Preterm Labor

Background

Despite recent technologic advances in obstetrical and neonatal care, the incidence of preterm birth has remained constant. Approximately 10–12% of infants are born prematurely (<37 completed weeks). Approximately 1% are very low birth weight (<1500 g). While birth weight-specific perinatal and neonatal mortality has declined, an infant with a very low birth weight is still much more likely to experience perinatal mortality or be neurologically impaired than those weighing ≥2500 g.

Etiology and Epidemiology

Historical factors
Certain epidemiologic and pregnancy characteristics have been associated with an increased risk for preterm delivery, including:

◆ Low socioeconomic status
◆ Nonwhite race
◆ Maternal age <18 or >40 years
◆ Previous 2nd-trimester loss
◆ Chemical dependency on cocaine or tobacco
◆ Multiple gestation
◆ Previous premature delivery (A woman with one previous preterm birth has a 15% recurrence risk for preterm delivery in a subsequent pregnancy. With two previous preterm births, the recurrence risk is 40%).

Reproductive-tract abnormalities
Congenital uterine malformations, such as bicornuate or unicornuate uterus, and in some instances, uterine myomata—especially submucosal—may increase the risk for preterm delivery.

Cervical incompetence may also predispose to premature labor and may be either:

◆ Congenital, as in association with uterine malformation, or
◆ As a result of a maternal in utero teratogen exposure from diethylstilbestrol, or
◆ Acquired from previous obstetrical trauma or conization of the cervix.

A dynamic cervix has been described as a predisposing risk for preterm delivery. (Dynamic cervix is a diagnosis describing dilation of the internal os and funneling of the lower uterine segment and membranes into the cervical canal. The diagnosis is best made in the second trimester by either a transabdominal or transvaginal ultrasound.)

Infectious etiologies and abnormal serum markers
Risk factors for preterm delivery also include infectious factors. Very early labor (prior to 28 weeks) is more likely the result of infection than labor occurring after 28 weeks. In one study, 83% of preterm labor of less than 28 weeks had chorioamnionitis. Patients with bacterial vaginosis are also at higher risk. The odds ratio for preterm birth in association with bacterial vaginosis in most studies ranges from 1.5 to 3.0. In high-risk patients with bacterial vaginosis, one study showed a decreased incidence of preterm labor with prophylactic metronidazole and ampicillin. Broad-spectrum antibiotics administered after premature rupture of membranes have also been shown to improve outcomes for the neonate.

Prevention

Because the prevalence of preterm delivery has not decreased, it is safe to say that an effective prevention program has not been established. According to studies, pregnancy risk-scoring systems, bed rest, home uterine-activity monitoring, and routine cervical examinations have not conclusively shown benefits. Additionally, the efficacy, timing, and duration of administration of antibiotics have yet to be determined. Of all preventive measures, early
access to prenatal care and frequent medical and nurse contact—along with active patient education—appear to be the best approach.

**Diagnosis**

The signs and symptoms of preterm labor may be subtle, including:

- Uterine contractions or menstrual-like cramps
- The feeling of pelvic pressure
- Increase in vaginal discharge
- Diarrhea

While the above symptoms frequently occur in the absence of preterm labor, patients with these complaints should warrant prompt evaluation. There is no question that preterm labor is over-diagnosed, most commonly in the presence of uterine contractions without cervical change.

*Uterine contractions in the presence of significant cervical effacement of ≥75%, cervical dilation ≥2 cm, and low presenting part or balloons of the lower uterine segment are associated with a high risk for preterm delivery and should be treated aggressively.*

Fetal fibronectin, a basement membrane protein produced by the placenta and membranes, is a predictor of the likelihood of preterm birth. Its presence in cervical mucus at 24 weeks led to a 60-fold increase in delivery prior to 28 weeks. If negative with preterm contractions, there is less than a 1% chance of delivery within 2 weeks. A rapid screening assay for its detection is now available.

**Management**

Patients with complaints consistent with preterm labor should be promptly evaluated, including evaluation of the cervix, initially with speculum if there is concern about premature rupture of membranes.

*If premature rupture of the membranes has occurred, digital examination of the cervix should NOT be done unless the patient is actively laboring, since the risk for infection is significantly increased.*

Initial therapy for preterm labor usually consists of IV hydration and evaluation for urinary tract infection; however, IV hydration has NO established benefit, and excessive hydration is best avoided.

After a diagnosis of premature labor has been made, consider the following issues:

- **Tocolysis**
  
  Available data suggest that tocolysis is effective in most cases for 48–72 hours. Commonly used agents include:
  - Magnesium sulfate
  - Beta-adrenergic agents (terbutaline, ritodrine)
  - Nonsteroidal anti-inflammatory drugs (indomethacin)
  - Calcium channel blockers (nifedipine)

  Contraindications to tocolysis for preterm labor are listed in Table I.

- **Group B streptococcus prophylaxis**
  
  Preterm infants are especially prone to neonatal GBS infection. Cultures from the introitus and anus area should be sent for GBS culture. In the meantime, treat the patient with IV antibiotics until the results return. Acceptable coverage would include penicillin G, ampicillin, cephalosporins, or vancomycin.
◆ Fetal-lung maturity assessment
Amniocentesis may play a role in evaluating patients in preterm labor. A sample of amniotic fluid may be sent for fetal pulmonary testing, including fluorescent polarization, which is commonly used in the Seattle area, with results available within two hours. The L/S ratio is an acceptable alternative. Since perinatal morbidity and mortality are closely linked to pulmonary status, knowing the fetal pulmonary maturity status may be helpful in guiding therapy with glucocorticoids and determining place of delivery. In addition, amniotic fluid may be sent for gram stain and culture and amniotic fluid glucose assessment, since as many as 15% of patients with idiopathic preterm labor may have infection as an underlying cause. Amniotic fluid containing white cells, bacteria, or a low glucose level has a high association with chorioamnionitis. In this situation, labor may not be postponed, and should be treated aggressively with antibiotics and delivery.

◆ Glucocorticoid treatment
A recent consensus conference on antenatal glucocorticoids concluded that antenatal treatment is effective in reducing the incidence of hyaline membrane disease in preterm deliveries and was significantly underutilized. If fetal pulmonary testing is performed and the fluorescent polarization is >270 or the L/S ratio is <2, glucocorticoids should be administered. Although tocolytics are not likely to be effective for more than 48–72 hours, their administration may stave off delivery long enough to allow for the beneficial effects of glucocorticoids. Acceptable dosing includes betamethasone (one dose, 12 mg IM, followed by a second dose 24 hours later) or dexamethasone (6mg IV q 6h X 4). Glucocorticoids may be used with ruptured membranes, but in these cases, amniocentesis may be performed prior to administration, if possible, to rule out amniotic fluid infection. In pregnancies of ≤30 weeks’ gestation, only 10% will have mature fetal lungs. At 32 weeks, 25–30% will have reached pulmonary maturity, and 95% will have mature lungs at 36 weeks. The benefits of glucocorticoid administration after 34 weeks of gestation have not been established.

◆ Maternal transport
Survival rates for preterm/very low birth weight infants and premature infants with pulmonary immaturity are higher in Level III centers than those born in Level I and II facilities. If time is available for safe maternal transport in these cases, such transport should be strongly considered. Each hospital, in conjunction with obstetric, pediatric, and neonatal consultation, should develop guidelines for maternal and neonatal transport.

◆ Continued tocolysis
After initial evaluation and a decision made to transport or keep a mother, tocolysis usually should be continued for a minimum of 48 hours. Tocolytic drugs may have major side effects to mother and fetus and should be administered only under careful supervision. The goal of tocolysis is to minimize uterine contractions with the least amount of drug possible. Potential complications of tocolytic agents are listed in Table II. The best outcomes result from a carefully constructed protocol for tocolysis. Each hospital, in conjunction with obstetric, neonatal, and pediatric staff, should develop a protocol for evaluation of preterm labor and safe administration of tocolytic agents.

◆ Consultation
As with any complicated case, consultation with obstetric, pediatric, neonatal, or perinatal colleagues should be encouraged.
♦ Risk management implications

Maintain a high index of suspicion for the patient with a previous history of preterm birth, as well as for the patient who reports subtle changes (e.g., cramps, backache, increased discharge). These patients need to be seen frequently and monitored carefully with screening for infection, cervical changes, and fetal fibronectin.

For those patients that deliver prematurely, ALL involved parties should be informed in anticipation, including neonatology and anesthesia. If possible, these babies should be transferred in utero to a Level III facility.

It is important to obtain the appropriate cultures from cervix and amniotic fluid and to send the placenta for pathological examination to document the presence of chorioamnionitis.

References


Table I

Contraindications To Tocolysis For Preterm Labor*

General Contraindications

- Acute fetal distress (except intrauterine resuscitation)
- Chorioamnionitis
- Eclampsia or severe preeclampsia
- Fetal demise (singleton)
- Fetal maturity
- Maternal hemodynamic instability

Contraindications for Specific Tocolytic Agents

**Beta-mimetic Agents**

- Maternal cardiac rhythm disturbance or other cardiac disease
- Poorly controlled diabetes, thyrotoxicosis, or hypertension

**Magnesium Sulfate**

- Hypocalcemia
- Myasthenia gravis
- Renal failure

**Indomethacin**

- Asthma
- Coronary artery failure
- Gastrointestinal bleeding (active or past history)
- Oligohydramnios
- Renal failure
- Suspected fetal cardiac or renal anomaly

**Nifedipine**

- Maternal liver disease

* Relative and absolute contraindications to tocolysis based on clinical circumstances should take into account the risks of continuing the pregnancy versus those of delivery.

### TABLE II

**Potential Complications Of Tocolytic Agents**

#### Beta-Adrenergic Agents

- Hyperglycemia
- Hypokalemia
- Hypotension
- Pulmonary edema
- Cardiac insufficiency
- Arrhythmias
- Myocardial ischemia
- Maternal death

#### Magnesium Sulfate

- Pulmonary edema
- Respiratory depression*
- Cardiac arrest*
- Maternal tetany*
- Profound muscular paralysis*
- Profound hypotension*

#### Indomethacin

- Hepatitis‡
- Renal failure‡
- Gastrointestinal bleeding‡

#### Nifedipine

- Transient hypotension

* Effect is rare; seen with toxic levels.
‡ Effect is rare; associated with chronic use.

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