Pregnancy In Pulmonary Hypertension: An Update

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FINANCIAL DISCLOSURE

Dianne L. Zwicke, MD

I have been an investigator and/or received study grants from the following companies:

- Glaxo – Welcome
- Medtronic
- *Gilead
- Lilly
- Reata

*United Therapeutics
Co Therix
Actileon
*Bayer
Elgier

Pfizer
Ikaria
Novartis
GENO
Univ of SD-CTEPH

* Appointed to Advisory Boards
Evolution of PAH and Pregnancy Data

2003
Observe & Counsel
CHEST

2016
Pre-Pregnancy Counseling
CPP / CHEST / PHPN

2011
Multidisciplinary Team
PHA / ERS

2008
Pharmacology & Team –
CHEST / CPP / ACC
### VOLUME
- Total Patients (Mothers) 170
- Total Infants 186

### Diagnosis of PAH
- Pre Pregnancy 10
- Post Pregnancy 8

### F/U of pre-pregnancy
- Chose Adoption 1
- Lost to F/U 1
- Proceeded with Pregnancy 8

### Infants
- Female 106 (57%)
- Male 80 (43%)

### Geography
- United States 32
- Foreign Countries 22
OUR NEIGHBORS / WORLD MAP
ETIOLOGY OF PAH / 170 PATIENTS

- Idiopathic PAH (44.7%)
- Congenital Heart Disease (24.7%)
- Connective Heart Disease (12.25%)
- Familial PAH (11.76%)
- Anorexic Drug Related (2.9%)
- CTEPH (6%)
Clinical symptoms at time of first evaluation

92% Dyspnea on exertion

77% Lower extremity edema

44% Pre-syncope

12% Syncope

82% Increased abdominal girth for gestational age

33% Chest pressure, discomfort, pain with exertion
WHAT IS CAUSE OF SYMPTOMS

• Serious altercations in normal pregnancy
  • Each trimester
  • Post partum
  • Manifests at 16-28 weeks gestation, especially weeks 24-28

• Systems
  • Cardiovascular System
    ↑ total blood volume by 20-30%
    ↑ red cell mass and plasma volume is 30-50%
    ↑ heart rate by 25 beats per minute
    ↑ Cardiac output throughout pregnancy, peak at 32 weeks (30-50%)
    ↑ SVR, PVR, BP decreases
    ↑ 500 cc of blood wash in/out of uterus with contractions
PAH SYMPTOMS

- Fixed pulmonary vascular resistance (PVR), with serious increase in blood volume.
- Decreased or fixed cardiac output (supply & demand).
- RV dysfunction → fluid retention.
- Impaired venous return secondary to compression of the IVC, as fetus grows.
- Worsening right to left shunt, if present.
- Evaluate nocturnal O₂.
- Hypercoagulability.
<table>
<thead>
<tr>
<th>Pharmacologic agents used in pregnant patients with PAH at our center</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled vasodilators</strong></td>
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<tr>
<td>Nitric oxide</td>
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<tr>
<td>Epoprostenol (Flolan, Veletri)</td>
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<tr>
<td>Treprostinil (Tyvaso)</td>
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<tr>
<td><strong>Inotropes agents</strong></td>
</tr>
<tr>
<td>Dobutamine (Dobutrex)</td>
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<tr>
<td>Digoxin (Lanoxin)</td>
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<tr>
<td>Dopamine</td>
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<tr>
<td><strong>Intravenous prostacyclins</strong></td>
</tr>
<tr>
<td>IV Epoprostenol</td>
</tr>
<tr>
<td>Flolan (early years)</td>
</tr>
<tr>
<td>Veletri (more recently)</td>
</tr>
<tr>
<td>IV Treprostinil</td>
</tr>
<tr>
<td>Remodulin</td>
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<tr>
<td><strong>Antiarrhythmic</strong></td>
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<tr>
<td>Antiarrhythmic (A-Fib)</td>
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<tr>
<td>Diltiazem (Cardizem)</td>
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<tr>
<td>Amiodarone (Cordarone)</td>
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<tr>
<td>Digoxin (Lanoxin)</td>
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<tr>
<td><strong>IV prostacyclins</strong></td>
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<tr>
<td>IV Treprostinil</td>
</tr>
<tr>
<td>Remodulin</td>
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<tr>
<td><strong>Oral prostacyclins</strong></td>
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<tr>
<td>Orenitram (Treprostinil Oral)</td>
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<tr>
<td>Selexipeg (Utravi)</td>
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<tr>
<td><strong>PDE-5</strong></td>
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<tr>
<td>Sildenafil (Revatio)</td>
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<tr>
<td>Tadalafil (Adcirca)</td>
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<tr>
<td><strong>Calcium channel blocker</strong></td>
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<tr>
<td>Nifedipine (Procardia)</td>
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<tr>
<td>Amlopidine (Norvasc)</td>
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<tr>
<td><strong>Anticoagulants</strong></td>
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<tr>
<td>Warfarin (Coumadin)</td>
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<tr>
<td>Enoxaparin (Lovenox)</td>
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<tr>
<td><strong>Diuretics</strong></td>
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<tr>
<td>Furosemide (Lasix)</td>
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<tr>
<td>Torsemide (Demadex)</td>
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<tr>
<td>Bumetanide (Bumex)</td>
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<tr>
<td><strong>Other</strong></td>
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<tr>
<td>Potassium chloride</td>
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<tr>
<td>Magnesium</td>
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</tbody>
</table>
Medications not recommended in pregnancy secondary to teratogenicity

- SCG DRUGS (Adempas)
- ERA Drugs (Letaris, Macitentan, Tracleer)
EVALUATION

- Multidisciplinary teams established early
- Written Delivery / Care plan
- Spinal anesthesia is mandatory
- Delivery – Cesarean Section 32 (17.4%)
  Vaginal delivery 148 (80.4%)
  Conversion 4 (2.2%)
- Degree of PAH
  Severe - 63 patients
  Moderate - 88 patients
  Mild - 19 patients
Long Term Follow up of patients

170 Patients – NO Deaths related to pregnancy.

Etiology of 8 deaths within observation time of study

- No deaths during or within 18 months after delivery of babies.
- 1 death secondary to progression of CTD (Lupus)
- 3 deaths secondary to progression of congenital heart disease awaiting heart-lung transplant
- 4 deaths from progression of primary disease
  1 Anorexic PAH, 1 Sickle Cell disease, 1 Idiopathic PAH, 1 Familial PAH