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Tocolytics for regular uterine contractions without cervical change; Cons

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Preterm uterine contractions

Physiologic vs. pathologic

1) Braxton-Hicks contraction
2) Presence of absence of progressive cervical change

Preterm labor

Diagnostic criteria of PTL

1) Uterine contraction ≥ 4/20 min or 8/60 min + progressive change in cervix
2) Cervical dilatation 〉 1 cm
3) Cervical effacement ≥ 80%

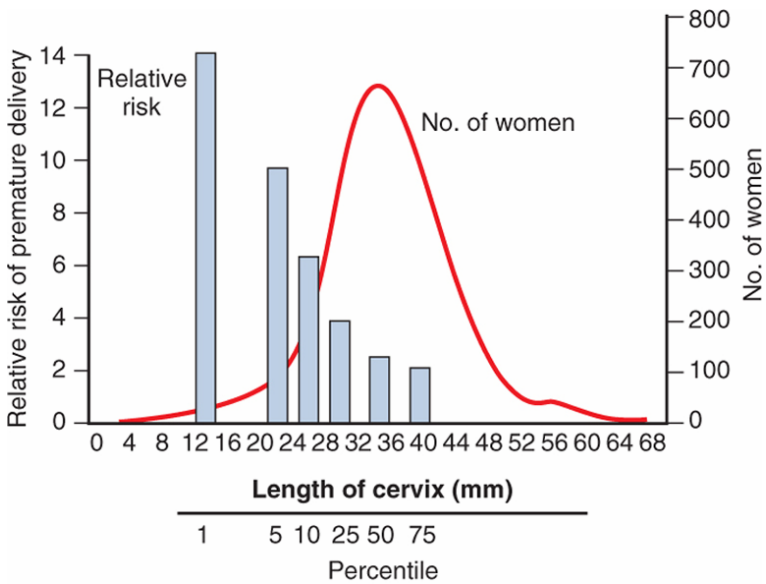
ACOG, 1997

Preterm UC Cervical change vs. No change

	Cervical change (n=44)	No change (n=195)	P
Delivered before hospital discharge	16 (36%)	4 (2%)	〈.001
Delivered before 37weeks' gestation	28 (64%)	50 (26%)	〈.001
Time between presentation and delivery			〈.001
〈1 wk	16 (36%)	9 (5%)	
1–2 wk	4 (9%)	8 (4%)	
〉 2wk	24 (55%)	178 (91%)	
NICU needed	5 (11%)	7 (4%)	.05

Hueston WJ et al., Obstet Gynecol, 1998

PTD risk of women with normal cervical length



Iams JD et al., N Engl J Med, 1996

Tocolytics for preterm labor

- Meta–analysis, 18 trials
  Tocolytics group: 1,434 patients
  Control group: 1,351 patients

Kristen Gyetvai et al. Obstet Gynecol, 1999

→ Tocolytics reduced delivery within 7 days
(Beta-mimetics, indomethacin, atosiban, ethanol, not magnesium sulfate)
→ No improvement of perinatal outcomes.

• ACOG Practice Bulletin (2003)
"Does tocolytic therapy improve neonatal outcomes?"
→ Tocolytics may prolong gestation for 2~7 days, which can provide time for administration of steroids and maternal transport to a facility with a NICU. (Level A)

Tocolytics for Preterm UC

• Randomized trial, 179 patients
observation vs. hydration vs. terbutaline
→ No differences in pregnancy outcome

	Observation (n=56)	Hydration (n=62)	Terbutaline (n=61)	Significance
Mean gestational age at delivery (wk)	38.2±2.5	38.1±2.8	38.2±2.4	P=0.99
Repeat triage visits (%)	34	41	48	P=0.32
Mean triage visits	1.4±0.7	1.7±1.1	1.9±1.2	P=0.10
Received tocolysis	10 (18%)	8 (13%)	8 (13%)	P=0.69
PTD 〈 34 wk	5 (9%)	4 (6%)	4 (7%)	P=0.88
PTD 〈 37 wk	13 (23%)	19 (31%)	10 (16%)	P=0.18
NICU admissions (%)	17	18	15	P=0.89

Guinn DA et al., Am J Obstet Gynecol, 1997

Management of preterm UC in community settings.

Premature contractions in community hospitals (n=239, cervical change in 44 (17%))
• Tocolytics agents were used regardless of whether cervical change occurred (61%) or not (76%, p=0.01)
• Tocolytics were prescribed frequently upon discharge
: 54% of those with cervical change
62% of those without changes (p=0.57)

OVERTREATMENT !!!

Hueston WJ et al., Obstet Gynecol, 1998

Tocolytics for preterm UC

Problems

1) Side effects of drugs
2) Inappropriately early administration of corticosteroid
3) Cost for hospital admission etc.

Side effects of tololytic agents

Pulmonary edema (0.3%)
Tachycardia
Hypotension
Tremor
Palpitations
Chest discomfort
Hypokalemia
Hyperglycemia

Pulmonary edema
Flushing
Diaphoresis, Nausea
↓Deep-tendon reflexes (9.6 ~12.0 mg/dl), Resp. paralysis (12.0~18.0mg/dl)
Cardiac arrest (24.0~30.0mg/dl)
Suppression of heart rate, contractility, Lt. ventricular systolic pressure & neuromuscular blockade with CCB

Hepatitis
renal failure
GI bleeding, nausea heartburn
Closure of the PDA
NEC
ICH
Pul. Hypertension
Hyperbilirubinemia
Reversible decrease in renal function with oligohydramnios

Hypotension
Tachycardia
Palpitation
Myocardial Ischemia
Hepatitis
Flushing
Headache
Dizziness
Nausea

Hypersensitivity
Injection-site reactions
Headache
Nausea
Vomiting

Antenatal corticosteroid

- 1994 NICHD Consensus Development Conference

" The benefits of antenatal administration of corticosteroids to fetuses at risk of PTD vastly outweigh the potential risks."

Am J Obstet Gynecol, 1995

- NICHD Recommendation (2000)

Multiple Courses

"– should not be routinely used."

"– should be reserved for women enrolled in clinical trials."

Obstet Gynecol, 2001

Cost

• Tocolytics에 따른 비용 비교

	Hydration	Yutopar	Magrol	Nifedipine	Atosiban
Tocolytics max dose 1 cycle	2,130	12,176원	45,870원	2,016원	184,646원
1주일간 tocotlytics 1주일간 병실료 및 식비	14,910	24,352원	321,090원	14,112원	553,938원
(고위험병실 2인실 기준)	1,162,364원	1,162,364원	1,162,364원	1,162,364원	1,162,364원
1주일간 총비용 (병실료+식비+ tocolytics)	1,177,274원	1,186,716원	1,483,454원	1,176,476원	1,716,302원

2008년 삼성서울병원 산부인과기준

And then…
For prediction of preterm delivery

CERVICAL LENGTH 〈30MM	FETAL FIBRONECTIN +	DELIVERY WITHIN 48 HOURS	DELIVERY WITHIN 7 DAYS	DELIVERY ≤32 WKS	DELIVERY ≤35WKS
No	No	2.2% (2/93)	2.2% (2/93)	0% (0/47)	1.1% (1/93)
No	Yes	0% (0/14)	7.1% (1/14)	0% (0/5)	21.4% (3/14)
Yes	No	7.1% (5/70)	11.4% (8/70)	6.5% (2/31)	17.1% (12/70)
Yes	Yes	26.3% (10/38)	44.7% (17/38)	38.9% (7/18)	47.4% (18/38)
Prevalence of the outcome		7.9% (17/215)	13.0% (28/215)	8.9% (9/101)	15.8% (34/215)

Gomez R, et al. Am J Obstet Gynecol, 2005

Conclusion

• Tocolytics for preterm UC without cervical change

→ No improvement in perinatal outcomes Unnecessary risk and cost

• USG and fetal fibronectin test

Fibronectin (−) & cervical length 〉 30 mm

→ delivery in the next week is less than 1%

Goldenberg RL, MD et al., Obstet Gynecol, 2002