Preterm Labor

CONTENTS

BACKGROUND
FACTORS ASSOCIATED WITH PRETERM LABOR
DIAGNOSIS
INTAKE ASSESSMENT
MANAGEMENT
ASSESSMENT OF FETAL LUNG MATURITY
SOURCES

KEY POINTS

1. Preterm labor is uterine contractions resulting in progressive cervical change prior to 37 weeks gestation. Preterm delivery is delivery prior to 37 weeks gestation; low birthweight infants are those that weight less than 2500 g at delivery.
2. Prior to 34 weeks gestation, most patients should be considered for tocolysis; from 34 to 37 weeks gestation such decisions must be made on a case-by-case basis.
3. Complications associated with preterm delivery include increased perinatal mortality and complications of prematurity (including respiratory distress, gastrointestinal dysfunction, hemorrhage, and abnormalities of growth and development).

BACKGROUND

Preterm labor is among the most common and most serious of prenatal complications. Preterm labor and its potential sequellae of preterm delivery and low-birthweight (LBW) infants remain one of the most significant challenges of current obstetrical practice. Preterm labor is defined as uterine contractions resulting in progressive cervical change prior to 37 weeks gestation. Preterm delivery is delivery prior to 37 weeks gestation. LBW infants are defined as those infants weighing less than 2500 g at delivery regardless of gestational age.

From: Current Clinical Practice: Obstetrics in Family Medicine: A Practical Guide
By: P. Lyons © Humana Press Inc., Totowa, NJ

55
LBW infants should be distinguished from small-for-gestational-age (SGA) infants who are defined as those infants below the fifth percentile for weight based on gestational age.

Preterm labor affects approximately 10% of all pregnancies. Preterm delivery affects approximately 13% of all live births. Preterm delivery and LBW infants represent approximately 70% of all perinatal mortality (~25,000 deaths annually) and 50% of all neurological morbidity.

FACTORS ASSOCIATED WITH PRETERM LABOR

A number of factors have been associated with an increased risk of preterm labor. These are summarized in Table 1. These factors can be divided into pre- and postconception factors. Although the mechanisms that link these factors to the onset of preterm labor is, in most instances, poorly understood, a thorough review of the patient’s history will allow providers to more carefully outline the risk of preterm labor, preterm delivery, and LBW infants.

Although preterm labor alone is not associated with perinatal complications, concomitant conditions and outcomes are. Preterm labor may be complicated by preterm premature rupture of membranes (PPROM). PPROM is associated with a variety of complications discussed in Chapter 8. Preterm labor may also result in preterm delivery. Prematurity, in turn, is potentially associated with pulmonary dysfunction, gastrointestinal abnormalities, neurological complications, abnormalities of growth and development, and a significant risk of perinatal mortality. Complications of preterm delivery are the leading cause of perinatal mortality, responsible for approximately two-thirds of all deaths.

Preconception Factors

ENVIRONMENTAL FACTORS

A number of environmental factors have been associated with an increased risk of preterm labor. The most significant environmental factor associated with preterm labor is lower socioeconomic status.

PATIENT-RELATED FACTORS

A number of pre-existing patient conditions also contribute to the risk of preterm labor. Patients may have a pre-existing genetic risk, a congenital anomaly (e.g., septate/bicornuate uterus or cervical incompetence), a pre-existing acquired obstetrical/gynecological risk (e.g., myomata, uterine surgery, diethylstilbestrol exposure), or a past history of preterm labor or second trimester spontaneous abortions. The recurrence rate of preterm labor is approximately 25%. Additionally, the risk of preterm labor is highest among younger (<18 years old) and older (>40 years old) obstetrical patients. These conditions can
be screened for early in pregnancy (or during preconception counseling). Although many of these factors are not modifiable, their presence can usefully contribute to a conversation between the provider and the patient concerning the risk for preterm labor during the current pregnancy.

**Postconception Factors**

Once conception occurs, a number of additional factors contribute to the risk of preterm labor. An increased risk for preterm labor is associated with tobacco and cocaine use. Infections such as group B streptococcus, gonorrhea, chlamydia, trichomonas, gardnerella, ureaplasma, and mycoplasma have all been associated with increased preterm labor risk. Such exposures should be screened for at the first prenatal history (either directly through testing or via history) and as appropriate throughout the course of pregnancy.

**DIAGNOSIS**

As noted earlier, the diagnosis of preterm labor consists of three components: gestational age less than 37 weeks, presence of uterine contractions, and progressive cervical change.

The diagnosis of preterm labor begins with confirmation of the gestational age of the fetus. All data that contributed to the estimated date of delivery (EDD) should be reviewed for accuracy. The patient’s last menstrual period should be reviewed for accuracy. Additional data such as prenatal ultrasound, sequential fundal height measurements and gestational age at quickening should also be reviewed. If no such data is available, an obstetrical ultrasound may be indicated. It should be emphasized, however, that an ultrasound

<table>
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<th>Table 1</th>
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<td><strong>Risk Factors for Preterm Labor</strong></td>
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<tr>
<td><strong>Preconception factors</strong></td>
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<tr>
<td>Lower socioeconomic status</td>
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<tr>
<td>Anatomic abnormalities (e.g., septate/bicornuate uterus, cervical incompetence)</td>
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<td>Prior uterine surgery</td>
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<td>Myomata</td>
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<tr>
<td>Diethylstilbestrol exposure</td>
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<tr>
<td>Past history of preterm labor</td>
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<td>Under 18 years old, over 40 years old</td>
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<tr>
<td>Possible genetic predisposition</td>
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<tr>
<td><strong>Postconception factors</strong></td>
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<tr>
<td>Tobacco</td>
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<td>Cocaine</td>
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<tr>
<td>Infection (e.g., Group B streptococcus, <em>N. gonorrhea</em>, <em>C. trachomatis</em>, trichomonas, gardnerella, ureaplasma, mycoplasma)</td>
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obtained late in pregnancy has significantly less accuracy for purposes of gestational dating.

The patient should be questioned concerning the presence of contractions (although the absence of patient reported contractions does not exclude the possibility of clinically significant contractile activity). If preterm labor is suspected, patients should be placed on tocometric monitoring to confirm the presence of uterine contractions.

Documentation of progressive cervical change, under most circumstances, requires serial cervical examinations. After confirming the absence of bleeding per vagina, providers should document cervical dilation and effacement as well as fetal station. Although the patient may demonstrate unequivocal cervical evidence of labor on initial examination, generally the diagnosis will require comparison of initial findings to findings on a follow-up examination.

INTAKE ASSESSMENT

History

In addition to the history noted earlier, patients should be asked about bleeding per vagina, rupture of membranes or fluid leak, and/or symptoms of infection. Special caution should be exercised if the patient reports a history of bleeding per vagina. The management of third trimester bleeding is covered in Chapter 10. A review of the past history should note the presence of cardiac, renal pulmonary, and/or endocrine abnormalities.

Physical Examination

In addition to the pelvic examination for assessment of cervical change, the intake physical examination should document blood pressure, pulse, temperature, rupture of membranes (see Chapter 8), fetal heart rate, and uterine contractions.

Laboratory Studies

Patients admitted with preterm labor should have all prenatal laboratory values reviewed with lab values ordered or updated as necessary. Patients may require testing for infection, including gonorrhea, Chlamydia, group B strep trichomonas, and bacterial vaginosis. Other studies that may contribute to evaluation of possible infection include increased interleukin-6 in amniotic or cervical samples, elevated ferritin in cervical or serum samples, and elevated granulocyte colony-stimulating factor in serum samples. Patients demonstrating clinical signs or symptoms of other obstetrical conditions (e.g., pregnancy-induced hypertension) should have laboratory evaluation as indicated for those conditions.

Controversy exists concerning the role of routine fibronectin testing in the management of suspected preterm labor. After 20 weeks gestation a result
greater than 50 ng/mL is associated with an increased risk for preterm delivery with a sensitivity of 70–90% and a specificity of 70–85%. The negative predictive value is approximately 99%. A negative test is a strong predictor of no preterm labor in the week following the test.

**MANAGEMENT**

The management of preterm labor is often limited in efficacy and duration and few modifiable factors have been identified. A general outline of management is shown in Fig. 1. Decisions concerning appropriate management should be tailored to the individual patient. Despite the challenge and variability involved in managing preterm labor a few general guidelines can be given.

**Management Prior to 34 Weeks Gestation**

In general, fetal lung maturity cannot be assumed in infants prior to 34 weeks gestation. For this reason, tocolysis is generally recommended. Although the efficacy and duration of such therapy is limited, a brief delay in delivery allows for administration of corticosteroids to enhance fetal lung maturity. All patients should be screened for contraindications to tocolysis (see Table 2). Contraindications to tocolysis include underlying medical contraindications (cardiac disease, renal insufficiency, pyelonephritis, pulmonary hypertension, untreated diabetes mellitus, and electrolyte abnormalities) and obstetrical contraindications (fetal stress, chorioamnionitis, eclampsia, fetal demise, and hemodynamic instability). Tocolytic options include the following:

1. Terbutaline (β-2-sympathomimetic): 250 μg subcutaneously every 3–4 hours.
2. Ritodrine (β-2-sympathomimetic): 100 μg per minute intravenous starting dose. Dose increased 50 μg per minute every 20 minutes until contractions cease.
3. Magnesium sulfate (MgSO₄): 6 g intravenous load over 15 minutes then 2 g per hour. May be increased every hour until contractions cease, maximum dose of 5 g per hour is reached or signs or symptoms of magnesium toxicity occur. Magnesium toxicity may be noted as neurological depression, cardiac depression or arrest, tetany, and hypotension. Monitoring of all patients on magnesium should include serum magnesium levels, maternal deep tendon reflexes, blood pressure, and strict recording of fluid input and output. Urinary retention is associated with magnesium use. Magnesium levels above 7 mEq/L are associated with diminished deep tendon reflexes; above 10 mEq/L with respiratory depression; above 12 mEq/L with cardiac depression and arrest. Magnesium toxicity is treated with calcium gluconate 1 g intravenous.
4. Indomethacin (nonsteroidal anti-inflammatory, prostaglandin inhibitor): 100 mg per rectum or 50 mg orally loading dose; 50 mg per rectum or 25 mg orally every 4–6 hours. Prior to 32 weeks, indomethacin has been shown to have equal efficacy to β-2-sympathomimetic agents probably by inhibiting
Use of indomethacin is associated with oligohydramnios and premature closure of the ductus arteriosus. For this reason, all patients on indomethacin should undergo frequent (every other day) ultrasound examinations to monitor for oligohydramnios. Because of the concern for premature ductus arteriosus, closure the use of indomethacin after 32 weeks gestation is controversial.

Fig. 1. Management of preterm labor.
5. Nifedipine (calcium channel blockade): 20 mg orally loading dose; 10 mg orally every 6 hours. Nifedipine’s action in blocking calcium channel function in smooth muscle is postulated to explain its efficacy in reducing uterine contractility. Studies have demonstrated efficacy similar to β-2-sympathomimetic agents.

Patients should be admitted and placed on bed rest. If significant cervical dilation has occurred, patients may be placed in a head-down position. Routine management includes monitoring of fluid status, hemodynamic status, and fetal well-being. If there is question concerning the gestational age or fetal lung status, fetal lung maturity testing may be considered. Mothers of infants at risk for fetal lung immaturity (24–35 weeks gestation) should be treated with 12 mg of betamethasone, intramuscularly. Two doses should be given 24 hours apart. Patients with evidence of contributory infection should be treated as appropriate for the infection.

**Management at 34–37 Weeks**

Fetal lung maturity in this range is highly variable and decisions to initiate tocolysis must be individualized. When time permits, assessment of fetal lung maturity may assist in decisions concerning tocolysis versus expectant management.

**ASSESSMENT OF FETAL LUNG MATURITY**

Delivery of an infant prior to fetal lung maturation is associated with considerable neonatal morbidity and mortality. For this reason, assessment of fetal lung maturity is critical in all instances where gestational age cannot be firmly established or when prenatal complications require consideration of an early delivery.
Confirmation of the gestational age is critical. Gestational age can be confirmed by review of the last menstrual period, early obstetrical ultrasound results, and key developmental milestones such as quickening and fetal heart tones. Although these data may allow for accurate gestational dating when available, not all data will be available in all cases. Even with such data, a more accurate assessment of fetal lung maturity may be necessary to guide management decisions. A variety of options are available to assist in this assessment.

**Lecithin-Sphingomyelin Ratio**

As fetal lung maturity progresses, pulmonary secretions are accumulated in the amniotic fluid allowing for assessment of fetal lung maturity based on amniotic fluid sampling. Lecithin and sphingomyelin are present in approximately equal quantities until approximately 8 weeks prior to the EDD. Beginning at this point, lecithin concentrations increase and sphingomyelin concentrations remain stable. As the fetus nears maturation, therefore, the ratio of lecithin to sphingomyelin will increase. Although the exact interpretation of the results may be site-dependent, a lecithin-to-sphingomyelin ratio of 2:1 is associated with generally favorable neonatal pulmonary outcomes.

**Phosphatidylglycerol**

The presence of blood or meconium in the amniotic fluid may alter the results of the lecithin-to-sphingomyelin ratio. For this reason, alternative tests have been developed that are not sensitive to the presence of these substances. One such test is phosphatidylglycerol, a component of surfactant that is present in increases quantities as fetal lung maturity advances. Amniotic fluid samples may be tested for phosphatidylglycerol alone or in conjunction with lecithin–sphingomyelin testing. The presence of phosphatidylglycerol is associated with more advanced fetal lung maturity and therefore with generally improved neonatal pulmonary outcomes. The results may be reported either qualitatively or quantitatively.

**SOURCES**


