The Pitocin Wars: Evidence-Based Use of Oxytocin for Induction and Augmentation of Labor

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Disclaimer
I have no relevant financial disclosures related to this topic

Recognize these Sayings?
“Pit through the pattern”
“Pit to distress”
“Push the Pit”

Let’s look at how well these practices work…..

Ms H is being induced at 41 weeks. It is now 12 hours after Pitocin was initiated. She is feeling mild cramps with contractions q 2 minutes that appear low amplitude, and high frequency with some coupling. The Pitocin is at 16 mU/min. Which is your recommendation

A. Stop the Pitocin and wait 1-2 hours to restart
B. Turn the Pitocin down to 8 mU/min
C. Continue increasing Pitocin at 2 mU/min every 30 minutes
D. Leave the Pitocin unchanged and reassess in an hour
Objectives

- Pharmacokinetics of oxytocin
- Evidence-based management of oxytocin infusions
  - Management of tachysystole
  - Dosing protocols for induction and augmentation
  - The fallacy of the Friedman curve

Why Focus on Oxytocin?

- Oxytocin is the most commonly used induction agent in the United States
- Large variability in dose and dosing intervals and no consensus about best practice
- Oxytocin is a “high-alert” medication
- Allegations of oxytocin misuse are present in ~ half of all paid obstetric litigation claims

Endogenous Oxytocin Action

- Oxytocin is a small nine-amino acid peptide
- Biologic half-life is 10-12 minutes
- Rapidly metabolized in the liver
- Maternal plasma levels ~2-4 mU/min during labor
- Fetal secretion is ~ 2-3mU/min during labor

Endogenous Oxytocin Action

- Unpredictable therapeutic index:
  - Plasma levels are not different from pre-labor values during latent and active labor
  - Plasma levels don’t correlate with uterine contractility or cervical dilation
  - Plasma levels rise significantly toward the end of the second stage
**Distribution of Oxytocin Receptors in Uterus**

- Uterine response to oxytocin is dependent upon density and distribution of receptors

Smith JG 2006

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**Pharmacokinetics of Exogenously Administered Oxytocin**

- Onset of action 3-4 minutes when given IV
- Half-life is ~ 10-15 minutes
- It takes ~ 30-40 minutes to reach steady state (3-4 half-lives)


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**Limitations of Uterine Activity Monitoring**

- External tocodynamometry measures frequency only
- Internal monitoring
  - MVU do not assess duration of each contraction
  - MVU do not assess direction of pressure applied by contracting uterus

Bakker PC 2007

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**Effect of Oxytocin in Uterine Activity**

- Initial increase in frequency, strength, and duration
- Followed by a stable phase during which uterine activity does not increase
- Studies of abnormal labor patterns suggest amplitude decreases during episodes of tachysystole

Bakker PC 2007
Adverse Pharmacologic Effects

- **Hyponatremia from water retention:**
  - More likely if infusion rate is >20 mU/min
  - Rare if isotonic solution is used

- **Hypotension**
  - Sudden hypotension, tachycardia and ↑ cardiac output if given in bolus dose
  - May cause transient myocardial ischemia that results in EKG changes
  - Most likely s/p cesarean section

  Ruchala PL 2002

Adverse Pharmacologic Effects

- **Desensitization**
  - Large doses or prolonged exposure can lead to desensitization of oxytocin receptors
    - 4 hours exposure causes ½ inactivation in in-vitro studies of myometrial cultures


Tachysystole

- **Definition**
  - > 5 contractions in a 10 minute window
  - Based on expert opinion from NICHD 2008 FHR committee

  Macones et al 2008

What is Too Much Uterine Activity?

- **Peebles DM 1994:**
  - Near infrared spectroscopy to measure fetal cerebral concentrations of oxyhemoglobin
  - UC interval of 2-3 minutes (average relaxation phase of ≥ 60 seconds) associated with stable cerebral oxyhemoglobin levels

  Peebles DM 1994, Johnson N 1994
What Is Too Much Uterine Activity?

- Bakker P 2007:
  - Compared uterine activity parameters to UA pH
  - Inter-contraction interval < 63 seconds is associated with an increased incidence of UA pH < 7.1

- Simpson KR 2008:
  - Compared UC frequency to FpO₂
  - > 6 UCs in a 10 minute window is associated with a gradual drop to low normal values over ~ 30 min

Tachysystole: Turning Down the Oxytocin

- Turn off:
  - Resolution in 14 minutes
- Turn off + IV bolus
  - Resolution in 9-10 minutes
- Turn off + IV bolus + change to lateral position
  - Resolution in 6 minutes

- Note: IV bolus = 500 cc LR

Simpson KR & James 2005
Management of Tachysystole: ACOG

- Uterine tachysystole
  - Spontaneous labor
  - Labor induction or augmentation
    - Category I or II FHR tracing
      - No interventions required
      - Intravenous resuscitative measures
        - If no resolution, consider tocolytic
    - Category III or IV FHR tracing
      - Intravenous resuscitative measures
        - If no resolution, consider tocolytic

Management of Tachysystole: AWHONN

- Normal FHR
  - Reposition, IV bolus
  - Decrease oxytocin by half if uterine activity is not normal in 10-15 minutes

- Indeterminate or abnormal
  - Stop oxytocin
  - Reposition, IV bolus, consider O2 via mask and terbutaline

Myth #1 and Myth #2

- "Pit through the pattern"
  - Inter-contraction intervals of ~ 60 seconds optimize fetal gas exchange and acid/base balance

- "Pit to distress"
  - The gradual drop in fetal oxygenation probably occurs prior to overt evidence in FHR patterns

Induction: High vs Low Dose Protocols

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Starting dose mU/min</th>
<th>Increase mU/min</th>
<th>Interval mU/min</th>
<th>Maximum dose mU/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose</td>
<td>0.5-2</td>
<td>1-2</td>
<td>30-60</td>
<td>20-40</td>
</tr>
<tr>
<td>High dose</td>
<td>4-6</td>
<td>4-6</td>
<td>15-30</td>
<td>≥ 40</td>
</tr>
</tbody>
</table>

Smith JG 2006, Patka JH 2005
High vs Low-Dose Protocols: Outcomes

<table>
<thead>
<tr>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ C/S for failed induction</td>
<td>↑ C/S for FHR distress</td>
</tr>
<tr>
<td>↑ Chorioamnionitis</td>
<td>↑ Tachysystole</td>
</tr>
</tbody>
</table>

Studies confounded by use of the Friedman curve and definitions of failed induction and failure to progress

Low Dose
- Change in Cervical Dilatation
- Time Interval hr (range)
- Cm/hr (range)

2-3
- 3.2 (0.6-15)
- 0.3 (0.1-1.8)

3-4
- 2.7 (0.6-10.1)
- 0.4 (0.1-1.8)

4-5
- 1.7 (0.4-6.6)
- 0.6 (0.2-2.8)

5-6
- 0.8 (0.2-3.1)
- 1.2 (0.3-5.0)

6-7
- 0.6 (0.2-2.2)
- 1.7 (0.5-6.3)

7-8
- 0.5 (0.1-1.5)
- 2.2 (0.7-7.1)

8-9
- 0.4 (0.1-1.3)
- 2.4 (0.8-7.7)

9-10
- 0.4 (0.1-1.4)
- 2.4 (0.7-8.3)

Zhang J et al 2002

Normal Labor Progress Today: 6 is the new 4
- Many nulliparous women are not in active labor until ≥ 6 cms
- There is wide variability in cervical dilation between 6-10 cms
- The slowest yet normal rate of cervical dilation is 1 cm/2 hrs in nulliparous women in active labor

Myth #3

“Push the Pit”
- Oxytocin receptors desensitize when oversaturated or exposed for a long period of time
- Optimal dose:
  - Most women achieve effective regular Ucs at 10-13 mU/min
  - Maximal doses 20-40 mU/min
- No data that higher doses improve birth outcomes
- Optimal interval is 30-40 min


Conclusion

Consider protocols and checklists for
- pre-initiation of oxytocin,
- in-use oxytocin
- rescue protocols
- But titrate to uterine activity rather than to protocol

Resources
- Hayes EJ AJOG 2008
- Krenig CF J Perinat Neonat Nsg 2012
- Clark SL AJOG 2007

Conclusion

Throw out the Friedman curve
- Consider delayed admission, amniotomy ↑ hydration and glucose, continuous support or ambulation in active phase
- Resources:
  - Zhang J AJOG 2010
  - Neal JL Med Hypoth 2012
  - Neal JL JOGNN 2011
  - Manusco MS Clin Perinatol 2008