Obstetric Management of Postpartum Hemorrhage

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Defining PPH

• Primary vs. Secondary
  – Primary
    • First 24 hours after delivery
  – Secondary
    • late or delayed PPH
    • between 24 hours and 12 weeks after delivery

• Classically defined by volume of blood loss
  – ≥ 500 ml at vaginal delivery
  – ≥ 1000 ml at cesarean delivery
Defining PPH cont.

• Royal College
  – Minor 500 – 1000 ml
  – Major > 1000 ml
    • moderate 1000 – 2000 ml
    • severe > 2000 ml

• International Expert Panel
  – “active bleeding > 1000 ml within the 24 hours following birth that continues despite the use of initial measures, including first-line uterotonic agents and uterine massage”

RCOG, Green-top Guideline No. 52. 2017
Incidence

• Varies widely depending on the criteria used to define
• US Data suggests incidence of 2-3% of deliveries (range most quoted is 1-5%)
Causes

• Atony
  – most common etiology
  – ~80% of cases
  – diagnosis made clinically

• Lacerations
  – cervical or vaginal lacerations
  – extensions of hysterotomy
  – ruptured uterus

• Retained products of conception

• Coagulopathy / medical bleeding

Incidence of atony with PPH

Annual rates of postpartum hemorrhage caused by atony, by mode of delivery, and by induction status (United States, 1994–2006)


Incidence of atony with PPH

### TABLE 2

**Estimated rates**\(^a\) of uterine atony and corresponding odds ratios, 1994 and 2006

<table>
<thead>
<tr>
<th>Delivery type</th>
<th>Rate (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1.6 (1.4–1.8)</td>
<td>2.4 (2.2–2.5)</td>
</tr>
<tr>
<td>Vaginal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induced</td>
<td>2.5 (2.3–2.8)</td>
<td>3.2 (3.0–3.5)</td>
</tr>
<tr>
<td>Not induced</td>
<td>1.7 (1.5–1.9)</td>
<td>2.5 (2.3–2.7)</td>
</tr>
<tr>
<td>Cesarean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induced</td>
<td>1.2 (0.9–1.6)</td>
<td>3.1 (2.8–3.5)</td>
</tr>
<tr>
<td>Not induced</td>
<td>0.7 (0.6–0.8)</td>
<td>1.6 (1.5–1.8)</td>
</tr>
</tbody>
</table>

\(\text{CI},\) confidence interval.

\(\text{a}\) Age-adjusted to the age distribution of the 1994 delivery hospitalization population.

Uterine atony pathogenesis

• Characterized by inadequate uterine contraction following delivery
  – uteroplacental arteries remain open
  – local hemostatic factors unable to contribute
• Etiology not known
  – OXTR desensitization as a possible explanation
• Well-described risk factors
  – but not all present with risk factors
Prevention?
Prevention of uterine atony

• Active vs. expectant management of the third stage of labor
  – Active management
    • prophylactic uterotonic
    • early cord clamping
    • controlled cord traction
  – Expectant management
    • await signs of placental separation

• Pluses and minuses to both approaches
  – Utilize prophylactic uterotonics almost universal

Begley, et al. Cochrane Review. 2015
Treatment
Uterine atony treatment cont.

• Make the diagnosis of PPH due to atony
  – highly subjective
  – with experience…“that’s too much”
  – tools exist to estimate blood loss
    • graduated measurement containers and drapes
    • visual aids that provide quantified examples
    • wet-dry weights
    • newer optical technologies
  – early intervention
    • prevent shock, coagulopathy
  – rule out lacerations and retained products
Uterine atony treatment cont.

• Unit-based PPH Protocols
  – allow for standardized management
  – multidisciplinary team approach
  – improved outcomes
    • time to cessation of bleeding
    • rates of DIC
    • decreased use of fewer blood products
  – California Maternal Quality Care Collaborative OB Hemorrhage Protocol

Uterine atony treatment cont.

• Medical management
  – first line
  – utilize various uterotonic agents
    • each target different receptors or signaling pathways

• Blood component therapy

• Surgical management
Oxytocin
Oxytocin history

- **W. Blair Bell, 1909**
  - British obstetrician
  - First to publish the clinical application of posterior pituitary extract, 1909
    - Administered IM
    - Prophylaxis and treatment of post-partum hemorrhage
    - First to use in Obstetrics
  - “There is no doubt, I think, that any one of these properties is sufficient to secure a permanent place in therapeutics for this much neglected portion of our anatomy.”
  - “it ought but rarely to be given before delivery.”
  - Concerned about tetanic contraction effects on fetus

Blair Bell W. Brit Med J. 1909
Oxytocin history cont.

THE SEQUENCE OF AMINO ACIDS IN OXYTOCIN, WITH A PROPOSAL FOR THE STRUCTURE OF OXYTOCIN*

BY VINCENT DU VIGNEAUD, CHARLOTTE RESSLER, AND STUART TRIPPETT

(From the Department of Biochemistry, Cornell University Medical College, New York, New York)

(Received for publication, July 13, 1953)

• du Vigneaud, 1953
  – In 1949, isolated pure oxytocin from the posterior pituitary
  – In 1953, proposed the amnio acid sequence and structure for oxytocin
  – Produced a synthetic product indistinguishable from the natural hormone
  – Won the Nobel prize for this discovery in 1955
Uterine atony medical management

• Oxytocin cont.
  – uterotonic agent of choice
    • no absolute contraindication
    • utilize even after prophylactic usage
  – various regimens
    • 40 Units in 1 liter of normal saline or LR
    • deliver via pump
    • rate to control hemorrhage
    • adjust rate to achieve/maintain contractility
  – 10 units IM if no IV access
  – avoid undiluted IV boluses
Ergots

ON SOME PHYSIOLOGICAL ACTIONS OF ERGOT.
BY H. H. DALE.

(From the Wellcome Physiological Research Laboratories, Herne Hill.)
Uterine atony medical management

• Ergots cont.
  – methylergonovine 200 mcg IM
    • do not give IV
    • avoid in
      – hypertension, Raynaud’s
    • response in 2-5 minus
    • if first dose ineffective, switch to next agent
    • dosing intervals every 2-4 hours up to 1mg
Uterine atony medical management

• Carboprost
  – PGF$_2$alpha (Hemabate) 250 mcg IM
    • do not give IV
    • avoid in asthma/bronchospasm
    • dosing intervals every 15-90 mins up to 8 doses, 2 mg
    • side effects
      – tachycardia, fever, diarrhea
Uterine atony medical management

• Misoprostol (PGE1)
  – useful when other uterotonic agents are contraindicated
  – optimal dose and route unclear
    • sublingual
      – 400 mcg
      – rapid absorption, 30 min peak,
      – avoids first-pass (higher peak, longer affect)
    • oral
      – 400 mcg
      – rapid absorption, 30 min peak
      – first pass effect (lower peak, shorter affect)
    • rectal
      – 800-1000 mcg
      – slow onset (one hour) but long duration (four hours)
Uterine atony medical management

• Misoprostol (PGE1) cont.
  – fever common
  – not contraindicated in hypertension or asthma
Uterine atony medical management

- Carbetocin
  - long-acting oxytocin analog
    - modified to have a long serum ½-life
  - not available in US
  - primarily used for prevention of PPH following cesarean delivery

- marketed due to it’s long ½-life, therefore longer duration of action…but
Uterine atony medical management

- Carbetocin cont.
Uterine atony medical management

• Tranexamic acid
  – anti-fibrinolytic agent
  – used for prevention and treatment of PPH
  – WOMAN trial on-going
    • early use of TXA in women with PPH
    • primary outcome
      – mortality, hysterectomy, severe morbidity

Shakur H, et al. Trials. 2010
Uterine atony medical management

• Explore uterine cavity
  – evacuate clots
  – facilitates further uterine contraction
# Duke L&D Bedside Cognitive Aid

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin — 1st Line</td>
<td>10-40 Units per 500-1000 ml</td>
<td>IV Infusion (10 Units IM)</td>
<td>Continuous infusion</td>
<td>Avoid undiluted rapid infusion</td>
</tr>
<tr>
<td>Methylergonovine (Methergine)</td>
<td>0.2 mg</td>
<td>IM (NOT IV)</td>
<td>Every 2-4 hours</td>
<td>Avoid if hypertensive</td>
</tr>
<tr>
<td>Prostaglandin F2α (Hemabate)</td>
<td>250 mcg</td>
<td>IM (NOT IV)</td>
<td>Every 15-90 mins (limit 8 doses in 24 hrs.)</td>
<td>Avoid in asthmatic</td>
</tr>
<tr>
<td>Misoprostol (Cytotec, PGE1)</td>
<td>800-1000 mcg</td>
<td>Rectal</td>
<td>Once</td>
<td>Rare</td>
</tr>
<tr>
<td>Tranexamic acid* (TXA)</td>
<td>1 g bolus</td>
<td>IV</td>
<td>May follow with infusion (1mg/kg/hr)</td>
<td>Avoid if hypertensive or recent DVT/PE</td>
</tr>
</tbody>
</table>

*Consult with Ob Anesthesia prior to giving
Uterine atony surgical treatment

• Surgical treatment
  – Occlude uterine cavity
    • Bakri balloon
    • Uterine packing
    • B-Lynch uterine suture braces
  – Uterine devascularization
    • Uterine artery ligation
    • Utero-ovarian vessel occlusion
    • Uterine artery embolization
  – Hysterectomy
Uterine atony treatment cont.

- Uterine Balloons

https://www.cookmedical.com/products/wh_sosr_webds/
Uterine atony treatment cont.

- B-Lynch Uterine Suture Brace

http://www.cblynch.co.uk/wp-content/uploads/tech-image.jpg
Continued atony despite medical mgt.

Mode of delivery

Cesaean

Vaginal
Lacerations

• Cervical and Vaginal lacerations
  – identified on initial presentation with PPH
  – repair
Retained products

- Careful visualization of placenta
- Manual uterine exploration
- Ultrasound
Fluids and blood products

- Discussed separately
Obstetric management of PPH

• Summary
  – Preparation and anticipation
  – Early diagnosis
  – Rule out lacerations and retained products
  – Uterine atony Rx
    • medical mgt
    • more medical mgt
    • more medical mgt
    • surgical options

• Research gaps
  – optimal drug combinations
  – personalized uterotonic approach to treatment
Questions?