Acute Preterm Labor

Symptoms of PTL 23.0-33.9 weeks

Symptoms include persistent contractions with pelvic pressure/backache, regulare uterine contractions, increased vaginal discharge, leakage of fluid, vaginal spotting/bleeding

(1) Evaluate fetal well being:

- Continuous external fetal monitoring and tocometry
- Perform basic ultrasound for fetal size, presentation, AFI, placental location

(2) Assess for pertinent co-existing conditions:

- **Chorioamnionitis:** abdominal exam/fundal assessment, CBC with diff, consider amniocentesis if exam findings are equivocal
- **Abruption:** abdominal exam/fundal assessment, CBC, coagulation panel
- **Urinary tract infection:** order urinalysis, urine culture

(3) Perform Vaginal Exam:

- **Sterile speculum exam**: obtain fetal fibronectin, GBS, wet prep, GC/CT swabs. Evaluate for rupture of membranes (nitrazine, pool, fern, other clinical tests including placental alpha microglobulin-1 protein) as appropriate.
- **Check digital sterile vaginal exam** if no evidence of PPROM and no previa

PPROM

Admit patient, initiate PPROM protocol

SVE ≥3cm or >80% effaced

(1) Admit patient: Initiate transfer to facility with higher level NICU care if applicable
(2) Corticosteroids for fetal lung maturity[1,2]

- Betamethasone 12mg IM q24 hours x 2 doses OR
- Dexamethasone 6mg IM q12 hours x 4 doses

(3) Antibiotics for GBS prophylaxis
(4) Tocolysis*

- First line: beta-adrenergic receptor agonists, calcium channel blockers, NSAIDs used singly or in combination are reasonable approaches based on local practice patterns[3,4,5]
- If <32 weeks, consider indomethacin first-line in combination with magnesium sulfate

(5) Magnesium sulfate for neuroprotection[6]

- If <32 wks; 6g IV bolus, then 2g IV per hour

(6) NICU consult
(7) Treat urinary tract infection, gonorrhea, chlamydia, trichomonas if applicable when results available

SVE <3cm and <80% effaced

Equivocal – Need Further Evaluation to confirm or rule out PTL
(choose one path based on resource availability)

CL <15 mm[7] ← TVUS CL[§7]

- CL 20-30 mm** → Repeat SVE as per boxes on right
- CL ≥30mm → D/C home

Repeat SVE

- Cervical change → Admit
- No change → D/C home

*Contraindications to tocolysis: intrauterine fetal demise, lethal fetal anomaly, non-reassuring fetal status, severe pre-eclampsia, maternal bleeding with hemodynamic instability, chorioamnionitis

** **Consider preterm birth risk factors, gest. age, presenting symptoms. Use clinical judgement to decide whether it is appropriate to proceed directly to treatment if CL 15-25mm**

§All cervical length measurements should be performed by credentialed sonographer or credentialed physician and interpreted by trained/credentialed physician. If qualified personnel are unavailable, further evaluation should be based on exam only (repeat SVE) per boxes on right.

Initial Equivocal Evaluation

- Women with an initial cervical dilation <3cm dilated and <80% effaced should undergo further evaluation to confirm or rule out preterm labor.
- **Transvaginal ultrasound cervical length** assessment is the preferred 'next step' for evaluation, provided it is available and is performed by trained/credentialed sonographers or physicians and interpreted by trained/credentialed physicians. In the US, credentialing is available through the CLEAR program of the Perinatal Quality Foundation.
  - Women who have a short cervical length (<15mm) are at high risk for preterm delivery. They should be considered to have 'confirmed preterm labor' and should be treated as described in the algorithm
  - Women who have an equivocal cervical length (15-25mm) in the setting of this cervical examination may benefit from further risk stratification by further clinical observation
  - Women who have a normal cervical length (≥ 25mm) in the setting of this cervical examination are at low risk for preterm birth.
    - It is estimated that 50% of women who present with symptoms of preterm labor will fall into this category. Their chance of delivering within one week is <2%
    - The fetal fibronectin does not add additional information regarding risk stratification in this situation
    - These patients should be discharged home with precautions
- The additional workup that is obtained depends on clinical resources available and local practice patterns.
  - Available resources may vary based on time of day, day of the week, and/or provider availability.
  - Though fetal fibronectin has good negative predictive value, it has not been proven to improve outcomes and is not recommended unless no other evaluation modalities are available[8,9]
    - FFN by itself has not been shown to increase the detection of acute preterm labor, decrease the incidence of PTB, or affect neonatal outcomes in women with symptoms of preterm labor, and may be associated with increased cost[8.9]
- **Clinical observation and repeat cervical examination:**
  - An alternative strategy- if cervical length screening is unavailable- is to continue to monitor the patient for 1-2 hours, and repeat the digital cervical examination after this monitoring period.
  - If there has been cervical change, the woman should be admitted and treated for preterm labor
  - If there has been no cervical change, discharge home with precautions is reasonable.
- **In all cases, clinical judgment should be used to determine the best plan of care for each woman, as well as individual factors cannot be accounted for in a single algorithm.**

Additional Notes:

- **Corticosteroids**[1,2]
  - **In general, administration is appropriate if there is risk for delivery within 7 days (per ACOG) at 24-34 weeks of gestation**[10]
  - **Periviability:** Administration of corticosteroids during the peri-viable period (22-24 weeks gestation) who are at risk for preterm delivery within 7 days is linked to a family's decision regarding resuscitation and should be considered in that context.
  - **Repeat dosing:** A single repeat course of antenatal corticosteroids may be considered in women who are <34 weeks who are at risk of PTB within 7 days, and whose prior course of antenatal corticosteroids was administered >14 days previously. Repeat dosing may be considered as early as 7 days from the prior dose if indicated by the clinical scenario
- **Tocolytic Therapy**
  - Provides for short-term (48 hour) prolongation of pregnancy only
  - No evidence exists supporting long term tocolysis
  - No evidences supporting direct favorable effect on neonatal outcomes

Agent	Maternal Side Effects	Neonatal Side Effects	Contraindications
Nifedipine[4]	Dizziness, flushing, hypotension, potential suppression of heart rate, contractility, and left ventricular systolic pressure when used with magnesium sulfate	No known adverse effects	Hypotension and pre-load dependent cardiac lesions (e.g., aortic insufficiency)
Indomethacin[5]	Nausea, gastritis, emesis	Premature closure of the ductus arteriosus, oligohydramnios, possibly necrotizing enterocolitis	Platelet dysfunction or bleeding disorder, peptic/gastric ulcer, renal dysfunction
Beta-adrenergic receptor agonists	Tachycardia, hypotension, tremor, palpitations, shortness of breath, hypokalemia, hyperglycemia	Fetal tachycardia	Tachycardia sensitive maternal cardiac disease, poorly controlled diabetes
Magnesium sulfate[3]	Flushing, diaphoresis, nausea, respiratory suppression, cardiac effects when used in combination with calcium channel blockers	Neonatal depression, reduction in fetal heart rate variability	Myasthenia gravis

References – Management of Acute Preterm Labor

(1) Antenatal Corticosteroid Therapy for Fetal Maturation. Committee Opinion No. 677. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016; 128:e187-94.

- ACOG recommends single course of corticosteroids for women 24 0/7 and 36 6/7 weeks, even w PPROM and multiples, at risk for PTB
- Periviable corticosteroids are a family's decision
- Single repeat course should be considered in those < 34 w 0/7 with an imminent risk for PTB within next 7 days whose prior course was given more than 14 days previously.

(2) Roberts D, Brown J, Medley N, Dalziel SR. Cochrane database of systematic reviews. 2017 Volume 3 page CD004454

- 30 studies of 7774 women and 8158 infants demonstrate antenatal corticosteroids compared with placebo or no treatment reduced perinatal and neonatal death, RDS, IVH, NEC, infection in first 48 hours of life.
- No benefit for chronic lung disease, childhood death, neurodevelopment delivery in childhood.
- A single course of antenatal corticosteroids could be considered routine for preterm delivery.

(3) Crowther CA, Borwn J, McKinlay CJD, Middleton P. Magnesium sulphate for prevent preterm birth in threated preterm labor. Cochrane Database of Systematic Reviews 2002 Issue 4 Page: CD001060. DOI 10.1002/14651858

- 37 randomized trials of magnesium sulphate as solo tocolytic in 3571 women (3600 infants) found that compared to placebo or no treatment, or other tocolytics, treatment with magnesium sulphate had no differences in giving birth within 48 hours after trial entry, no difference in serious infant outcome.

(4) Flenady V, Wojcieszek, Papatsonis DNM, Stock OM, Jurray L, Jardine LA, Carbonne B. Cochrane Database of Systematic Reviews 2003 Issue 1 Page: CD002255

- 38 trials of 3550 women with threatened preterm labor found that compared to placebo (1 trial) or no treatment, calcium channel blockers have benefit in delaying delivery
- Compared to beta mimetics, calcium channel blockers have benefit in pregnancy prolongation and reduced maternal adverse effects
- Data limited by lack of blinding and no long term follow up.

(5) Reinebrant HE, Pileggi-Castro C, Romero CLT, dos Santos RAN, Kumar S, Souza JP, Flenady V. Cochrane database of systematic reviews. 2015 Issue 2 Page: CD001992

- 20 studies of 1509 women; indomethacin most commonly used COX inhibitor, used in 15 studies
- No clear benefit for COX inhibitors was shown over placebo or any other tocolytic agents
- Data limited by small studies, minimal safety data, no long-term outcomes, and general low study quality.

(6) Rouse DJ, Hirtz DJ, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. N Engl J Med 2008;359:895-905.

- RCT of 2241 women enrolled at 24-31 weeks, randomized to mag sulfate (6gm bolus then 2 gm/hr) versus placebo
- Primary outcome of composite of stillbirth or infant death by 1 year of corrected age or moderate or severe cerebral palsy at or beyond 2 years of corrected age was not significantly different in the magnesium sulfate group and the placebo group (11.3% vs. 11.7%)
- In a pre-specified secondary analysis, moderate or severe cerebral palsy was significantly less frequent in the magnesium sulfate group (1.9% vs. 3.5%, RR 0.55, 95% CI 0.32-0.95)

(7) Fuchs IB, Henrich W, Osthues K, Dudenhausen JW. Sonographic cervical length in singleton pregnancies with intact membranes presenting with threatened preterm labor. Ultrasound Obstet Gynecol 2004;24:554-7.

- TV cervical length measured in 253 women with painful uterine contractions at 24-35 weeks.
- ROC curve showed cervix length 15 mm as best predictor of preterm delivery within 7 days.
- 47% with cervical length <15mm delivered within 7 days; 1.8% with a cervical length ≥ 15 mm delivered within 7 days

(8) Peaceman AM, Andrews WW, Thorp JM, Cliver SP, Lukes A, Iams JD, Coultrip L, Eriksen N, Holbrook RH, Eliott J, Ingardia C, Pietrantoni M. Fetal fibronectin as a predictor of preterm birth in patients with symptoms: a multicenter trial. Am J Obstet Gynecol 1997 Jul; 177(1): 13-8.

- 763 women with acute PTL symptoms 24+0 to 34+6 and dilation <3cm were studied; FFN was obtained for study purposes only and results were not made available to managing physicians. 20% had + FFN. Those with a positive result were more likely to be delivered within 7 days (RR 25), 14 days (RR 20), and <37 weeks (RR 2.9).
- The negative predictive values for delivery within 7 days, 14 days, and <37 weeks were 99.5%, 99.2%, and 84.5%, respectively

(9) Berghella V, Saccone G. Fetal fibronectin testing for prevention of preterm birth in singleton pregnancies with threatened preterm labor: a systematic review and meta-anlysis of randomized controlled trials.

- 6 trials including 546 singleton pregnancies with symptoms of preterm labor were included.
- Management using fetal fibronectin test required higher hospitalization charges (mean difference, $153), but no improvements in neonatal outcomes or rates of preterm birth or antenatal corticosteroid use
- The authors conclude that FFN testing in singletons is not associated with PTB prevention or improvements in outcomes but is associated with higher costs.

(10) ACOG Practice Bulletin #159: Management of Preterm Labor. Obstet Gynecol 2016 Oct; 128(4):e155-64. PMID 27661654.

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