10/18/18njm

ANMC WOMEN'S HEALTH SERVICE
PRETERM PRELABOR RUPTURE OF MEMBRANES

1. Definition:

Rupture of the membranes prior to 37 weeks gestation and prior to the onset of labor.
(To be distinguished from "prelabor rupture of membranes" prior to the onset of labor at term, and from premature rupture of membranes without labor prior to viability at 23-24 weeks, which is most commonly associated with "hour-glassing" of the membranes secondary to cervical insufficiency.)

a. Associations with PPROM:
-same as for preterm birth above, current theory is that PPROM is the result of occult infection at the choriodecidual interface with production of microbial collagenases resulting in membrane rupture.

Midtrimester PPROM: KEY POINTS

- Midtrimester PPROM is associated with the same risk factors at PPROM later in gestation
- Mean latency is 17 days, median latency is 7 days because the majority of pregnancies deliver soon after rupture of membranes
- The frequency of chorioamnionitis is higher early in the latency period and at lower residual amniotic fluid volumes
- Abruptio placentae and cord prolapse are more common in pregnancies complicated by PPROM
- Neonatal survival is primarily related to gestational age at delivery, and is comparable to that in preterm deliveries matched for gestational age without PPROM.
- The neonatal risk of both pulmonary hypoplasia and musculoskeletal deformation decrease with advancing gestational age, shorter latency, and greater residual amniotic fluid volume.
- Maternal risks from midtrimester PPROM are lower than fetal/neonatal risks and include infection, need for cesarean delivery, and need for classical hysterotomy.
- Absence of amniotic fluid leakage associated with resealing of membranes and reaccumulation of amniotic fluid confers a prognosis comparable to that of pregnancies without PPROM.

Corticosteroids
A single course of corticosteroids is recommended for pregnant women between 23 weeks and 34 weeks of gestation who are at risk of preterm delivery within 7 days.

'Rescue' Steroids
A single course of 'rescue' therapy is reasonable if the patient is clinically estimated to be at high risk of delivery within the next seven days, at least two weeks have passed since the initial course of antenatal corticosteroids, and the initial course was given at

<28 weeks of gestation. However, regularly scheduled repeat courses or multiple courses (more than two) are not recommended.

Antibiotics
There are 3 separate indications to give antibiotics in this setting:
-GBS prophylaxis
-prolong latency period
-treat overt chorioamnionitis

2. Management:

Review pregnancy dating criteria
Perform sterile speculum examination for evidence of amniotic fluid
Refrain from performing a digital examination unless absolutely necessary to document advanced labor prior to transport. (Remember that if you can visualize a portion of the presenting part, the cervix is most likely significantly effaced and dilated at least 4 cm, but if it appears "closed" it may be any dilation <4cm…) Digital examination "winds the clock of infection" and significantly decreases the latency period for the onset of labor, and increases the risk of infection, and is to be avoided in this setting if at all possible.
Confirm presentation by Leopold's and/or ultrasound
Perform level I ultrasound to assess GA, EFW, AFI, presentation, and anatomy
A sample of vaginal pool amniotic fluid for fetal lung maturity testing may be appropriate if the patient is between 34 and 36 weeks gestation
Obtain fetal monitor strip and maternal vital signs
Administer group B strep prophylaxis per guideline
Tocolysis (see above) may be appropriate to facilitate transport, but is otherwise not indicated
Consult with OB-GYN is advised for further management and transport
At ANMC PPROM is managed as an inpatient*
Daily NST should be carried out
Maternal temperature and fetal heart rate are monitored q4h, but the onset of uterine contractions is the most common sign of incipient infection. Overt chorioamnionitis mandates delivery.
Labor may be induced at 34 weeks documented gestation, or sooner with consultation with the Pediatrics service
Patients may be induced with either vaginal or oral misoprostol or IV oxytocin
Group B strep prophylaxis should be re-instituted in labor
If chorioamnionitis is suspected, gentamicin 2 mg/kg IV q8h should also be administered to cover gram negative pathogens
Patients with rupture of membranes **at term** who are not in labor have a better outcome without an increase in their cesarean birth rate if induced as soon as they present.

*In cases of extreme prematurity, expectant management should be individualized. There is 2B data to support antibiotic prophylaxis at 23-24 weeks. The data is only 2C from 20-23 wks. Please consult with either MFM or Neonatalogy.

(Please see ACOG/STFM Consensus Summary: Periviable Birth)

EGA < 34 weeks

Step 1

If less than 23-34 weeks gestation, administer
Betamethasone (12 mg) given intramuscularly 24 hours apart for two doses
or
Dexamethasone (6 mg) given intramuscularly every 12 hours for four doses

Step 2

If GBS status is unknown, obtain a rectovaginal GBS specimen and for 48 hrs administer:

Ampicillin 2 gm IV q 6 hours X 48 hrs

If penicillin allergy is reported, but it is not urticaria or anaphylaxis, the drug of choice is then cefazolin (1 g IV q8h x 48 hrs), not clindamycin. This is followed by cephalexin 500 mg orally four times daily for five days.

plus

Azithromycin 500 mg IV q 24 hr x 48 hrs

If erythromycin allergy is reported, cross-reactivity with azithromycin should likewise be uncommon.

Step 3

To increase the latency period **after 48 hrs,** administer azithromycin 250 mg daily orally for an additional 5 days

Plus

Amoxicillin (500 mg orally three times daily or 875 mg orally twice daily) for an additional 5 days

Use of Magnesium Sulfate for Fetal Neuroprotection

Women with preterm premature rupture of membranes at **26*- 32 weeks** gestation who are expected to deliver within the next 24 hours are eligible for magnesium sulfate for fetal neuroprotection
-upon diagnosis
-in active labor

Exclusion:
Women who have not delivered within 12 hours of admission for PPROM.

1. A loading dose of magnesium sulfate 6 g IV over 20 minutes should be given.
2. A maintenance dose of magnesium sulfate of 2 g/h should be continued for 12 hours.

3. Other orders for antenatal corticosteroids, and group B strep prophylaxis as per guideline.
4. The infusion should be stopped at 12 hours if delivery has not occurred.
5. If delivery is again considered imminent (resumption of active labor and cervix >4 cm dilated) within 12 hours after the infusion has been discontinued, a repeat 6 g bolus is suggested and the infusion may be resumed at 2 g/h. The total length of maternal exposure should be less than 24 hours, even if magnesium sulfate is given in divided doses.
6. < 25 wks: only give 4 gm bolus and 1 gm per hour*

Rescue Steroids
A single course of 'rescue' therapy < 34 wks is reasonable if the patient is clinically estimated to be at high risk of delivery within the next seven days, and at least two weeks have passed since the initial course of antenatal corticosteroids. However, regularly scheduled repeat courses or multiple courses (more than two) are not recommended.

Management of Late Preterm (> 34 wk < 37 wks)
1. In women with a singleton pregnancy between 34 weeks 0 days -36 weeks 6 days of gestation who are at high risk for PTB within the next 7 days (but before 37 weeks of gestation), we recommend treatment with betamethasone (two doses of 12 mg IM twenty four hours apart).

2. In women with preterm labor symptoms in the late preterm (LPT) period, please wait for evidence of preterm labor, such as a cervical dilatation of at least 3 cm or effacement of at least 75%, before treatment with betamethasone.

3. Late preterm antenatal corticosteroid administration should NOT be used in women diagnosed with chorioamnionitis.

4. Administration of late preterm antenatal corticosteroids should NOT be given if the pregnancy was already exposed to antenatal corticosteroids.

5. In women with LPT pregnancies receiving betamethasone, please avoid the use of tocolysis in an attempt to delay delivery to complete the steroid course since it is unclear if the benefits of betamethasone administration are outweighed by the risks of attempts to delay delivery.

6. In women with LPT pregnancies with a potential medical indication for delivery, betamethasone need not be given unless there is a definitive plan for LPT delivery.

7. These recommendation exclude patients with:
Pregestational diabetes, multifetal gestations, previous exposure to steroids during this pregnancy, or pregnancies with one major or two minor non-lethal fetal malformations. (see Appendix 1)

References:

-Prelabor rupture of membranes. ACOG Practice Bulletin No. 188. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e1–14.

- Management of preterm labor. Practice Bulletin No. 171. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e155–64.(Reaffirmed 2018)

- Antenatal corticosteroid therapy for fetal maturation. Committee Opinion No. 713. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e102–9.

-Periviable birth. Obstetric Care Consensus No. 6. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e187–99.

-Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2017 Mar 21:3: Issue 3. Art. No.: CD004454. DOI: 10.1002/14651858.CD004454.pub3.

- Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD001058. DOI: 10.1002/14651858.CD001058.pub3

-Crowther CA, et al. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. (ACTOMagSO4 Trial). JAMA 2003; 290:2669-76.

-Magnesium sulfate before anticipated preterm birth for neuroprotection. Committee Opinion No. 455. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;115:669–71. (Reaffirmed 2018)

-SMFM Publications Committee. SMFM Statement: Implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery. Am J Obstet Gynecol 2016; DOI: 10.1016/j.ajog.2016.03.013.

-Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal betamethasone for women at risk for late preterm delivery. NICHD Maternal-Fetal Medicine Units Network. N Engl J Med 2016; DOI: 10.1056/NEJMoa1516783.

Rescue corticosteroids in PPROM

Crowther CA, et al. Mid-Childhood Outcomes of Repeat Antenatal Corticosteroids: A Randomized Controlled Trial. Pediatrics. 2016 Oct;138(4). pii: e20160947. Epub 2016 Sep 20.

Crowther CA, Haslam RR, Hiller JE, Doyle LW, Robinson JS; Australasian Collaborative Trial of Repeat Doses of Steroids (ACTORDS) Study Group. Neonatal respiratory distress syndrome after repeat exposure to antenatal corticosteroids: a randomised controlled trial. Lancet. 2006 Jun 10;367(9526):1913-9.

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7/31/97
10/11/95
October 1994
January 1988
June 1980

Appendix 2 (See Table 1 and Table 2)

Table 1: Major Fetal Anomalies / Congenital Malformations

(Need one major anomaly for exclusion)

Pulmonary
Congenital diaphragmatic hernia (CDH)
Congenital cystic adenomatoid malformation
Pleural effusions
Chylothorax
Bronchogenic cyst
Bronchpulmonary sequestration

Cardiac
Anomalous pulmonary venous return
Tricuspid atresia
Mitral atresia
Double right ventricle
Ebsteins's malformation
Pulmonary atresia
Hypoplastic left heart syndrome
Transposition of great vessels
Tetrology of fallot
Double outlet right ventricle
Aortic stenosis
Aortic coartation
Fetal arrhythmia (tachycardia, bradycardia, or supraventricular tachycardia)

Genito-urinary
Any genitor-urinary lesion accompanied by oligohydramnios at <24 wks
Bilateral renal agenesis
Cystic renal disease (polycystic or multicystic)
Obstructive uropathy
Horseshoe kidney
Megacystis microcolon
Cloacal abnormality

CNS
Anencephaly
Holoprosencephaly
Dandy-walker malformation or variant
Septo-optic dysplasia
Neural tube defect
Vein of Galen aneurysm

Skeletal
Acondrogenesis
Thanatophoric dysplasia
Osteogenesis imperfecta

Thoracic dysplasia
Hypophosphatemia
Short rib polydactyly
Any skeletal defect with suspected small thorax

Other
Any karyotype abnormality
Any suspected genetic syndrome
Cleft lip/palate
Micrognathia
Hydrops
Fetal anemia
Neck mass
Gastroschisis

Table 2: Minor Fetal Anomalies / Congenital Malformations

(Need two minor anomalies for exclusion)

Cardiac
ASD
VSD
Intracardiac echogenic focus

CNS
Choroid plexus cysts (unilateral or bilateral)
Mild ventriculomegaly (defined by a lateral ventricle measurement of <1.5cm)
Agenesis of the corpus callosum
Arachnoid cyst

Genito-urinary
Pyelectasis
Hydronephrosis
Unilateral renal agenesis (normal AFI)
Pelvic kidney
Hypospadias

Skeletal
Achondroplasia (with normal thoracic circumference)
Clubbed foot (unilateral or bilateral)

Other
Echogenic bowel (Cystic fibrosis negative)
Polydactyly