PRETERM LABOUR/BIRTH

DEFINITION

Preterm birth (PTB) is defined as birth before 37 completed week's gestation (up to 36^{+6} weeks) and is one of the most significant causes of perinatal morbidity and mortality. Incidence is between 5-10% in most developed countries.

Preterm labour is diagnosed by regular painful uterine contractions and evidence of cervical change. It may be associated with rupture of membranes or positive fetal fibronectin.

PTB is the major cause of neonatal morbidity and mortality, and results in 75-90% of all neonatal deaths not due to lethal congenital malformations, and 50% of childhood neurological disabilities, including cerebral palsy, blindness and deafness.[1]

Preterm babies are ten times more likely to die than the babies born at term. The risk of death and neurosensory disability increases with decreasing gestational age. PTB is associated with psychosocial and emotional effects within the family and huge cost implication on the healthcare system.

Prevention of PTB has the potential to reduce adverse outcomes. Management involves identification of high-risk women, prevention and treatment.

RISKS

- Previous preterm birth
- Infection/inflammation
- Cervical weakness – congenital and acquired
- Uterine abnormality
- Multiple pregnancy
- Haemorrhage
- Intrauterine growth restriction
- Caesarean section at full dilatation

IDENTIFICATION AND PREVENTION

PREVIOUS PRETERM BIRTH

Identification of women at high-risk of PTB is important as the risk of PTB after one and two previous PTB is 15% and 41% respectively.[2]

FETAL FIBRONECTIN

Fetal fibronectin is an appropriate screening test to use for women presenting with suspected preterm labour from 24^{+0} to 36^{+0} weeks gestation. A negative test has a high negative predictive value: 99.5%

of women with a negative result will not give birth spontaneously in the 7 days following the test. The predictive value of positive test is less useful. Only 13-30% of women with a positive test result will deliver preterm in next 7days[3].

CERVICAL LENGTH

The rate of PTB below 32weeks was 1%, 4% and 78% with cervical length of > 25 mm, < 15 mm and < 5 mm respectively in one study.[4] Cervical length < 25 mm in women with previous cone biopsy is associated with increased risk of PTB < 35 weeks (likelihood ratio is 4.7).[5]

CERVICAL CERCLAGE[6-12]

Cervical cerclage will provide a degree of structural support to a weak cervix, as well as maintain the cervical length and the endocervical mucus plug as mechanical barrier to ascending infection.

Women who fulfil the following criteria should be offered elective cerclage

- History indicated cerclage: women with three or more previous preterm births (< 33+6 weeks') and/or second trimester losses
- Ultrasound indicated cerclage: women with one or more spontaneous PTB (< 33^{+6} weeks') or second trimester loss **and** with cervical length ≤ 25 mm before 24 weeks of gestation, who are undergoing transvaginal sonographic surveillance

Indications for serial sonographic surveillance of cervical length

- Women with history of spontaneous PTB (< 33^{+6} weeks') or second trimester loss
- Women with three or more previous preterm birth (< 33^{+6} weeks) who have decided against cerclage
- History of a cone biopsy or more than one LLETZ procedure with known depth excision ≥10mm[22]

It is reasonable to commence the sonographic surveillance of cervical length from 14 and until 24 weeks of gestation. The frequency can be fortnightly or monthly and should be individualised.

There is no evidence to support cerclage in the following situations

- Incidental finding of short cervix in the absence of past history of spontaneous PTB or second trimester loss
- Funnelling of cervix in the absence of shortening ≤ 25 mm
- Multiple pregnancies
- Uterine anomalies
- Cervical trauma (cone biopsy, LLETZ, laser ablation or diathermy) with normal cervical length.

BACTERIAL VAGINOSIS

Bacterial vaginosis is a polymicrobial condition associated with PTB. Women deemed high risk (with history or symptoms of bacterial vaginosis and preterm labour) should be screened, and if found positive for bacterial vaginosis, should be treated. Metronidazole and topical clindamycin are equally effective.[13] Topical clindamycin is not currently a registered drug in New Zealand. The recommended regimen is oral metronidazole 400 mg twice daily for seven days. As metronidazole is not

recommended in the first trimester, treatment may need to be delayed until after 13 weeks of gestation.

UREAPLASMA

Uncertainty exists as to whether treatment of ureaplasma or mycoplasma is indicated, but when isolated should be treated with erythromycin. When previous PTB has been associated with chorioamnionitis and positive ureaplasma screening, treatment may be considered.[14]

PROGESTERONE

Progesterone promotes pregnancy and uterine quiescence. There is good evidence that progestagenic agents such as 17Hydroxy progesterone and natural progesterone reduce the risk of preterm labour.[15] The drug of choice is progesterone 100 mg (Utrogestan® Capsules) inserted vaginally once a day until 34 weeks of gestation. (Request Special Authority)

ASSESSMENT

EXAMINATION AND INVESTIGATION

- Maternal temperature, pulse and blood pressure
- General examination including abdominal palpation
- Palpate for uterine activity
- Fetal heart rate monitoring to ascertain fetal response to contractions (>28 weeks)
- Vaginal assessment with sterile speculum
- Fetal fibronectin – from 24^{+0} to 36^{+0} weeks gestation
  - take first before any digital examination or any further swabs as any physical manipulation of the cervix may cause release of fetal fibronectin from the membranes, thus resulting in a positive test result.
  - false positives likely if any vaginal bleeding, or vaginal examination or sexual intercourse in last 24 hours
  - not appropriate if cervix > 3 cm dilated or obvious ROM
- Use warm water only as a lubricant for the sterilized speculum exam. Do not use lubricants, soaps or disinfectants (K-Y, Monistate) before, or during specimen collection. The presence of lubricants or creams may interfere with the test.

  Microbiology:
  - Endo cervical chlamydia and gonorrhea
  - Endo cervical swab for Ureaplasma, Mycoplasma bacteriology, etc.
  - High vaginal swab
- Assess effacement and dilatation (visual – not digital before fibronectin swab)
  - exclude obvious rupture of membranes (ROM)
- Mid-stream urine

- Blood testing
  - full blood count
  - CRP
- Other investigations as clinically indicated
- Ultrasound scan if needed to assess fetal wellbeing, presentation, fetal growth, and placental morphology
- Fetal monitoring
  - cardiotocograph is appropriate beyond 28 weeks
  - intermittent auscultation < 28 weeks

MANAGEMENT

STEROID ADMINISTRATION

For women < 24 weeks gestation steroids must not be given before consultation with the neonatal consultant.

Any woman presenting between 24 and 36 weeks with threatened preterm labour and a positive fetal fibronectin result should be offered a course of steroids, to improve neonatal outcome.

The recommended dose is Betamethasone 11.4 mg IM 2 doses 24 hours apart, however if the birth is imminent consideration may be given for a 12 hourly dose regimen.

The effect of steroids last for approximately 7 days after the last dose.

Repeated courses are not routinely given.

If 14 days have lapsed and a woman remains at risk of giving birth within 48 hours, and the gestation remains below 36 weeks, a single dose of steroids should be offered to the woman, in consultation with the obstetric consultant.

Between 36-39 weeks of gestation, if a woman requires a caesarean section she should be offered steroids, as outlined above.

TOCOLYSIS

Tocolysis should be considered to gain a few days, to complete the course of steroids or for in-utero transfer.[16]

A Cochrane review comparing calcium channel blockers with other tocolytic drugs showed the use of calcium channel blockers was associated with reduction in the number of women giving birth within 7 days of receiving treatment and before 34 weeks of gestation.[15] Calcium channel blockers are associated with fewer side effects and reduced need to stop treatment because of side effects. Nifidepine is the drug of choice. The reported adverse effects of Nifedipine are flushing, nausea, vomiting and hypotension.

Precautions before prescribing nifedipine

- Congestive heart failure
- Aortic stenosis
- Angina

Contraindications to nifedipine as a tocolytic

- Cardiac disease (myocardial infarction in last seven days)
- Porphyria
- Severe hypotension

In such circumstances discuss the appropriateness of salbutamol for tocolysis with the obstetrician and obstetric physician on call.

Appendix 1 and Appendix 2 for regimen

Contraindication to tocolysis

1. Gestational age > 34 weeks
2. Significant vaginal bleeding or suspected abruption
3. Intrauterine infection
4. Fetal anomaly not compatible with life
5. Maternal indication for birth exists (eclampsia, preeclampsia)
6. Pathological fetal heart rate tracing
7. Maternal refusal of treatment.

ANTIBIOTIC ADMINISTRATION

The risk of EOGBS (Early Onset Group B Streptococcus) disease in infants of those women who deliver preterm term is estimated to be 2.3/1000 [17] and the mortality rate from infection is 20-30% compared to 2-3% at term. For this reason, IAP (Intrapartum antibiotic prophylaxis) is recommend for women in confirmed preterm labour. However, IAP is not recommended for women requiring caesarean section with intact membranes.

Appendix 3 for regimen

RESCUE CERVICAL CERCLAGE

The decision to place emergency cerclage should be individualised and decision should be made by a senior (SMO) obstetrician. Rescue cerclage may delay birth by further 5weeks on average compared with bed rest/expectant management alone [18, 19, 20, 21]

Rescue cerclage is performed in rare cases between 18 and 24 weeks where the following criteria are met for the preceding 12 hours:

- Intact membranes
- No bleeding
- Cervical dilatation
- Uterine activity has subsided
- No intrauterine infection is suspected
- Normal detailed anatomy scan.

Contraindications for cerclage insertion:

- Active preterm labour
- Clinical evidence of chorioamnionitis
- Continuing vaginal bleeding
- PPROM
- Evidence of fetal compromise
- Lethal fetal defect
- Intrauterine fetal demise

FETAL AND MATERNAL MONITORING

FETAL MONITORING

- Continuous EFM while uterine activity continues, and the woman is over 28 weeks gestation
- Intermittent fetal heart auscultation once uterine activity settles
- Arrange interval ultrasound assessment if pregnancy ongoing to assess fetal wellbeing.

MATERNAL WELLBEING

Before treatment begins:

- Temperature, pulse and blood pressure.

First hour:

- Every 30 minutes, temperature, pulse and blood pressure.

Subsequently:

- Hourly for 2 hours and then four times a day.

ONGOING MANAGEMENT

MODE OF BIRTH

If baby is cephalic and there is no other contraindication- plan for a vaginal birth.

There is no indication for prophylactic instrumental birth or episiotomy (these should be reserved for the usual obstetric indications).

Caesarean section for breech presentation at early gestational age is controversial and discussion between senior obstetrician, staff and the woman and her family, should precede any decision about planned mode of birth.

If a decision is made for preterm caesarean section – assistance of a consultant obstetrician at birth is required for any registrar who has not been credentialed to be able to perform such a birth unsupervised.

NEONATAL TEAM

The neonatal consultant should be advised of any women in preterm labour from 22 weeks gestational age onward.

Where possible they will discuss the likely events, which might occur with respect to the baby at birth and in the neonatal period. The parents may be offered the opportunity to visit the neonatal unit, and to meet the neonatal social worker.

TRANSFER TO MATERNITY WARD

Most women should be transferred to the Maternity ward from the Birthing Suite, once uterine activity settles. This decision should be made in consultation with the obstetric team.

LONG TERM MANAGEMENT

If uterine activity has ceased and no other additional risk factors are present, care may be transferred back to the LMC

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APPENDIX 1 NIFEDIPINE REGIMEN[22]

NIFEDIPINE SLOW RELEASE: DOSE	TIME
Max dose 60 mg/24 hours after loading dose completed	
Loading dose: 20 mg orally – crushed tablet*	Stat *and* at 60 min
20 mg orally – swallowed whole	8 hourly until the completion of steroids

** First and second tablets of nifedipine should be crushed prior to administration to hasten absorption. All subsequent tablets should be swallowed.*

APPENDIX 2 SALBUTAMOL REGIMEN

Commence at 10 microgram/min IV increase according to response until contractions diminish (max 45 microgram/min) maintain rate for 1 hour after contractions have stopped then reduce by 50% every 6 hours until steroid course is completed.

Monitor for signs of fluid overload and heart failure.

Reference - 2008 British National Formulary

APPENDIX 3 ANTIBIOTICS IN PRETERM LABOUR (REGARDLESS OF GROUP B STATUS)

GESTATION	ANTIBIOTIC THERAPY
<37 weeks of gestation	**Amoxicillin** IV 2g q6h (in 100 mL 0.9% Sodium Chloride over 30-60 minutes)
With signs of infection **add**	**Gentamicin** 5 mg/kg OD IV infusion (in 100 mL 0.9% Sodium Chloride over 30 minutes) *(if more than one dose required contact CWH pharmacist on Pager 5009 for advice on monitoring serum concentrations)* **and** **Metronidazole** 500 mg IV (over 30 minutes) 12 hourly in labour (*To consult with pharmacist if required postnatally)*
If the woman is allergic to penicillin , replace penicillin component with:	**Low risk of anaphylaxis*** Cephazolin IV 2g q8 hourly until birth **High risk of anaphylaxis*** Clindamycin IV 600mg q8h

** Low risk of anaphylaxis - women who do not have history of anaphylaxis, angioedema, respiratory distress or urticaria after penicillin or a cephalosporin*