Pulmonary Hypertension (PHTN)

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SERIES
WORLD SYMPOSIUM ON PULMONARY HYPERTENSION

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

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Eur Respir J 2019; 53: 1801916

Outline

Definition

Classification

Aetiology

Diagnosis

Medical management

Definition

Increased pulmonary pressures

- Mean PAP≥ 20 mmHg at rest (previously 25)
- PVR ⩾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)

Rosenzweig EB, Abman SH, Adatia I, et al. Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management. **Eur Respir J 2019;** 53: 1801916 [https:// doi.org/10.1183/13993003.01916-2018].

Classification/Aetiology in children

- Primary PAH or idiopathic pulmonary arterial hypertension (IPAH)
- Familial (heritable PAH)
    - Gene mutations implicated in some sporadic and HPAH
- PPHN

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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,

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Classification

Group	Definition	Etiology
Group 1	Pulmonary arterial hypertension (PAH)	Idiopathic PAH, Connective tissue disease associated PAH, Congenital heart disease associated PAH, Heritable PAH, Persistent PH of the newborn
Group 2	PH due to left heart disease	Left ventricular systolic dysfunction, Left ventricular diastolic dysfunction, Aortic or mitral valvular heart disease
Group 3	PH due to lung diseases and/or hypoxia	Chronic obstructive pulmonary disease, Interstitial lung disease, Sleep-disordered breathing, Developmental lung disease
Group 4	Chronic thromboembolic PH	
Group 5	PH with unclear multifactorial mechanisms	Sarcoidosis, metabolic disorders, Chronic hemolytic anemia

Adapted from:
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 O_2 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, tadafil
   - ***Blood vessel relaxation***
   - Increases the levels of cycline guanosine monophosphate (cGMP), thereby promoting vasodilatation in the pulmonary vascular bed

Management of PHTN

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