Pulmonary Hypertension (PHTN)

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Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management

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Outline

Definition

Classification

Aetiology

Diagnosis

Medical management
Definition

Increased pulmonary pressures

– Mean PAP $\geq$ 20 mmHg at rest (previously 25)
– PVR $\geq$ 3 WU/m$^2$

Fontan circulation

– Do not usually fulfil the definition of PH

(Paediatric Task Force of the 6th World Symposium on Pulmonary Hypertension, 2018, Fr)

Classification/Aetiology in children

• Primary PAH or idiopathic pulmonary arterial hypertension (IPAH)

• Familial (heritable PAH)
  • Gene mutations implicated in some sporadic and HPAH

• PPHN

Persistent pulmonary hypertension of the newborn (PPHN) and associated disorders

Idiopathic PPHN
Down syndrome
Meconium aspiration syndrome
Respiratory distress syndrome
Transient tachypnoea of the newborn
Pneumonia/sepsis
Developmental lung disease
Peri-natal stress

Myocardial dysfunction (asphyxia, infection)
Structural cardiac diseases
Hepatic and cerebral arteriovenous malformations

Associations with other diseases:
  Placental dysfunction (pre-eclampsia, chorioamnionitis, maternal hypertension)
  Metabolic disease
  Maternal drug use or smoking

Proportion of newborns with PPHN is inversely related to gestational age
Secondary PAH

– Heart or vascular disease: shunts, flow

– Developmental lung diseases: bronchopulmonary dysplasia (BPD), congenital diaphragmatic hernia (CDH) and congenital pulmonary vascular abnormalities

– Others: infection (HIV, Schistosomiasis), drugs, toxins, thrombo-embolic diseases, space occupying lesions/pressure,
<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Pulmonary arterial hypertension (PAH)</td>
<td>Idiopathic PAH, Connective tissue disease associated PAH, Congenital heart disease associated PAH, Heritable PAH, Persistent PH of the newborn</td>
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<tr>
<td>Group 2</td>
<td>PH due to left heart disease</td>
<td>Left ventricular systolic dysfunction, Left ventricular diastolic dysfunction, Aortic or mitral valvular heart disease</td>
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<td>Group 3</td>
<td>PH due to lung diseases and/or hypoxia</td>
<td>Chronic obstructive pulmonary disease, Interstitial lung disease, Sleep-disordered breathing, Developmental lung disease</td>
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<td>Group 4</td>
<td>Chronic thromboembolic PH</td>
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<tr>
<td>Group 5</td>
<td>PH with unclear multifactorial mechanisms</td>
<td>Sarcoidosis, metabolic disorders, Chronic hemolytic anemia</td>
</tr>
</tbody>
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Adapted from: [https://www.researchgate.net/publication/281736900_Statement_on_pregnancy_in_pulmonary_hypertension_from_the_Pulmonary_Vascular_Research_Institute](https://www.researchgate.net/publication/281736900_Statement_on_pregnancy_in_pulmonary_hypertension_from_the_Pulmonary_Vascular_Research_Institute) [accessed Apr 09 2019]
Pathophysiological changes

- Severe and sudden
  - Right sided failure >>> heart failure

- Chronic PHTN
  - Hypertrophy and dilatation of RV
  - Increase RV pressure
Pathophysiological changes

• Reduced cardiac output
  – RV hypertrophy
    • Impaired cardiac perfusion
      – Impairs LV function
      – Increased LA, LV pressure

  – Increased pulmonary vascular resistance
    • Reduced pulmonary vascular return
Clinical presentation

• Subtle and nonspecific

• Clear cardiorespiratory signs & symptoms
  • Could have a delay of up to 3 years
    – Breathlessness, easy fatigability
    – Chest pain
    – Syncope

• Examination
  – Respiratory signs
  – Loud P2
  – Others based on cause
Diagnosis/Investigations

• Best to exclude:
  • Common respiratory problems
  • Treatable causes

• Exercise testing (6-minutes walk test)
  – After ECG
  – Gives estimate of cardiopulmonary capacity
Cardiac Investigations

• ECG: Rhythm
  – Right Ventricular hypertrophy
  – ST-T wave abnormalities in inferior leads
  – RA enlargement,

• CXR
  – Right atrial enlargement
  – Pulmonary vascular markings

• Cardiac Echo
  – TR,
  – In PR: EDP,
  – Pressure gradient across: In VSD, PDA
  – IVS shape
Cardiac Investigations

• Catheterization
  – Pressure measurements
  – Include acute pulmonary vaso-reactivity study

• CT
  – High resolution CT lungs
  – CT angiography
    • PAs

• Cardiac MRI
Other investigations

• Respiratory
  – Blood gas analysis
  – Lung function tests
  – Nocturnal O₂ sats. monitoring
    • <90%---Supplement
  – Pulmonary function tests
  – Ventilation perfusion scan : ?emboli

• Airway obstruction (PNS, Polysomnography)
• BNP and NT-proBNB levels (severity and response to Rx)
• Coagulation profile
• Thyroid function
• HIV
• Others based on likely cause: Genetic testing, lung biopsy
Management in practice

• Sildenafil caution!

• Diuretics, oxygen, anticoagulation and digoxin should be considered on an individual basis

• Don’t overly decrease intravascular volume due to the pre-load dependence of RV
  – If, sustained and improved response, CCBs may be continued,
Management of PHTN

1. Prevention
2. **Treat primary disease**
3. Oxygen
   - ?Hyperoxia
4. Diuretics
   - Fluid overload
5. Nitrous oxide
6. Calcium channel blockers: Nifedipine – muscle relaxant
   - Not all respond
7. Phosphodiesterase-5 inhibitors: sildenafil, tadalafil
   - **Blood vessel relaxation**
   - Increases the levels of cycline guanosine monophosphate (cGMP), thereby promoting vasodilatation in the pulmonary vascular bed
8. Endothelin receptor antagonists:
   - Bosentan, ambisentan
   - Block endothelin >>> no narrowing

9. Prostacyclin: IVI or subQ
   - Slow down progression
   - Prostacyclin analogs:
     - Epoprostenol (Flolan) IVI – off label

10. Anti-platelet/ anti-coagulation: Aspirin/warfarin
    - Minimize clot formation in pulmonary vessels

11. ECMO to Lung transplant
Costs

• Sildenafil
  – 10 mg at about 100/=  
  – Dose:
    • UK: 0.5 mg/kg/dose up to a maximum of 2 mg/kg/dose/every 6 h  
    • US: 0.5-2 mg/kg three times daily

• Epoprostenol (Flolan)
  – 0.5 mg at about 2,800/=  
  – Dose: start 1-2 nanograms/kg/min up to 60-80 ng/kg/min
The end

Todah raba

Ahsante sana

Mbuya mono