CRASH 2015
Pulmonary Hypertensive Crisis

Mark Twite  MA MB BChir FRCP
Children’s Hospital Colorado & University of Colorado
Anschutz Medical Campus
Mark.Twite@UCDenver.edu

Disclosures

• No financial disclosures
• Some drugs discussed are an off-label application

Objectives

After 30 minutes, understand:

1. Pathophysiology of pulmonary hypertension (PH)
2. Anesthetic management of PH
3. Strategies to prevent and treat a PH crisis

Case Scenario

• 18yr old, 70kg female with PH
• Requires Broviac® catheter placement and lung biopsy
• Last Echocardiogram report
  – Tricuspid regurgitant (TR) jet 5m/sec   (BP 110/70)
  – No PFO
• Patient’s medications
  – Epoprostenol sodium (Flolan®)
  – Sildenafil (Revatio®)
  – Bosentan (Tracleer®)
  – Aspirin
  – Nifedipine

Question

What is the degree of this patient’s PH?

1. Supra-systemic
2. Systemic
3. Sub-systemic

Definition: Pulmonary Hypertension

• mPAP ≥ 25 mmHg at rest
  • Normal mean pulmonary artery pressure (mPAP)=15mmHg
    = independent of age, gender, ethnicity
  • During exercise mPAP increases slightly
    = dependent on age and level of exertion

• PVRI ≥ 3 Wood units m²
  • In association with variable degrees of:
    • Pulmonary vascular remodeling
    • Vasconstriction
    • In-situ thrombosis

Twite, Mark, MA, MB, BChir, FRCP
CRASH 2015: Pulmonary Hypertensive Crisis
Case Scenario
• 18yr old, 70kg female with PH
• Requires Broviac® catheter placement and lung biopsy

Last Echocardiogram report
– TR jet 5m/sec (BP 110/45)
– No PFO

Patient’s medications
– Epoprostenol sodium (Flolan®)
– Sildenafil (Revatio®)
– Bosentan (Tracleer®)
– Aspirin
– Nifedipine

ECHO: Systolic TR Velocity
Bernoulli Equation
\[ sPAP = 4v^2 + RAP \]
\[ sPAP = 4(5^2) + 10 \]
\[ sPAP = 110 \text{ mmHg} \]

Limitations:
• Need TR
• Assumes perfect alignment between Doppler and TR jet

Definition: Pulmonary Hypertension
• mPAP ≥ 25 mmHg at rest
  • Normal mean pulmonary artery pressure (mPAP)=15mmHg

  • PVRI ≥ 3 Wood units m²

Cardiac Cath: Gold standard
1. Hemodynamics
   \[ \text{PVR} = \frac{\text{mPAP} - \text{LAP}}{\text{CO}} \]
   Normal PVR 1-1.4 Wood units m² (90 – 120 dynes/s/cm⁵)
   PH PVR > 3 Wood units m² (240 dynes/s/cm⁵)
   Wood units x 80 = dynes/s/cm²
2. Vasoreactivity testing
   Short acting pulmonary vasodilator
   • iNO, IV adenosine
   Drop in mPAP > 10 mmHg
   Responders (<10%) may benefit from calcium channel blockers
3. Rule out associated disease states
   Pulmonary vein disease
Non-invasively monitor patients with PH?

- Right ventricle (RV) function
  - Ability of the RV to cope with progressive increase in PA pressure
  - Determines patient’s functional capacity and survival

- Other ECHO parameters (observer angle dependent):
  - TAPSE (Tricuspid Annular Plane Systolic Excursion)
  - Tei index

Increase of 0.1 in S:D ratio associated with 13% increase in yearly risk for lung transplant or death.

S:D ratio > 1.4 associated with worse:
- RV function
- Hemodynamics
- Exercise capability
- Clinical status

PH Classification: What increases mPAP?

- PVR = mPAP – LAP/CO
- mPAP = LAP + (CO x PVR)

1. ↑LAP
   - LV systolic / diastolic dysfunction
   - Mitral valve stenosis / regurgitation

2. ↑CO
   - Congenital heart disease with L to R shunt

3. ↑PVR
   - Pulmonary parenchymal disease
   - Thromboembolic disease

WHO Classification Conferences

- 1973 Geneva
- 1988 Evian
- 2003 Venice
- 2008 Dana Point
- 2011 Panama
  - Pulmonary Vascular Research Institute
  - Classification specific to children
- 2013 Nice, France

WHO Classification

- Group I PAH
- Group II Left sided heart disease
- Group III Lung disease and/or hypoxia
- Group IV Chronic embolic/thrombotic
- Group V Miscellaneous
WHO Classification

- **Group I** PAH
  - Idiopathic
  - Heritable: TGF-β Family (BMPR2, ALK-1, Endoglin)
  - Drugs: Fenfluramine, methamphetamine
  - Herbal supplements: St. John’s Wort
  - Associated with:
    - Congenital heart disease
    - Connective tissue disease (SLE)
    - HIV
    - Chronic hemolytic anemias (Sickle cell disease)
    - Schistosomiasis
    - Pulmonary veno-occlusive disease (PVOD)
- **Group II** Left heart disease
  - Mitral valve disease
- **Group III** Lung disease and/or hypoxia
  - COPD
  - BPD
  - Interstitial lung disease
  - Sleep-disordered breathing
  - High altitude
- **Group IV** Chronic embolic/thrombotic
- **Group V** Miscellaneous
  - Myeloproliferative disorders
  - Metabolic disorders

Pediatric Pulmonary Hypertension

PH: Congenital Heart Disease

Biventricular Circulation
- mPAP > 25mmHg & PVRI > 3 Wood units m²
- Positive vasodilator response is a fall in mPAP and PVRI by 20% with no change in CO

Univentricular Circulation
- following cavopulmonary anastomosis
- PVRI > 3 Wood units m² or TPG > 6 mmHg
  - EVEN IF mPAP < 25mmHg

Adult: Epidemiology & Survival

- Rare disease 5-15 cases / million
- REVEAL
  - Age of presentation increased from 35yrs in 1980s to 53yrs
  - Male:Female 1:4
  - 1yr survival 80-90%
  - 3yr survival 60%

Pediatric: Epidemiology & Survival

**TOPP**

- Global registry
- At diagnosis:
  - Median age 7yrs
  - Dyspnea & fatigue
  - 43% other disorders
    - 85% CHD, 12% BPD
    - Chromosome anomalies
      - 13% (Trisomy 21)

**REVEAL**

- USA registry
- At diagnosis:
  - Median age 7yrs
  - Dyspnea
  - mPAP 56mmHg
  - PVRI 17 Wood units m²
  - 5yr survival 75%
Case Scenario

- 18yr old, 70kg female with PH
- Requires Broviac® catheter placement and lung biopsy
- Last Echocardiogram report
  - TR jet 5m/sec (BP 110/45)
  - No PFO
- Patient’s medications
  - Epoprostenol sodium (Flolan®)
  - Sildenafil (Revatio®)
  - Bosentan (Tracleer®)
  - Aspirin
  - Nifedipine

Question

With no PFO on ECHO, what may happen during an acute increase in PVR?

<table>
<thead>
<tr>
<th>Option</th>
<th>BP</th>
<th>SpO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>↓</td>
<td></td>
</tr>
</tbody>
</table>

Physiology of Pulmonary Circulation

- Pulmonary vascular bed is a high-flow low-pressure circulation system
  - Large cross sectional area
  - High compliance arterioles with thin walls (less smooth muscle cells)
  - Pressure and resistance are 10% of systemic circulation
  - Sympathetic nervous system innervation
- Pulmonary arteries
  - Constrict with hypoxia (Euler-Liljestrand reflex) and relax with hyperoxia
  - Respond to changes in cardiac output and airway pressure

Pathophysiology of Pulmonary Circulation

- Poiseuille’s Law: \( R = \frac{\pi r^4 p}{8nl} \)
- 8mm ≈ 1 x R
- 4mm ≈ 16 x R
- 2mm ≈ 256 x R

PH: Pathology

A. Vasculopathy of the pulmonary arteriole cells
1. Endothelial
   - Intimal hyperplasia
2. Smooth muscle cell (SMC)
   - Medial hypertrophy
3. Adventitial
   - Proliferation

B. Vasoconstriction

C. Thrombosis
**Discussion**

What will be your airway and ventilation strategy to facilitate the lung biopsy?

Concerns?

Does anyone want a type & screen or cross match?

---

**Case Scenario**

- 18yr old, 70kg female with PH
- Requires Broviac® catheter placement and lung biopsy
- Last Echocardiogram report
  - TR jet 5m/sec (BP 100/45)
  - No PFO

**Patient’s medications**
- Epoprostenol sodium (Flolan®)
- Sildenafil (Revatio®)
- Bosentan (Tracleer®)
- Aspirin
- Nifedipine

---

**Case Scenario**

- 18yr old, 70kg female with PH
- Requires Broviac® catheter placement and lung biopsy
- Flolan® running via PIV
- NPO status good
**Question**

What is this patient’s risk of cardiac arrest under general anesthesia?

1. 10 times LESS
2. SAME
3. 10 times GREATER
4. 40 times GREATER

---

**PH: Peri-operative risk**

<table>
<thead>
<tr>
<th>Population</th>
<th>Procedures (n)</th>
<th>Cardiac arrest (%)</th>
<th>Death (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children</td>
<td>All (1,089,200)</td>
<td>0.027</td>
<td>0.004</td>
<td>Morray et al. Anesthesiology 2000;93:6-14</td>
</tr>
<tr>
<td>All children</td>
<td>All except cardiac surgery (88,639)</td>
<td>0.029</td>
<td>0.016</td>
<td>Flick et al. Anesthesiology 2007;106:226-237</td>
</tr>
<tr>
<td>Children with heart disease</td>
<td>Cardiac cath (4,454)</td>
<td>0.49</td>
<td>0.08</td>
<td>Benattar et al. Pediatr Anesthesiology 2003;15:1083-88</td>
</tr>
<tr>
<td>Children with PAH</td>
<td>All except cardiac surgery (256)</td>
<td>1.17</td>
<td>0.78</td>
<td>Carmosino et al. Anesthesiology 2007;104:521-527</td>
</tr>
<tr>
<td>Children with PAH</td>
<td>Cardiac cath (141)</td>
<td>2.13</td>
<td>1.42</td>
<td>Carmosino et al. Anesthesiology 2007;104:521-527</td>
</tr>
<tr>
<td>Children with PAH</td>
<td>Cardiac cath (128)</td>
<td>0.8</td>
<td>0</td>
<td>Williams et al. Pediatr Anesthesiology 2010;20:28-37</td>
</tr>
</tbody>
</table>

Adapted from Friesen. Pediatr Anesthesia 2008;18:208-216

---

**Discussion**

What is your plan for induction of anesthesia?

Use the existing PIV?

Drugs?

---

**PH: Goals of anesthetic management**

1. Avoid increases in pulmonary vascular resistance (PVR)
   - Hypoxia, Hypercarbia, Metabolic acidosis
   - Sympathetic stimulation secondary to noxious stimuli
     (endotracheal intubation, surgery, tracheal suctioning)

2. Avoid systemic hypotension
   - Decreases coronary artery blood flow leading to myocardial ischemia and ventricular dysfunction
   - A rapid increase in PVR to a point where PAP > SBP leads to RV failure especially if there is no PFO (or atrial septostomy)

---

**Hemodynamic effects of anesthetic drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>MAP</th>
<th>SVR</th>
<th>PAP</th>
<th>PVR</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheologic</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>→</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Desflurane</td>
<td>→</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Propofol</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Ketamine</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Etomidate</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>↑</td>
<td>→</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>→</td>
<td>↑</td>
<td>↑</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Opioids</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>→</td>
</tr>
</tbody>
</table>

MAP = mean arterial pressure; SVR = systemic vascular resistance; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; HR = heart rate; ↓ decreases; ↑ increases; → no significant change. Ketamine decreases contractility in vitro and in catecholamine-depleted patients. Dexamethasone can increase PVR during loading dose administration.
Preparation

- iNO in the room
  - Set-up and working, weaning plan to avoid rebound PH
- Anesthesia drugs
  - 4% topical lidocaine spray for vocal cords
  - Balanced technique
  - Resuscitation drugs ready
- Communicate with surgeon
  - High risk patient
  - Local anesthetic
- Post-op plan
- Communicate with PH team

Pulmonary Hypertensive Crisis

- Pulse-oximetry desaturation  Sats 70%
- Hypotensive  BP 60/30
- Tachycardia ➔ Bradycardia  HR 30
- ECG ST segment changes

PH: Pathophysiology of RV Failure

Disposition and Follow-up

- Extubated and returned to the ICU
- Returned emergently to the OR 3 hours later
  - Bleeding via Chest Tube
  - Hypoxic and hypotensive

Summary

- Knowledge & therapy of PH is an evolving field
- Patients with systemic PH are HIGH risk
- Goals for anesthesia in PH
  - Preparation
  - Good airway management
  - Balanced anesthetic drug technique

Treatment | Rationale / Therapy
---|---
Administer 100% O₂ | ↑P₅O₂ and P₅O₂ will ↓PVR
Hyperventilate | PVR is directly related to PaCO₂
Exclude pneumothorax | Optimize ventilation
↓Mean Airway Pressure | Avoid P₅A > P₅es
Correct metabolic acidosis | PVR is directly related to H⁺ level
Administer pulmonary vasodilators | NO
Analgesia | Decrease sympathetic mediated ↑PVR
Support cardiac output | Adequate preload, epinephrine, vasopressin
ECMO | Support cardiac output and oxygenation
Thank you!