PRETERM LABOUR

Keywords: threatened preterm labour, TPL, fetal fibronectin, tocolytic therapy

PURPOSE

• To diagnose preterm labour i.e. labour at less than 37 completed weeks
• To establish a cause, if possible, of preterm labour, which may allow treatment of the primary cause of the preterm labour e.g. urinary tract infection.
• To assess the maternal and fetal condition in the situation of preterm labour.
• To establish effective suppression of labour (unless contra-indicated) prior to 34 weeks gestation without undue delay.

KEY POINTS

• There is good evidence\(^1\) that tocolysis alone does not improve neonatal outcome. However, tocolysis should be considered if the few days gained can be used for corticosteroid therapy.
• In the case of preterm labour occurring at a site without appropriate nursery facilities, the time gained with tocolytic therapy can be used for transport.
• The evidence suggests there is no benefit to the fetus in the following situations:
  ➢ Using tocolytic therapy longer than 48 hours.
  ➢ Prolonged or repeated tocolytic therapy after corticosteroids have been given and are current.
  ➢ Employing tocolysis at a gestation greater than 34 weeks.
• It may not be appropriate to suppress labour in situations such as:
  ➢ Birth required immediately or as soon as possible because of maternal or fetal condition.
  ➢ Labour is too far advanced to attempt suppression.
  ➢ The fetus is sufficiently mature that the risks of suppression therapy outweighs benefits to the fetus (>34 weeks gestation).
• The Consultant Obstetrician and / or Senior registrar on call must be notified of all such admissions, and participate in the decisions regarding treatment. Their involvement in the management plan shall be documented in the woman’s notes.
• Labour is diagnosed on the basis of regular contractions (at least 1 per 10 minutes) which are associated with effacement and / or dilatation of the cervix.
• The absence of fetal fibronectin (fFN) in the cervical secretions is a very useful negative predictor of imminent birth (negative predictive value for birth within 7 days 97-98%).
• Like fFN, a cervical length is a good negative predictor, but not a good positive predictor i.e. greater than or equal to 30mm is highly reassuring
• In cases of threatened preterm labour, a threshold of 30 mm has been consistently reported to exclude preterm labour, but there is no threshold of cervical length that establishes the diagnosis. In women with contractions and cervical length less than 30 mm, additional testing (such as fetal fibronectin) may help predict the patient’s risk of preterm delivery within the next several days.\(^8\)
• It is important to ascertain maternal and fetal well-being before instituting tocolytic and corticosteroid therapy. Fetal factors such as chorioamnionitis, antepartum haemorrhage and intrauterine growth restriction may make delay unwise.
• The best results in postponing birth are obtained in women who have intact membranes and who are less than 5 cm dilated. However, ruptured membranes or excess dilatation are not absolute contraindications to treatment.

This clinical guideline applies to women when the outcome for the fetus may be improved by delaying birth.
MANAGEMENT

ADMISSION AND INVESTIGATION

On admission, a thorough assessment of the woman shall include:

- History - particularly relating to rupture of the membranes, contractions and antepartum haemorrhage. Gestational age must be confirmed by menstrual history and any available previous ultrasound data.
- Examination - noting particularly temperature, uterine tone and tenderness, amniotic fluid volume and fetal size and presentation.
- Vaginal examination - a speculum examination shall be performed with full aseptic technique and not touching the cervix with the speculum. Cervical swabs shall be taken for immediate bacteriological assessment. If the cervix is closed and there is no blood or amniotic fluid to be seen in the vagina, a fetal fibronectin (fFN) test shall be performed (see below). Digital examination shall be avoided unless there is a significant possibility of a cord presentation or prolapse, or the cervix cannot be adequately visualised.
- Urine microbiology - if a mid-stream urine is unsatisfactory a catheter specimen of urine shall be obtained for microscopy and culture.
- Ultrasound - this may be necessary to assess presentation, gestation, fetal weight, fetal normality, and the possibility/ advisability of amniocentesis. Additionally, a trans-vaginal ultrasound is the best way of detecting early changes in the internal cervical os in women who continue to contract.
- Electronic fetal heart monitoring (EFM) - shall be performed to assess fetal wellbeing in the case of a viable fetus. On going, continuous electronic fetal monitoring (EFM) at gestations of less than 25 weeks is a decision which shall be taken in discussion with a consultant.
- Amniocentesis - this investigation may be appropriate to assess the presence or absence of intra-amniotic sepsis, or to assess fetal lung maturity. The use of this investigation shall be made only by a consultant obstetrician.
- The on-call Paediatric registrar shall be notified of the woman’s presence in the Birth Suite.

Ruptured membranes
- If there is evidence of ruptured membranes, continue as per the guidelines for premature rupture of membranes.

Maternal fever
- Any maternal temperature of 37.5°C or more MUST lead to formal review of the woman and review of the treatment plan with the Consultant on call.

Fetal fibronectin (fFN) test
- Fetal fibronectin is a screening test used to assess the risk of preterm delivery within the next 7 days. “Point of Care” fFN testing should be utilised in the assessment of preterm labour.

| INDICATIONS | • Symptomatic preterm labour between 24 and 36 weeks gestation  
| • Intact membranes and  
| • Cervical dilatation less than 3cm |
| CONTRAINDICATIONS | • Ruptured membranes  
| • Visual evidence of moderate or gross bleeding  
| • Cervical cerclage insitu |
| RELATIVE CONTRAINDICATIONS | • After the use of lubricants or disinfectants  
| • Within 24 hours of coitus  
| • Within 24 hours of vaginal examination |
PROCEDURE
• Performed using a sterile speculum examination prior to any examination or manipulation of the cervix or vagina
• Use only sterile water as a lubricant
• Obtain the sample for testing from the posterior fornix of the vagina
• As per test instructions

POSITIVE RESULT
• Consider transvaginal ultrasound of cervical length
• Admit for tocolysis and steroids
• A false positive result may occur as a result of recent coitus, digital vaginal examination or transvaginal ultrasound

NEGATIVE RESULT
• Low risk of delivery within 7 days
• False negative result may occur due to the use of a lubricant with speculum examination or intravaginal disinfectants

Transvaginal Ultrasound
Transvaginal ultrasound of the cervical length (TVCL) is an additional screening test that can aid in assessing the risk of preterm delivery. TVCL must be performed by a credentialed clinician. Lack of local capability to perform this test is not a reason for transfer.

Interpreting TVCL Results
A cervical length less than 15mm is associated with an increased risk of spontaneous preterm birth. Due to the distances required for transfer from WA regional centres, a TVCL ‘cut off’ of 20mm is appropriate.

MANAGEMENT OF PRETERM LABOUR
Tocolysis and steroids are the main strategies to manage preterm labour.

Negative fFN and no evidence of cervical change / TVCL > 20mm
There is a low risk of delivery within the next 7 days therefore:
• If contractions are infrequent / irregular: offer discharge home with follow up as an outpatient within 7 days
• If contractions are regular and painful: admit for observation, offer analgesia and reassess in 2 hours
• If contractions are persistent and painful: consider steroids and tocolysis.

Positive fFN and / or evidence of cervical change / TVCL < 20mm
There is an increased risk of delivery within the next 7 days therefore:
• Admit and offer analgesia
• Administer steroids and commence tocolysis (if no contraindications)
• Continuous fetal monitoring with a CTG.
• In established labour IV antibiotics should be given

Administration of Magnesium Sulphate Infusion
• For information regarding the administration of antenatal magnesium sulphate prior to preterm birth for neuro protection of the fetus post birth see Clinical Guideline Antenatal Magnesium Sulphate Prior to Preterm Birth for Neuroprotection of the Fetus Post Birth
Administration of corticosteroids

- For prophylaxis against neonatal respiratory distress syndrome, a single course of betamethasone is given to women with a gestation of between 23 to 34 weeks.
- The course is administered as two intramuscular injections of 11.4 mg of betamethasone given 24 hours apart.\(^2\), \(^3\)
- No repeat courses are given. In the event of maternal diabetes, and difficulty controlling the blood glucose level, the on call Diabetes Physician shall be consulted regarding blood glucose level (BGL) control.

Administration of antibiotic therapy

- If progressive labour occurs group B Streptococcus antibiotic prophylaxis shall be prescribed as per Clinical Guideline Group B Streptococcus
- If evidence of urinary tract sepsis is seen on urine microscopy antibiotics shall be prescribed. See Clinical guideline Antibiotic Treatment for Urinary Tract Infection
- If there is clinical chorioamnionitis or generalised sepsis associated with preterm labour, blood cultures, a urine specimen and vaginal swabs shall be taken and broad spectrum intravenous antibiotics shall be commenced. See Pharmacy and Medication guidelines

Tocolytic Therapy

- The decision to suppress labour with tocolytic medication shall only be made by a registrar, senior registrar or the consultant on call.
- Any decision to change tocolytic medication shall only be made by the consultant.

First line: Nifedipine

- Unless contra-indicated, the first line tocolytic to be used shall be Nifedipine.\(^4\)
- Contraindications to the use of nifedipine include:
  - Contraindications to any suppression of labour including antepartum haemorrhage, pre-eclampsia, chorioamnionitis and fetal distress
  - Cardiac disease including cardiac conduction defects and left ventricular failure
  - Hypotension
  - Concomitant use of betamimetics such as Salbutamol
  - Caution should be taken with simultaneous administration of Magnesium Sulphate (MgSO4). This is not an absolute contraindication but care must be taken since hypotension may result.

Dosage

- Give an initial dose of 20mg of Nifedipine orally (not slow release Nifedipine)
- After 30 minutes, if contractions persist, give another 20mg oral dose
- After a further 30 minutes, if still contracting, follow up with a further 20mg orally
- If BP is stable, a maintenance dose of 20mg three times a day for 48-72 hours may be given where indicated.

  Note: The maximum dose of Nifedipine is 120mg / day.

Precautions

- IV shall be inserted and baseline electrolytes, urea and creatinine and LFT levels measured
- Half hourly maternal pulse, BP and respiratory rate until the contractions cease. Maternal hypotension should be treated with IV fluids in the first instance.
- Continuous electronic fetal heart rate monitoring until contractions have settled.
- Cardiovascular examination including auscultation of lung bases every 8 hours for first 24 hours of therapy.
Action
Onset of tocolysis is at 30-60 minutes and institution of second line tocolysis should not be considered in the first 2 hours. If contractions do not abate after this time a second line tocolytic may be considered by the consultant on call.

Side effects
- Facial flushing
- Headache
- Nausea
- Tachycardia
- Dizziness
- Hypotension – this is unusual in normotensive patients
- Cardiac failure
- Increase in liver enzymes

Contraindications
- Cardiac disease including cardiac conduction defects and left ventricular failure.
- Hypotension.

OTHER TOCOLYTICS WHICH MAY BE USED IN THE EVENT OF THE FAILURE OF NIFEDIPINE TOCOLYSIS

1: Salbutamol
- Salbutamol may be used as a second line tocolytic, in the absence of contraindications.
- It must not be used in addition to Nifedipine, as the two drugs have potentially synergistic actions.
- Salbutamol is contra-indicated in the presence of
  - Maternal or fetal cardiac disease
  - Insulin dependent diabetes
  - Thyroid disease
- Salbutamol should be used with care, as it is associated with maternal tachycardia, hypotension, tremor, pulmonary oedema, hyperglycaemia and hypokalaemia.

Dosage
- If Salbutamol is to be used for tocolysis, 5mg (5mL ampoule Ventolin Obstetric Injection) is added to 100mL of normal saline to produce a 50 mcg/mL solution.
- An IV infusion pump must be used for administration.
- Following the establishment of intravenous access, the salbutamol infusion is commenced at 12 mL/hour (10 mcg/minute) and increased by 4 mL/hour (3.3 mcg/minute) every 30 minutes until:
  - Contractions cease
  - Maternal pulse rate reaches 120 beats/minute or
  - The infusion rate reaches a maximum of 36 mL/hour (30 mcg/minute).

Precautions
- Baseline electrolytes, urea and creatinine before commencement of infusion; repeat as necessary if abnormal.
- Baseline maternal blood sugar level; repeat 4 hourly if abnormal
- Cardiovascular examination including auscultation of lung bases every 8 hours
- No additional intravenous fluids to avoid fluid overload
- Half hourly maternal pulse, BP and respiratory rate until the maintenance dose is reached
- Reduce the infusion if the maternal pulse >120bpm
- CEASE the infusion and request medical review immediately if there is chest pain, dyspnoea or the respiratory rate >30/min
- Baseline electronic fetal heart rate monitoring
Do not exceed 48 hours of salbutamol therapy. Only in exceptional circumstances should the treatment be continued for more than 24 hours.

**Side effects**
- Tachycardia
- Tremor
- Nausea
- Dizziness
- Hypotension
- Pulmonary oedema and cardiac failure
- Hypokalaemia

**Contraindications**
- Maternal or fetal cardiac disease
- Thyroid disease
- Insulin dependent diabetes

### 2: Glyceryl Trinitrate (GTN)
Glyceryl Trinitrate (GTN) is a nitric oxide donor and causes smooth muscle relaxation via the metabolite nitric oxide (NO) which acts as a 2nd messenger to increase Ca²⁺ uptake. Nitric oxide promotes uterine quiescence in pregnancy; current evidence does not support the routine administration of nitric oxide donors in the treatment of threatened preterm labour. Peak action occurs 1-2 hours after application. It acts as a vasodilator. GTN patches provide continuous plasma nitrate concentration up to 24 hours.

**Dosage**
- Apply a 5-10mg transdermal GTN patch to abdominal skin, and repeat the dose in 1 hour if the contractions persist (maximum dose 20mg in 24 hours).

**Side effects**
- Headache
- Facial flushing
- Hypotension and Tachycardia

### 3: Indomethacin
- Indomethacin use may be indicated in association with the insertion of a cervical suture at pre-viable gestations.
- Indomethacin, short term, may be considered when there is a failure or a contraindication to other tocolytics. Theoretical risks of fetal pulmonary hypertension and reduced renal function are debatable in short-term use but clear in the event of extended use.

**Dosage**
- Indomethacin is administered as a 100 mg rectal suppository followed by a 25 mg oral dose every 4 hours for 48 hours.
- If regular uterine contractions persist 1-2 hours after the initial 100 mg suppository an additional 100 mg suppository is administered before beginning oral therapy.

**Side effects**
- Prolonged use of indomethacin, especially in the presence of a relatively mature fetus, may lead to narrowing or occlusion of the fetal ductus arteriosus and/or reduction in fetal renal function.
- As there are no evidence-based indications to continue tocolysis for greater than 48 hours, or at gestations greater than 34 weeks, these potential side effects do not contraindicate the use of indomethacin if other regimens are not safely available (e.g. in the absence of the ability to adequately monitor the possibility of side effects of other regimens and in transport situations).

**Contraindication**
- Peptic ulceration.
REFERENCES (STANDARDS)


National Standards – 1 Clinical care is Guided by Current Best Practice
Legislation - Nil

Related Guidelines – Preterm Labour
Other related documents – Nil

RESPONSIBILITY

<table>
<thead>
<tr>
<th>Policy Sponsor</th>
<th>HoD Obstetrics</th>
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<tbody>
<tr>
<td>Initial Endorsement</td>
<td>June 2003</td>
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</tr>
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