OXYTOCIN: WHEN TO START & WHEN TO STOP

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DISCLOSURES

- I have received honorarium from Smith + Nephew for educational lectures on wound care and negative pressure wound therapy
- I trained and practiced primarily with oxytocin use for labour induction and augmentation but have recently become a big fan of misoprostol

COMING SOON!

THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Watch this space for the new SOGC Clinical Practice Guidelines: Cervical Ripening and Induction of Labour
OBJECTIVES

- Review the risks
- Discuss different regimens
- Red flags / when to worry

WHAT IS OXYTOCIN?

- Oxytocin is a peptide
- Three primary oxytocin-signaling genes:
  - OXT (20p13, structural gene for oxytocin)
  - OXTR (3p25.3, oxytocin receptor)
  - CD38 (4p15.32, oxytocin secretion)
- Primarily synthesized by the hypothalamus in the supraoptic nucleus and the paraventricular nucleus for both systemic and central release
- From a physical perspective:
  - Rhythmic uterine contractions
  - Let down reflex (breastmilk expression)
- From a psychosocial perspective:
  - Interactions with dopaminergic and muscarinic acetylcholine signaling to modulate cognitive state processes involved in complex human behaviors
  - Recognition
  - Trust
  - Parent-infant bonding
  - Romantic attachment
  - Sexual arousal and orgasm

MYOMETRIAL OXYTOCIN RECEPTORS

- Oxytocin receptor activation triggers the release of intracellular calcium and local prostaglandin production
- Receptors are produced by the myometrium from 13 weeks’ onwards, reach a clinically significant concentration at ~20 weeks’ and peak at term
- Oxytocin action is limited by the concentration of receptors in the smooth muscle of the uterus. Repeated doses may cause desensitization of the receptors and decreased response (Vallen 2017).
EXOGENOUS INTRAVENOUS PHARMACOKINETICS

- Onset of action (uterine contractions): 1 minute
- Steady state achieved (true response): 40 minutes
- Duration of action: 1 hour
- Half-life: 1 to 6 minutes, decreased in late pregnancy
- Excretion: Urine (small amount unchanged)
- Cost: 10 units/mL (per mL): $2.31 - $4.61 CAD

**DELIVERY IN FOCUS: STRENGTHENING OBSTETRICAL CARE IN CANADA**

**Institute for Safe Medication Practices (ISMP)**

- Since 1997, the Institute for Safe Medication Practices (ISMP) has included IV oxytocin among its list of medications that have a heightened risk of causing significant patient harm when used in error
- **Maternal death:** Caused by hypertensive episodes, subarachnoid hemorrhage, or rupture of the uterus
- **Fetal death:** When used for induction of labour or for augmentation in the first and second stages of labour
- ISMP suggests there may be benefit from mitigation strategies, including standardized use (e.g., order, storage, preparations, and overall administration), proper labeling, applying clinical decision supports, and/or applying independent double checks

**FIGURE 5.**

- Note: A single case may involve more than one high-risk area.

**FIGURE 6.**

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**TABLES 4 to 7: TOP CONTRIBUTING FACTORS TO ISSUES FOR BOTH ORGANIZATIONS**

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ADVERSE REACTIONS

- Cardiovascular: Cardiac arrhythmia, hypertensive crisis, hypotension, subarachnoid hemorrhage, tachycardia, ventricular premature contractions.

- Endocrine & metabolic: Water intoxication with hyponatremia (severe water intoxication with seizure and coma is associated with a slow infusion rate of >24 hours and in cases using >40 μg/min).

- Gastrointestinal: Nausea, vomiting.

- Gynecologic: Uterine rupture.

- Hematologic & oncologic: Pelvic hematoma.

- Hypersensitivity: Anaphylaxis.

CONTRAINDICATIONS (PRODUCT LABEL)

- Hypersensitivity.
- Significant cephalopelvic disproportion.
- Unfavorable fetal presentation or positioning.
- Fetal distress when delivery not imminent.
- Hypertonic or hyperactive uterus.
- Contraindicated vaginal delivery (invasive cervical Ca, active genital HSV, cord prolapse, funic presentation, placental abruption, other surgery involving the uterus).
- Severe toxemia (preeclampsia).
- Prematurity or unripe cervix.
- Predisposition to uterine rupture (eg., grand multiparity, overdistention of the uterus, previous caesarian delivery, other surgery involving the uterus).
- Prolonged use in uterine inertia.
- Factors predisposing to thromboplastin or ATE (eg., prolonged retention of dead fetus, placental abruption).
- Serious medical or obstetric conditions and any condition in which fetal distress already occurs.
- Unavailability of physician to be in attendance.

INDICATIONS FOR INDUCTION

HIGH PRIORITY

- Chorioamnionitis.
- PET without severe features ≥37 weeks gestation.
- PET with severe features at any gestational age.
- PROM or near term, anti GBV.
- Preeclampsia pregnancy (>10 weeks).
- Significant maternal disease not responding to treatment.
- Significant perinatal or neonatal morbidity.
- Supported fetal compromised.
**IS THE CERVIX FAVOURABLE?**

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<tr>
<th>Position</th>
<th>Posterior</th>
<th>Mid</th>
<th>Anterior</th>
</tr>
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<tbody>
<tr>
<td>Consistency</td>
<td>Firm</td>
<td>Medium</td>
<td>Soft</td>
</tr>
<tr>
<td>Cervical Length (prev effacement)</td>
<td>≤ 4 cm (prev 0-30%)</td>
<td>2-3 cm (prev 31-50%)</td>
<td>1-2 cm (prev 51-80%)</td>
</tr>
<tr>
<td>Dilatation</td>
<td>0 cm</td>
<td>1-2 cm</td>
<td>3-4 cm</td>
</tr>
<tr>
<td>Fetal Station</td>
<td>-3</td>
<td>-2</td>
<td>-1/0</td>
</tr>
</tbody>
</table>

**INDICATIONS FOR AUGMENTATION**

- Latent phase labour: > 20 hours if nulliparous, > 14 hours if parous
- Slow progress of active labour: cervical dilatation rate of < 0.5-1 cm per hour
- Active phase labour with arrest of dilatation > 2 hours with inadequate uterine activity
- Second-stage arrest of descent with inadequate contractions, defined as:
  - A contraction pattern > 2-3 minutes apart, lasting > 80-90 seconds, and not palpating strong
  - A contraction pattern demonstrating < 220 MVU with IUPC
- If oxytocin is utilized for 1st stage augmentation, the time to delivery is shortened by ~2 hours (Alhafez 2020)

**PROVINCIAL RECOMMENDATIONS**

- “Obstetric care providers are reminded to decrease or stop oxytocin when the fetal heart rate tracing is abnormal.”
- Safe Administration of Oxytocin: Guidelines Report (Ontario 2019, revised 2022)
- Endorsed by SOGC, Ontario College of Family Physicians, Association of Ontario Midwives, Canadian Association of Perinatal and Women’s Health Nurses, HRDC
### HOW TO PREPARE OXYTOCIN
- All hospitals should use a standardized low-dose oxytocin protocol and order set
- Minimizes medication errors and ensures precise and transparent drug administration
- Verbal or remote orders for oxytocin should not be given to RN staff
- Continuous fetal heart rate monitoring should be instituted and assessed prior to oxytocin

- Independent double check should be performed
  - Preparing the medication
  - Setting the initial pump infusion rate via an IV Smart Pump
  - 10 units in 500mL RL or NS (final concentration 20 mU/mL)

### HOW TO ADMINISTER OXYTOCIN
- Only low-dose protocols should be used
- To reduce errors, must be administered/document in mU/min rather than mL/hr
- Patients should receive continuous one-to-one care by a registered healthcare professional for support, laboring, comfort measures, and monitoring
- The oxytocin protocol and order set must provide clear start, stop, and restart guidelines:
  - An in-person assessment and written order by the prescriber is required before the nurse or midwife can start or restart the infusion
  - The need to reduce or stop the infusion when there is:
    - Atypical or abnormal fetal heart rate (FHR) findings
    - Uterine tachysystole with or without FHR changes
  - The oxytocin rate should not be increased if there is adequate uterine activity
  - In the event that a healthcare practitioner provides care that deviates from the protocol, the indication must be justified and documented in the patient’s chart
  - Oxytocin must not be administered for the convenience of the staff or in the presence of concerning fetal health surveillance (FHS) as defined by the SOGC

### COMMONLY USED PROTOCOLS

<table>
<thead>
<tr>
<th></th>
<th>Low-Rate Protocol</th>
<th>Expedited-Rate Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial rate of oxytocin</td>
<td>1-2 mU/minute</td>
<td>4-6 mU/minute</td>
</tr>
<tr>
<td>Rate increment</td>
<td>1-2 mU/minute</td>
<td>4-6 mU/minute</td>
</tr>
<tr>
<td>Maximum rate</td>
<td>20-30 mU/minute</td>
<td>20-30 mU/minute</td>
</tr>
<tr>
<td>Benefits</td>
<td>Less tachysystole</td>
<td>Shorter time to delivery</td>
</tr>
<tr>
<td>Relative contraindications</td>
<td>Longer time to delivery</td>
<td>More tachysystole with or without FHR changes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TOLAC, parity 25, second stage, augmentation of labour</td>
</tr>
</tbody>
</table>
WHEN TO STOP

- Seizure-like convulsions frequently occurring
- Infants in distress
- Severe maternal hypotension
- Hemorrhage
- Fetal distress
- Expanding fetal head
- Active or latent station greater than 5 cm
- العامة الأعراض الأخرى
- Oxytocin should be stopped in the presence of:
  - Abnormal cord pulsation
  - Prolonged or irregular decelerations
  - Absence of acceleration
  - Absent or absent variability
  - Persistent abnormal cardiotocographic patterns
  - Persistent non-repetitive late decelerations
  - Persistent non-repetitive variable decelerations
  - Persistent non-repetitive sinusoidal decelerations

- The physician should be immediately notified and re-evaluate the patient

- Intrauterine resuscitation interventions may include:
  - Attempt to decrease UA
  - Check maternal pulse and replace with another
  - Consider aspiration of uterine contents or amniotic fluid

- The patient may be considered for immediate delivery or cesarean delivery

- Monitoring of fetal status should continue until birth

- The patient may continue to receive oxytocin if necessary

Table 7. Classification of normal or abnormal uterine activity and tachysystole

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal</th>
<th>Tachysystole</th>
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<tr>
<td>Frequency</td>
<td>&gt;5 contractions in 10 minutes, averaged over 30 minutes</td>
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<tr>
<td>Duration</td>
<td>&lt;90 seconds</td>
<td></td>
</tr>
<tr>
<td>Identity</td>
<td>Developed, unchanged, or changing</td>
<td></td>
</tr>
<tr>
<td>Resting period</td>
<td>5 contractions in 10 minutes, averaged over 30 minutes</td>
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<td>IUPC</td>
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Table 11. Classification of late deceleration and MHR findings

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<th>Term</th>
<th>Non-term</th>
</tr>
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<tr>
<td>Baseline</td>
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Table 16. Classification of intrapartum EFM findings

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STOPPING ONCE IN ACTIVE LABOUR?

- Can outcomes be improved by discontinuation of IV oxytocin (for IOL) once active labour established?
- 10 completed RCTs involving 1888 subjects (1998 – 2016), analysed by intention to treat
- Many trials had design limitations and were judged to be at either high or unclear risk of bias
- Compared with continuation of IV oxytocin, discontinuation of IV oxytocin may:
  - Reduce the CS rate, risk ratio (RR) 0.49, 95% CI 0.36 to 0.66 (low certainty)
  - (Analysis of those who reached the active phase of labour showed no difference, RR 0.92, 95% CI 0.65 to 1.21)
  - Reduce the risk of ane. hyperoxygenation with abnormal FHR, RR 0.55, 95% CI 0.32 to 0.91 (moderate certainty)
  - Reduce prolongation of labour, RR 0.54, 95% CI 0.31 to 0.93 (moderate certainty)
- However, no effect on overall neonatal, or set of adverse maternal/baby/steric or abnormal cord gases

RESTARTING

- FHR tracing should be normal
- If <30 mins have elapsed since stopping:
  - Restart at 50%–100% of the previous rate
- If >30 mins have elapsed since stopping:
  - Restart from initial protocol rate (1–2 mU/min)

IF GOING ABOVE HOSPITAL PROTOCOL

- Obstetrician consultation, guidance and oversight
- Consider placement of intraterine pressure catheter to make things objective
  - Terate oxytocin up to optimal contraction pattern
  - Aim for 200–250 Monevideo units (MVU) per 10 minutes
- If >30 mU/min with administration >24 hours consider laboratory surveillance for hypernatremia every 4–6 hours
SPECIAL POPULATIONS

- Intrauterine fetal death
- Significant maternal arrhythmias or risk
- Previous cesarean section
- Breech presentation
- Second twin at vaginal delivery

FINAL THOUGHTS & TAKE HOME

- Use a hospital-based protocol and order set
- Educate all staff and promote in-room one-to-one care
- Use a low-rate/low-dose protocol
- Once in active labour, continue with oxytocin (perhaps reduce, but don't stop)
- Follow SOGC guidelines for labour care, fetal monitoring and induction/augmentation of labour
- If you are deviating from the standard of care: see the patient and document your rationale/discussion
- Remember the pharmacokinetics
- Tocolysis probably doesn't fix things, time does
- Please try not to become complacent with oxytocin

THANKS FOR HAVING ME 😊
ANY QUESTIONS?