemia, headache, dizziness, tachycardia and hypotension.

Monitoring:

- Pulse and blood pressure every 15 minutes
- Continuous CTG until tocolysis effective (IFM and contraction palpation <26wks)
- Once effective, hourly observations and 4 hourly CTG
- Input-output fluid balance chart
- Regular review by a senior Obstetrician and urgent review if concerns re observations, bleeding, pain, CTG concerns etc.
- If labour does not ensue after discontinuation of tocolysis a plan for subsequent assessment is to be decided by a senior Obstetrician

Contraindications:

- maternal/fetal indication for immediate delivery
- chorioamnionitis
- abruption

Magnesium Sulphate Administration

Loading dose: 4g IV Bolus over 30 min
Maintenance infusion 1g/hr IV for 24 hours or until birth, whichever comes first

For RDH:
For both loading dose and maintenance infusion:
Make up 20ml (10g) of 50% MgSO4 diluted with 30ml of 5% Dextrose (to make 10g in 50ml) in a 50ml syringe.

Use pre-set menu on a Syramed syringe pump to administer both the initial loading dose and to initiate maintenance dose. However, **pre set protocol for Magnesium Sulphate initial bolus needs to be amended to administer over 30 minutes as not given to lower blood pressure. Once changed, confirm pre set load of 4g MgSO4 over 30 minutes and** confirm maintenance start rate of 1g/hr (5mls/hr).

For QHB:
Loading dose: make up 8ml (4g) of 50% MgSO4 diluted with 12ml of 5% Dextrose (to make 4g in 20ml) and give at 40ml/hr
Maintenance dose: make up 20ml (10g) of 50% MgSO4 diluted with 30ml of 5% Dextrose (to make 10g in 50ml) and give at 5ml/hr (1g/hr).

Monitoring and Management of Patients on Magnesium Sulphate

- Blood pressure 2 hourly
- Respiratory rate before treatment and hourly thereafter
- Urine output hourly
- Reflexes before treatment, 30 minutes after loading dose and hourly thereafter

Routine checking of magnesium levels is not necessary unless:

- Urine output is low ≤100mls over 4 hours
- Absent reflexes
- Urea is > 10 mmol / l

Magnesium sulphate **toxicity** signs include:

- Weakness
- Nausea
- Flushing
- Double vision
- Slurred speech
- Loss of reflexes
- Muscle paralysis,
- Respiratory arrest
- Cardiac arrest

If any of the following occur:

- Urine output is less than 100mL in 4 hours
- Reflexes are absent
- Respiratory rate is less than 12 breaths / minute
- Oxygen saturation is less 90%

Then:

- STOP the Magnesium sulphate infusion,
- Consider Calcium gluconate10%(1g), 10ml IV over 10 minutes
- Do Magnesium levels (therapeutic levels 2-4mmol/l).

Contraindications and Cautions for Use of Magnesium Sulphate

Concurrent use of digoxin is contraindicated. Neuromuscular blocking agents are potentiated by magnesium sulphate and should be used in lower doses. When GA is used, neuromuscular function monitoring is mandatory.

Appendix C

Carrying out the Actim Partus Test

Do not perform if large amount of blood present or ruptured membranes

1. Take cervical secretion sample with sterile Dacron swab from endocervix. Leave the Dacron swab in the endocervix for 10-15 seconds to allow the swab to absorb cervical secretions
2. Place Dacron swab in extraction solution and swirl vigorously for 10 seconds, then remove.
3. Dip yellow area of dipstick into extraction solution and hold there until the liquid reaches the result area
   Remove from solution and place horizontal
   If after 5 minutes there is one blue line only (control line) this is a negative result If there are 2 blue lines (control + positive lines) this is a positive result.

The Actim partus packs must be kept in the fridge

Documentation Control

Version: **UHDB Version 2**		**Status: FINAL**	**Reference Number:** UHDB/Obst/04:21/L1
Version	Date	Author	Reason
UHDB version 1	Jan 2021	Miss Raouf – Fetal Medicine Obstetric consultant Dr A Subramanium	Merged Trust, introduction Amnisure, in line with Precept
UHDB version 2	April 2021	Cindy Meijer – Risk Support Midwife	In line with extreme preterm guideline. For antibiotics during active labour prophylaxis for GBS for all preterm labour below 37 weeks
Version 2.1	Aug 2021	Pharmacy and senior labour ward teams	Amendment of Magnesium Sulphate
2.2	June 2023	Miss S Raouf	Amendment to section 6.3 to bring in line with RCOG
No new version required	March 2024	Joanna Harrison-Engwell	Clarification on antibiotic cover added to table, no new information added.

Intended Recipients: All staff with responsibility for caring for women in the case of preterm labour/Preterm pre-labour rupture of membranes	
Training and Dissemination: Cascaded electronically through clinical leads/midwives/doctors Published on Intranet: Articles in divisional newsletter	
To be read in conjunction with: Pre Eclampsia guidelines	
Consultation with:	Julia Lacey – Lead Pharmacist
Business unit sign off:	06/04/2021: Maternity Guidelines Group: Miss S Rajendran - Chair 19/06/2023: V2.2 15/04/2021: Maternity Governance Committee/CD – Mrs K Dent 19/06/2023: Maternity Governance Committee/CD – Mr R Deveraj 21/04/2021: Neonatal sign off: Dr N Ruggins
Divisional Sign off: 27/04/2021 Notification Overview sent to TIER 3 Divisional Quality Governance Operations & Performance: V2.2 20/06/2023	
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Key Contact:	Joanna Harrison-Engwell