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PREMATURE RUPTURE OF MEMBRANES (PROM)

Background

1. Definition:
    - PROM: Spontaneous rupture of membranes (SROM) before onset of labor, regardless of gestational age.
    - PROM at term = SROM at gestational age ≥37wks
    - PPROM (Preterm Premature Rupture of Membranes) = SROM at gestational age <37wks
2. General Information[1,2,3,4,5]
    - Treatment based on gestational age (GA) at the time of rupture.
    - Assess for infection and fetal status; treat appropriately regardless of GA
    - If Preterm PROM, be sure to transfer as necessary to facility that can provide appropriate level of care for the neonate.

Pathophysiology[1,2,3]

1. Pathology of Disease:
    - In normal pregrnancy, membranes weaken with increasing gestational age due to:
        - Matrix metalloproteinases (MMP's)
        - Decreased Tissue Inhibitors of MMP's (TIMP's)
        - Increased poly[ADP ribose] polymerase (PARP) cleavage
        - Increased physical stress, specifically intrauterine pressure with contractions.
    - Abnormal balance of cytokines, inhibitors, and physical stress in conjunction with certain risk factors, leads to accelerated breakdown in PROM and PPROM. [3]
2. Incidence, Prevalence:
    - PROM occurs in 8-10% of all pregnancies [1,2,3,5,6,7]
    - PPROM occurs in 3 % of pregnancies; responsible for 1/3 of all preterm births [2,3,4,5]
    - 16-32% risk of repeat PPROM[1]
3. Risk Factors[1,2,4]
    - African American
    - Low socioeconomic status
    - Smoking
    - Nutritional deficiency (Cu, Ascorbic acid)
    - Uterine overdistention (e.g. polyhydramnios, multiple gestations)
    - Vaginal bleeding (2nd or 3rd trimester)
    - Intrauterine infection, GU infections (esp. GC, Chlamydia, Trichomonas, GBS)
    - Connective tissue d/o
    - Pulmonary dz
    - Recent coitus
    - Procedures (cerclage, amniocentesis)
4. Morbidity / Mortality [1,2,3,4]
    - PROM is associated with the following complications:
        - Cord prolapse, cord compression (32-76%)[4]
        - Emergent delivery for non reassuring fetal heart tracing

- Fetal hypoxia and asphyxiation
- Fetal demise (1-2%)
- Neonatal infection
- Neonatal respiratory distress syndrome (35%)[4]
- Chorioamnionitis (13-60%)[4]
- Abruptio placenta (4-12%)[4]
- Retained Placenta, PPH[5]

Diagnostics

1. **History**:
    - *Gush of fluid, LOF (90% accuracy)[5]
2. **Clinical findings**:
    - Pooling of amniotic fluid in posterior vaginal canal on Sterile Speculum Exam
    - Nitrazine test
        - Amniotic fluid pH = 7-7.5, paper turns blue
        - Vaginal secretions pH = 4.5 - 5.5, paper stays yellow
        - Blood pH = 7.4, turns paper blue (false positive)
        - False positive nitrazine test can occur with cervical mucus, semen, bacterial vaginosis , and alkaline antiseptics
        - Sensitivity 93-100%, Specificity 16-52.6% [7,8]
    - Ferning or Arborization of fluid on microscopy
        - False positive ferning can occur with cervical mucus/blood, but ferning pattern will be more floral or skeletonized respectively
        - False negatives can occur with an insufficiently dry slide (<10mins).
    - If unsure with clinical signs, obtain U/S for AFI (<5cm, < 5th percentile, or absence of pocket measuring 2cm x1cm) or ultrasound guided amnioinfusion of indigo carmine dye and observe for passage of dye per vagina within 30mins. [2]

Differential Diagnosis

1. Cervicitis
2. urinary incontinence
3. mucus ‘show’ with cervical dilation and effacement
4. semen
5. vaginal douches

Management [1,2,4,5,9]

1. Digital cervical exams should be avoided in PPROM unless delivery anticipated, because digital exams associated with shortened latency. (SOR:A)[1,4]
2. Assess for infection and fetal status; treat appropriately regardless of GA
3. If PPROM, be sure to transfer as necessary to a facility that can provide the appropriate level of neonatal care.
4. Monitoring of fetal status indicated, but no consensus exists regarding best modality or frequency of monitoring.
5. Long-term tocolysis not indicated for patients with PPROM, although short-term tocolysis may be considered to facilitate maternal transport and administration of corticosteroids/antibiotics (SOR:C)[1,4]

6. GA≥ 37wks: Induction of labor (IOL) and antibiotics if GBS positive, or unknown with risk factors (delivery <37weeks gestation, rupture of membrane for >18hrs, fever >38.0C, intrapartum nucleic acid amplification tests positive for GBS).[10]
7. GA 34-36wks: IOL and antibiotics if GBS positive or risk factors for chorioamnionitis.
8. Multiple courses of corticosteroids or use of corticosteroids after 34 weeks GA not recommended (SOR:B)[1,4,5,11]
9. GA 32-33wks: Give one course of steroids
    - Give antibiotics for GBS and to increase latency (erythromycin and ampicillin)
    - Deliver at 34 wks or when documented evidence of lung maturity
    - Tocolytics may be given to allow for administration of corticosteroids but are otherwise of no proven clinical benefit (SOR:C)[1,4,5]
10. GA 24-32 wks:
    - Corticosteroids should be given to patients with PPROM between 24 and 32 weeks GA to decrease risk of intraventricular hemorrhage, respiratory distress syndrome, and necrotizing enterocolitis. (SOR:A)[1, 12, 13, 14]
    - Antibiotics should be administered to patients with PPROM because they prolong the latent period and improve outcomes. (SOR:A)[15, 16, 17, 18]
    - Deliver at 34wks or at 32-33 wks if documented evidence of lung maturity
11. GA <24wks
    - Expectant management or IOL
    - No steroids
    - No antibiotics unless clinically indicated for infection

Agents for IOL [19,20]

1. Oxytocin (Pitocin)
    - Synthetic hormone analog
    - Stimulates uterine contractions, increases frequency, force, and duration of contractions by increasing intracellular calcium and activating phospholipase C inositol pathway.
    - Use in patient with favorable cervix
    - Start at 1or 2 mU/min. Increase by 1-2 mU/min to max of 20 mU/min for augmentation and 40 mU/min for induction. (Rate of increase and maximum dose varies based on hospital guidelines)
    - FDA approved for labor induction or augmentation
    - Adverse effects include: tachysystole, water intoxication, fetal distress, hypotension, hypertension, hyponatremia, arrhythmia.
2. Prostaglandins:
    - Ripen cervix through relaxation of cervical smooth muscle; cause uterine contractions by increasing intracellular calcium levels; alter extracellular ground substance of cervix; increase cervical glycosaminoglycan, hyaluronic acid, dermatan sulfate, and elastase; PGE2 increases cervical collagenase activity[19].
    - Risks associated include uterine hyperstimulation, nausea, vomiting, diarrhea, and fever.
        - Dinoprostone gel (prepidil)
            - PGE2 prostaglandin
            - 0.5mg gel preparations

- Warm to room temperature before insertion
- Insert with 20mm endocervical catheter if no effacement
- Insert with 10mm endocervical catheter if >50% effacement
- Pt remains recumbent for 15-30mins after insertion
- Dose q6hrs x 2 after initial dose
- Max 1.5mg /24hrs
- Allow 6-12hrs after last dose before starting oxytocin
- Monitor fetal heart rate 15-20mins before insertion and 30-120mins after insertion
- Pregnancy category C
- FDA approved for cervical ripening
- Adverse effects include: uterine hyperstimulation, uterine rupture, nausea, vomiting, diarrhea, hypotension, arrhythmias,

▪ Dinoprostone insert (Cervidil)
- PGE_2 prostaglandin
- 10mg preparations; releases 0.3mg/hr x 12hrs.
- Insert into posterior vaginal fornix
- Pt remains recumbent for 2hrs after insertion
- Remove by pulling string 12 hrs after insertion, or if onset of labor, or hyperstimulation
- Monitor fetal heart rate 15-30mins before insertion and continuously after insertion and up to 15mins after removal
- FDA approved for cervical ripening
- Adverse effects include: uterine hyperstimulation, uterine rupture, nausea, vomiting, diarrhea, hypotension, arrhythmias,
- Approximately $215 per 10mg dose

▪ Misoprostol:
- Synthetic PGE_1analog
- 25-100mcg every 4-6hrs (max 3doses)
- Off label use for cervical ripening. FDA approved for management of gastric ulcer
- May be used PO or PV
- Allow at least 4 hrs after last dose before starting oxytocin
- Risk of uterine tachysystole
- Less expensive than PGE_2 (about $1 per 100 mcg pill) and can be stored at room temperature

3. When Oxytocin, misoprostol and PGE2 agents are compared with each other and placebo, the evidence shows:
   - Misoprostol significantly decreased latency for women with PROM and unfavorable cervix compared to placebo and PGE2 [6, 21] (SOR:A)
   - The number of deliveries within 12 hours was significantly higher with misoprostol compared to placebo or PGE2, but there was no difference at 24hrs [2,19,21,23].
   - When compared with oxytocin, misoprostol does not decrease latency with statistical significance, but the time difference may be clinically relevant.[4]

- Reduction of latency with Misoprostol is similar for nulliparous and multiparous women. [22]
- An increased trend of abnormal uterine activity was noted with Misoprostol compared to oxytocin and PGE2, but the finding was not statistically significant. [4,19,22,23]
- Abnormal uterine activity associated with Misoprostol may be dose dependent. [4,19,22]

Prognosis

1. Time to delivery, or latency, increases with decreasing GA.
2. 50% of women with PROM at term deliver within 5hrs; 95% deliver within 28hrs.[1,4,7]
3. Most women with PPROM deliver within 1wk[1,4,7]

Prevention

1. None identified.

Patient Education

1. AAFP Patient Education Handout: Preterm Premature Rupture of Membranes

References

1. ACOG Practice Bulletin No.80: premature rupture of membranes. Clinical management guidelines for obstetrician-gynecologists. *ACOG Committee on Practice Bulletins-Obstetrics. Obstet Gynecol*. 2007 Apr;109(4):1007-19.
2. Gabbe SG, Mebyl JR, Simpson JL. Obstetrics: Normal and problem pregnancies. 5th ed. 2007. Churchill Livingstone
3. Modena AB, Kaihura C, Fieni S. Prelabor rupture of the membranes: recent evidence. Acta *Biomed*. 2004;75 suppl 1:5010.
4. Medina TM, Hill DA. Preterm Premature Rupture of Membranes: diagnosis and management. *AFP* 2006;73(4):659-664.
5. Simhan H N, Canavan TP. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. *BJOG* 2005; 112, supp1:32-37.
6. Levy R, Vaisbuch E, Furman B, Brown D, Volach V, Hagay ZJ. Induction of labor with oral misoprostol for premature rupture of membrane at term in women with unfavorable cervix: a randomized, double-blind, placebo-controlled trial.Erdemoglu E, Mungan T. Significance of detecting insulin-like growth factor binding protein-1 in cervicovaginal secretions: comparison with nitrazine test and amniotic fluid Volume assessment. *Acta Obstet Gynecol Scand* 2004: 83: 622-626
7. Frohn, WE, Simmons S, Carlans Y. Prostaglandin E2 gel versus misoprostol for cervical ripening in patient with premature rupture of membrane after 34weeks. *Obstetrics and gynecology*. 2002; 99(3):206-210.
8. Kishida T, Hirao A, Matsuura T, Katamine T, Yamada H, Sagawa T, Fujimoto S. Diagnosis of premature rupture of membranes with an improved alpha-fetoprotein monoclonal antibody kit. *Clin Chem*. 1995;41(10):1500-3.
9. Mozurkewich E. Prelabor rupture of membranes at term: induction techniques. *Clinical obstetrics and gynecology*. 2006;49(3):672-683.

10. CDC. Prevention of perinatal group B streptococcal disease. Revised guidelines from cdc, 2010. *MMWR* 2010; 59(no.RR#):1-32.
11. R.J. Wapner, Y. Sorokin, E.A. Thom, F. Johnson, D.J. Dudley, C.Y. Spong, A.M. Peaceman, K.J. Leveno, M. Harper and S.N. Caritis *et al.*, Single versus weekly courses of antenatal corticosteroids: evaluation of safety and efficacy, *Am. J. Obstet. Gynecol.* **195** (2006), pp. 633–642.
12. Murphy KE, Hannah ME, Willan AR, Hewson SA, Ohlsson A, Kelly EN, Matthews SG, Saigal S, Asztalos E, Ross S, Delisle MF, Amankwah K, Guselle P, Gafni A, Lee SK, Armson BA; MACS Collaborative Group. Multiple courses of antenatal corticosteroids for preterm birth (MACS): a randomised controlled trial. *Lancet*. 2008 Dec 20;372(9656):2143-51.
13. Manktelow BN, Lal MK, Field DJ, Sinha SK. Antenatal corticosteroids and neonatal outcomes according to gestational age: a cohort study. *Arch Dis Child Fetal Neonatal* Ed. 2010 Mar;95(2):F95-8.
14. Arch Dis Child Fetal Neonatal Ed. 2010 Mar;95(2):F95-8. Single vs weekly courses of antenatal corticosteroids for women at risk of preterm delivery: A randomized controlled trial. *JAMA.* 2001 Oct 3;286(13):1581-7.
15. Hutzal CE, Boyle EM, Kenyon SL, Nash JV, Winsor S, Taylor DJ, Kirpalani H. Use of antibiotics for the treatment of preterm parturition and prevention of neonatal morbidity: a metaanalysis. *Am J Obstet Gynecol.* 2008 Dec;199(6):620.e1-8. Epub 2008 Oct 30
16. Tanir HM, Sener T, Tekin N, Aksit A, Ardic N. Preterm premature **rupture** of **membranes** and neonatal outcome prior to 34 weeks of gestation. Int J Gynaecol Obstet. 2003 Aug;82(2):167-72.
17. Bar J, Maayan-Metsger A, Hod M, Ben Rafael Z, Orvieto R, Shalev Y, Sirota L. Effect of **antibiotic** therapy in preterm premature **rupture** of the **membranes** on neonatal **mortality** and morbidity. Am J Perinatol. 2000;17(5):237-41.
18. Lovett SM, Weiss JD, Diogo MJ, Williams PT, Garite TJ. A prospective, double-blind, randomized, controlled clinical trial of ampicillin-sulbactam for preterm premature **rupture** of **membranes** in women receiving antenatal corticosteroid therapy. Am J Obstet Gynecol. 1997 May;176(5):1030-8.
19. Briggs GG, Wan SR. Drug therapy during labor and delivery, part 2. American journal of health-system pharmacy. 2006;63:1131-1139.
20. Tenore JL. Methods for cervical ripening and induction of labor. *Am Fam Physician*. 2003 May 15;67(10):2123-8.
21. McCaul JF, Rogers LW, PerryKG, Martin RW, Allbert JR, Morrison JC. Premature Rupture of membranes at term with unfavorable cervix: comparison of expectant management , vaginal prostaglandin, and oxytocin induction. *Southern Medical Journal.* 1997;90(12):1229-1233.
22. Nagpal MB, Raghunandan C, Saili A. Oral misoprostol versus intracervical prostaglandin #2 gel for active management of premature rupture of membranes at term. *BJOG*. 2009; 106: 23-26.
23. Ngai SW, Chan YM, Lam SW, Lao TT. Labour characteristics and uterine activity: misoprostol compared with oxytocin in women at term with prelabour rupture of the membranes. BJOG. 2000; 107:222-227

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