Evidence-based Methods for Induction of Labor

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Objectives

- Review the safety and efficacy of the some of the most common methods of cervical ripening
- Highlight a few evidence-based adjuncts that can improve the efficacy and/or safety of induction of labor (IOL)
- Discuss racial inequities in women undergoing IOL and their outcomes, and how an evidence-based induction protocol might help to mitigate these inequities
Outline

● Background
● Patient Case
● Methods of Cervical Ripening
  ○ Misoprostol
  ○ Balloon catheter
  ○ Catheter + misoprostol
  ○ Catheter + oxytocin
● Induction of Labor (IOL) Adjuncts
  ○ Stripping of Membranes
  ○ Early amniotomy
  ○ Active Phase Management of Oxytocin
● Addressing Racial Inequities with a Standardized Induction Protocol
● Discussion: Implications for Practice
Background

- >25% of pregnancies in the US are delivered via IOL\textsuperscript{1}
- Increasing elective IOLs after the 2018 ARRIVE trial\textsuperscript{2}
- Term IOL in low risk women (34 RCTs, N>21,000):\textsuperscript{3}
  - C-sections (RR 0.90, CI 0.85-0.95)
  - Operative vaginal delivery, tears, and hemorrhage
- After adjusting for medical comorbidities, BIPOC are 15-27% less likely to undergo IOL compared to White women\textsuperscript{4}
- Non-Latina Black women are 60% more likely to have their IOL result in c-section than Non-Latina White women\textsuperscript{5}

1. Martin, 2019
2. Grobman, 2018
3. Middleton, 2020
4. Singh, 2018
5. Rossi, 2020
Patient Case

- 26 yo G1P0 Black woman at 40w6d
- Planned IOL at 41 weeks
- Wants to know detailed risks & benefits
- Is aware of increased maternal morbidity & mortality for black women and wants to know how that impacts her IOL
- SVE 1/thick/high/post/mod
Methods of Cervical Ripening

- Misoprostol
- Balloon catheter
- Combination of catheter + misoprostol
- Combination of catheter + pitocin
Misoprostol

- **Vaginal misoprostol** vs. **prostaglandin E2** tab / gel (38 RCTs, N=7022):\(^6\)
  - Failed vaginal delivery in 24 hours (RR 0.77, CI 0.66-0.89)
  - Hyperstimulation causing FHR changes
  - C-sections

6. Hofmeyr, 2010
Misoprostol

- **Oral** vs. **vaginal** misoprostol, 50 mcg (37 RCTs, N=6417):\(^7\)
  - Hyperstimulation causing FHR changes (RR 0.41, CI 0.23-0.70)
  - Low apgars (RR 0.54, CI 0.33-0.87)
  - Overall maternal side effects
  - Failed vaginal delivery in 24 hours
  - C-sections

*Methods of Cervical Ripening*
Misoprostol

- **Low-dose vs. high-dose** (network meta-analysis, 611 RCTs, N> 100,000)⁸
  - Hyperstimulation
  - C-section
  - NICU Admission

Consider a low dose oral regimen for misoprostol

poor quality, mixed results
Balloon Catheter

- **Balloon vs. low dose oral misoprostol:**
  - Failed vaginal delivery in 24 hours (2 RCTs N=782, RR 1.28, CI 1.23-1.46)
  - C-section (7 RCTs, N=3178, RR 1.17, CI 1.04-1.32)
  - Hyperstimulation
  - Infection
  - Neonatal outcomes
Balloon Catheter: Infection risk

- Balloon vs. oral misoprostol (1 RCT, N=188)\(^9\)
  - Infection risk

- Balloon vs. vaginal prostaglandins (26 RCTs, N=5563)\(^10\)
  - Infection risk
Balloon Catheter: Volume

- 60-80 ml balloon volume vs. 30 ml balloon volume:
  - Time to delivery (~2 hours) (7 RCTs, N=1432).¹¹
Balloon Catheter: Double vs. Single

- **Double** vs. **single** balloon catheter:
  - Failed vaginal delivery in 24 hours (3 RCTs, N=608)
  - C-section (5 RCTs, N=862)\(^9\)
  - Pain at insertion (1 RCT, N=188)\(^9\)
  - Pain during ripening (1 RCT, N=217, RR 1.41, CI 1.04-1.92, all nulliparous patients)\(^12\)

9. De Vaan, 2019
12. Yang, 2018
Balloon Catheter: Outpatient vs. Inpatient

- **Outpatient vs. Inpatient** foley balloon placement (2 RCTs, N=111 and N=130)\textsuperscript{13,14}
  - Inpatient admission time (\~10h)
  - Induction time
  - NICU Admissions
  - C-sections

- **Outpatient vs. Inpatient** with oxytocin protocol
  - Inpatient admission time (\~4.3h), \textit{nulliparous} patients (1 RCT, N=126)\textsuperscript{15}
  - Inpatient admission time, \textit{multiparous} patients (1 RCT, N=129)\textsuperscript{16}

14. Policiano, 2017
15. Ausbeck, 2020
16. Kuper, 2018
Balloon Catheter:

Less effective than misoprostol. Consider a single, 60-80 ml balloon. Okay to place outpatient if desired.
Balloon + Misoprostol

- *Balloon + misoprostol* vs. *misoprostol* alone:¹⁷
  - Time (~2h) to vaginal delivery (14 RCTs, N=2160)
  - NICU admissions (11 RCTs, N=1848, RR 0.75, CI 0.58-0.97)
  - Hyperstimulation (1 RCTs, N=1040, RR 0.39, CI 0.23-0.67)
  - C-section (15 RCTs, N=2476)
Balloon + Oxytocin

- **Balloon + oxytocin** vs. **Foley balloon** alone:\(^1^\)
  - Time (~30 min) to delivery (6 RCTs, N=1133)
  - C-section (6 RCTs, N=1133)
  - Neonatal outcomes (6 RCTs, N=1133)
Balloon + Oxytocin

- **Balloon + oxytocin** vs. **balloon + misoprostol** (1 RCT, N=492)\(^1\)\(^9\)
  - Time to delivery, adjusted for c-sections (HR 1.38 CI 1.03-1.87)
  - Neonatal outcomes
  - C-section
  - Maternal morbidity

Consider combination methods for cervical ripening, preferably balloon + misoprostol

Labor Induction Adjuncts

- Stripping of Membranes
- Early amniotomy
- Active phase management of oxytocin
Stripping of Membranes

- **Membrane stripping vs. no treatment / sham** (17 studies, N=3170)\(^20\)
  - Spontaneous labor (RR 1.21, CI 1.08-1.34)
  - Other comorbidities / outcomes

- **Membrane stripping + IOL vs. IOL alone** (4 RCTs, N=1377)\(^21\)
  - Vaginal delivery (RR 1.12, CI 1.05-1.18)
    - nulliparas (RR 1.32, CI 1.18-1.48)
    - multiparas (RR 1.00, CI 0.96-1.04)
  - Meconium staining
  - NICU admission

\(^{20}\) Finucane, 2020

\(^{21}\) Liu, 2018
Early Amniotomy

- **Early amniotomy ≤ 4 cm vs. amniotomy > 4 cm** (4 RCTs, N=1273)
  - Time to delivery (~5 h)
  - C-section
Active Phase Management of Oxytocin

- **Discontinuation** after the active phase of labor with adequate contractions vs. **routine continuation** of oxytocin infusion (9 RCTs, N=1538).\(^{23}\)
  - C-sections (RR 0.64, CI 0.48-0.87)
  - Tachysystole (RR 0.53, CI 0.33-0.84)
  - Active phase duration (≈30 min)
  - 30% of patients in the discontinuation group required restarting of oxytocin
Addressing racial disparities with a standardized induction protocol
A Standardized labor induction protocol

A standardized labor induction protocol: impact on racial disparities in obstetrical outcomes

Rebecca F. Hamm, MD; Sindhu K. Srinivas, MD, MSCE; Lisa D. Levine, MD, MSCE

BACKGROUND: There are marked disparities between black and nonblack women in the United States in birth outcomes. Yet, there are little data on methods to reduce these disparities. Although the cause of racial disparities in health is multifactorial, implicit bias is thought to play a contributing role. To target differential management, studies in non-obstetrical populations have demonstrated disparity reduction through care standardization. With wide variation by site and provider, labor management practices are the ideal target for standardization.

OBJECTIVE: In this study, we aimed to evaluate the effect of a standardized induction of labor protocol on racial disparities in cesarean delivery rate and maternal and neonatal morbidity.

RESULTS: A significant reduction in cesarean delivery rate in black women managed with the induction protocol was noted when compared with those in the observational group (25.7% vs 34.2%; P=.02), whereas there was no difference in cesarean delivery rate in nonblack women (34.6% vs 29.9%; P=.41). The induction protocol reduced the racial disparity in cesarean delivery rate (interaction term, P=.04), even when controlling for parity, body mass index, indication for labor induction, and Bishop score at induction start. In addition, a significant reduction in neonatal morbidity was found in black women managed with the induction protocol.
A Standardized labor induction protocol

Prospective cohort study from 2013-2015\textsuperscript{24}

<table>
<thead>
<tr>
<th>Population</th>
<th>855 full term women, unfavorable cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>IOL with a standardized protocol</td>
</tr>
<tr>
<td>Comparator</td>
<td>IOL by physician discretion</td>
</tr>
<tr>
<td>Outcome</td>
<td>Cesarean delivery &amp; maternal and neonatal morbidity by race</td>
</tr>
</tbody>
</table>
A Standardized labor induction protocol

The induction protocol

- RCT with either:
  - Misoprostol
  - Foley balloon
  - Foley + misoprostol
  - Foley + pitocin

- Regular cervical checks for progression
- Early AROM by 4 cm
- Oxytocin
- Strict adherence to failed 2012 NICHD failed IOL definitions
# A Standardized labor induction protocol

Outcomes: Patients *induced with a standardized protocol* vs. *physician discretion*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Black Patients</th>
<th>Non-Black Patients</th>
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</thead>
<tbody>
<tr>
<td>Induction Time</td>
<td>1.1h (p=0.008)</td>
<td>3.9h (p=0.02)</td>
</tr>
<tr>
<td>C-Section</td>
<td>RR 0.36 (p=0.02)</td>
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<td></td>
<td></td>
<td>RR 1.16 (p=0.41)</td>
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<tr>
<td>NICU Admission</td>
<td>RR 0.27 (p=0.03)</td>
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<td></td>
<td></td>
<td>RR 0.84 (p=0.56)</td>
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<tr>
<td>Need for neonatal resuscitation</td>
<td>RR 0.27 (p=0.001)</td>
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<tr>
<td></td>
<td></td>
<td>RR 0.23 (p=0.69)</td>
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</table>
Patient Case

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**Discussion: Implications for Practice**

- **No contraindication to misoprostol:**
  - Combine with oral misoprostol 25 mcg q2-4 hrs or 50 mcg q4-6 hrs

- **Contraindication to misoprostol:**
  - Combine with oxytocin

- **Remove foley at 12 hours if not expelled**
  - Start/continue oxytocin

- **AROM as soon as possible > 3-5 cm**

- **Consider active phase oxytocin discontinuation**

*2020 MFM AJOG Evidence-based labor series proposed induction algorithm*
References

17. L Ornat et al. Misoprostol combined with cervical single or double balloon catheters compared with misoprostol alone for labor induction in singleton pregnancies: a meta-analysis of randomized trials. J Matern-Fetal Neonatal Med. 2020; 23(20):.
24. RF Hamm e al. A standardized labor induction protocol: impact on racial disparities in obstetrical outcomes. AJOG MFM. 2020;2(3).
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