

Preterm Labor

This document describes guidelines for the initial evaluation, diagnosis, and management of a patient with preterm labor with a focus on the use of tocolytic medications.

I. Preface

Definition

Preterm labor is defined as regular uterine contractions before 37 weeks GA associated with either(1):

1. Progressive cervical effacement and/ or dilatation
2. \geq 2cm cervical dilation.

General

Preterm labor resulting in preterm delivery continues to be the leading cause of perinatal morbidity and mortality.

Decisions regarding tocolysis necessitate discussion with the patient regarding risk, benefit and efficacy.

Requirements for Consideration of Labor Suppression

1. Absence of maternal or fetal conditions dictating delivery
2. Generally, should not be attempted if cervix is 6 cm or more dilated. However, tocolysis may still be considered to allow time for corticosteroid therapy if <34 weeks. For patients with preterm labor in the late preterm period, 34 0/7 – 36 6/7 weeks, ANCS may be indicated but tocolysis is not advised (See ANCS protocol).
3. PPROM warrants special considerations (See PPROM protocol)

Gestational age considerations

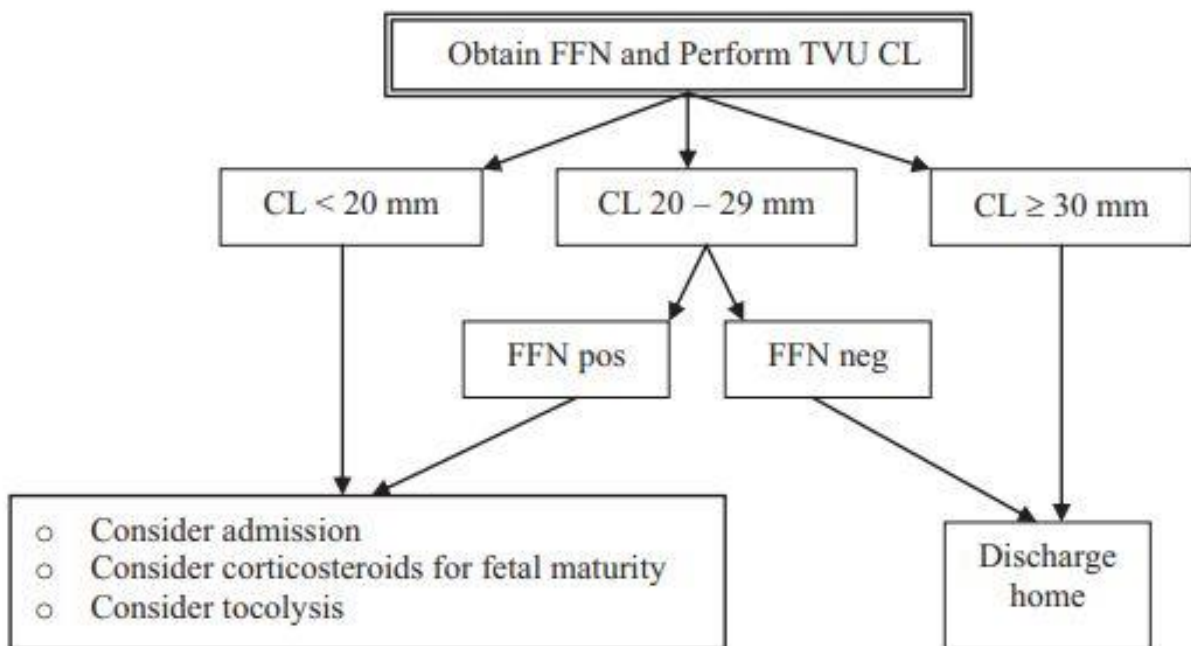
1. Patients at <34 0/7 weeks with demonstrated cervical change are candidates for tocolysis.
2. In patients 34 0/7 - 36 6/7 weeks with reliable dates, tocolysis is not advised(1). These patients may be considered for administration of late preterm ANCS (See ANCS protocol)
3. In general, tocolytics are not indicated for use prior to neonatal viability. Some exceptions may include (1) the post-operative period in patients undergoing abdominal surgery in pregnancy and (2) preterm contractions in a patient with placenta previa.

Contraindications to tocolysis(1)

1. Intrauterine fetal demise
2. Lethal fetal anomaly
3. Non-reassuring fetal status
4. Severe preeclampsia or eclampsia
5. Maternal bleeding with hemodynamic instability
6. Clinical chorioamnionitis
7. Maternal medical contraindications to tocolysis

II. Diagnosis

1. Confirm the diagnosis of preterm labor (PTL)
 - a. Document regular contractions, with either:
 - i. Progressive cervical effacement and/ or dilatation
 - ii. ≥ 2 cm cervical dilation
 - b. Verify estimated gestational age (EGA) < 34 wks.
 - c. Use of TV ultrasound cervical length and fFN may assist with diagnosis of PTL in patients with contractions but without significant cervical dilation (< 2 cm). See flow diagram below (3)
 - i. Collect fFN **prior to cervical check or TVUS**, hold this
 - ii. Perform TVUS CL assessment
 - iii. -if CL ≥ 30 mm low risk, do not send fFN
 - if CL 20-29mm send fFN: negative fFN=low risk, positive fFN= manage as PTL
 - if CL < 20 mm manage as PTL



PTL, preterm labor; CTX, contractions; FFN, fetal fibronectin; TVU CL, transvaginal ultrasound cervical length. Modified from³.

Berghella and Saccone. Am J Obstet Gynecol 2017.

III. Evaluation

1. Evaluate for evidence of clinical chorioamnionitis
 - a. Amniocentesis may be considered for Gram stain, culture, cell counts & glucose when there is suspicion for intra-amniotic infection, but the patient does not meet clinical diagnostic criteria.
2. Confirm absence of maternal or fetal conditions necessitating expeditious delivery
 - a. Evaluate fetal well-being

- i. NST or BPP as indicated
 - Caution in the setting of vaginal bleeding or concern for abruption
3. Ultrasound
 - a. Document: fetal number, presentation, and amniotic fluid volume (AFV)
 - b. Estimate gestational age/ fetal weight
 - c. Rule-out major fetal anomalies
 - d. Preferably ultrasound will be performed by trained sonographer, unless unavailable. Bedside ultrasound on admission may be performed by resident, fellow, and/ or attending. Formal ultrasound will be ordered when available.
 - e. Outside ultrasound reports that are not available at the time of admission should be obtained.
4. Perform a sterile speculum exam
 - a. Evaluate for evidence of PPRROM
 - b. Obtain swabs for GBS, GC (optional), and chlamydia (optional)
5. Labs
 - a. CBC
 - b. Clean catch or catheter UA with culture
 - c. Rapid HIV as indicated per protocol
 - d. Other labs as indicated

IV. Management

1. Admit to labor and delivery
 - a. Tocolytics may be initiated in triage if concern for rapid progression of PTL
 - i. Transfer to labor and delivery as soon as practical.
 - b. External fetal monitoring and tocometry for the first 12-24 hours during tocolysis
 - i. Monitoring should be continued for as long as patient is on magnesium for neuro protection
 - c. If the patient has premature uterine contractions but does not experience cervical change, the contractions may be treated with judicious hydration and sedation and observed over several hours for cervical change.
2. Administer first dose of corticosteroids for FLM acceleration(4).
 - a. Betamethasone 12.5mg IM q24h x 2 doses is the preferred agent
 - b. Dexamethasone 6mg IM q12h x 4 doses is an alternative regimen (See antenatal corticosteroid protocol)
3. Administer antimicrobial agents
 - a. PTL – antibiotics for GBS prophylaxis
 - b. PPRROM – antibiotics for latency (see PPRROM protocol)
 - c. Antibiotics or antifungals as indicated for suspected cervicitis/vaginitis
4. Consider magnesium for neuroprotection when appropriate
5. Call NICU on admission for counseling

- -Consider peri-viable birth counseling when appropriate

6. Consider tocolysis

a. **First-line agent = Nifedipine (Procardia)**

Although no tocolytic agent has been shown to be definitively superior(1), nifedipine has a favorable safety and side effect profile compared to the other first-line tocolytic agents (which include beta-adrenergic receptor agonists, calcium channel blockers, and NSAIDS).(5)

- i. Regimen: Oral (not sublingual) loading dose of 10 mg (immediate release) Q 10 mins (for a total loading dose of 30 mg) then standard starting dose of 20 mg q6 (begin 6 hours after loading dose).
 - Dose may be adjusted 10-20 mg PO q 4-6 hours
 - Maximum daily dose 160 mg/day
- ii. Contraindications
 - Patients with known or suspected cardiac conduction disorders (including Wolf Parkinson White Syndrome, etc.)
 - Caution with hepatic or renal disease
 - Maternal hypotension (<90/50)
- iii. Modest decrease in diastolic blood pressure expected
 - ~20 minutes after second oral dose
 - generally transient and not clinically significant
 - often accompanied by a mild unsustained increase in maternal heart rate
 - little to no effect on uterine perfusion
- iv. Side-effects:
 - Common:
 - Flushing (96%) - transient
 - Headache (38%) - Often resolves after initial 1-2 doses
 - Nausea - uncommon
 - Less common: Transient lightheadedness, Palpitations, Chest pain, Nasal congestion, Heartburn,

Comment: Nifedipine is a calcium channel blocking agent, which typically has minimal cardiac conduction effects. Although there have been case reports of profound hypotension with use of nifedipine and magnesium together, with close monitoring the risk of profound hypotension may be minimized.

b. Second line tocolytic agent = Indomethacin: If <32 0/7 weeks and evidence of persistent cervical change (dilatation or effacement) while on Nifedipine then consider Indomethacin as the second-line agent

- i. Regimen: Oral loading dose of 50mg followed by 25 mg PO q6h X 48 hours
- ii. Document normal amniotic fluid volume (AFV) prior to administration
- iii. Contraindications to the use of Indomethacin
 - Peptic ulcer disease
 - Uncontrolled hypertension
 - Bleeding diatheses
 - Renal disease

- Hepatic dysfunction
 - Aspirin-induced reactive airway disease
 - Fetal renal disease
 - Oligohydramnios
- iv. Prolonged bleeding time has been documented (PT/PTT not affected)
- v. Other side effects rare in healthy adults
- I/O's should be monitored as fluid retention and decreased urine output are possible
 - Could exacerbate electrolyte imbalance (\uparrow K⁺, \downarrow Na⁺)
- vi. Potential fetal side-effects(1,7):
- Reduction in AFV
 - Reduction (not oligohydramnios) has been documented as early as 4h after first dose
 - Repeat AFV assessment not required as therapy will be limited to 48h and AFV reduction is limited & reversible with short term therapy
 - Neonatal necrotizing enterocolitis
 - Constriction of ductus arteriosus
 - Of minimal concern as therapy will be limited to <32 0/7 weeks and \leq 48h duration

ix. Although allowable to give second line tocolysis between 32 0/7 - 33 6/7 weeks of gestation, the benefit is less clear than at <32 0/7 weeks. Second line tocolysis should be individualized.

c. Magnesium sulfate tocolysis may be considered if a patient is transferred from an outside hospital on a magnesium sulfate infusion and is stable or if specific clinical consideration warrants its use- gestational age considerations as with nifedipine and indomethacin

- i. Loading dose is 6g given over 30 minutes
- ii. Infusion is to be run by controlled infusion pump "piggy back" into primary IV line.
- iii. Maintenance dose: 3 g IV per hour starting dose (range 2-4 g IV / hour)
- iv. Clinical examination and serum Mg levels can be used to monitor dose effect.
- v. Serum levels of 5-8 mg/dL are thought to be therapeutic
- vi. 6g bolus followed by 3-4 g/h have been shown to give serum levels of 6.5-7.5 mg/dL
- vii. Serum magnesium levels are to be checked 2 hours after the loading dose and then every 8 hours while on the continuous infusion.
- viii. Patients transferred on magnesium should have serum magnesium levels drawn on arrival and then every 8 hours while on the continuous infusion.

7. Long-Term maintenance tocolysis:

- a. Maintenance tocolysis is generally not recommended following the 48 hour primary tocolytic course as it has not been shown to be effective in reducing neonatal morbidity or mortality and may increase maternal-fetal risk without offering clear benefit.(1)

b. Prophylactic therapy with tocolytic drugs in patients at high risk for preterm delivery is also not recommended.

8. Combining tocolytic drugs:

- a. Generally not recommended as combining tocolytic drugs may increase maternal morbidity without proven efficacy. There may be some special circumstances in which combined tocolytics can be considered.
- b. If combination tocolysis is considered, recommend MFM consultation and management.

9. Tocolysis in patients with preterm contractions without cervical change:

- a. No evidence exists to support the use of tocolytic drugs in patients with preterm contractions but no cervical change

V. References:

1. American College of O, Gynecologists, Committee on Practice B-O. ACOG practice bulletin no. 171: Management of preterm labor. *Obstet Gynecol.* 2016;119(6):1308-17 reaffirmed 2020.
2. DeFranco EA, Lewis DF, Odibo AO. Improving the screening accuracy for preterm labor: is the combination of fetal fibronectin and cervical length in symptomatic patients a useful predictor of preterm birth? A systematic review. *Am J Obstet Gynecol.* 2013;208(3):233 e1-6.
3. Ness A, Visintine J, Ricci E, Berghella V. Does knowledge of cervical length and fetal fibronectin affect management of women with threatened preterm labor? A randomized trial. *Am J Obstet Gynecol.* 2007;197(4):426 e1-7.
4. Practice ACoO. ACOG Committee Opinion No. 475: antenatal corticosteroid therapy for fetal maturation. *Obstet Gynecol.* 2011;117(2 Pt 1):422-4.
5. Flenady V, Wojcieszek AM, Papatsonis DN, Stock OM, Murray L, Jardine LA, et al. Calcium channel blockers for inhibiting preterm labour and birth. *Cochrane Database Syst Rev.* 2014(6):CD002255.
6. Reinebrant HE, Pileggi-Castro C, Romero CL, Dos Santos RA, Kumar S, Souza JP, et al. Cyclo-oxygenase (COX) inhibitors for treating preterm labour. *Cochrane Database Syst Rev.* 2015(6):CD001992.
7. Macones GA, Marder SJ, Clothier B, Stamilio DM. The controversy surrounding indomethacin for tocolysis. *Am J Obstet Gynecol.* 2001;184(3):264-72.