RESPIRATORY DISORDERS ASSOCIATED WITH BRONCHOPULMONARY DYSPLASIA

Respiratory 2 Department
CONTENT:

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**INTRODUCTION**

*Bronchopulmonary dysplasia* is a chronic lung disease in premature infants who required long-term oxygen.

<table>
<thead>
<tr>
<th></th>
<th>&lt;32 weeks GA</th>
<th>&gt;32 weeks GA</th>
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<tbody>
<tr>
<td><strong>Treatment with oxygen</strong></td>
<td>&gt;21% for at least 28 days</td>
<td>&gt;21% for at least 28 days</td>
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<tr>
<td><strong>Time point of assessment</strong></td>
<td>36 weeks PMA or discharge*</td>
<td>&gt;28 days but &lt;56 days postnatal age or discharge*</td>
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<tr>
<td><strong>Grade:</strong></td>
<td></td>
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<tr>
<td>Mild</td>
<td>Breathing room air at 36 weeks PMA or discharge*</td>
<td>Breathing room air at 56 days Postnatal age or discharge*</td>
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<tr>
<td>Moderate</td>
<td>Need for &lt;30% oxygen at 36 weeks PMA or discharge*</td>
<td>Need for &lt;30% oxygen at 56 days Postnatal age or discharge*</td>
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<tr>
<td>Severe</td>
<td>Need for ≥30% oxygen and/or positive pressure (IMV/CPAP) at 36 weeks PMA or discharge*</td>
<td>Need for ≥30% oxygen and/or positive pressure (IMV/CPAP) at 56 days Postnatal age or discharge*</td>
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INTRODUCTION

• Have advances in perinatal care and a steady decline in mortality rates among very low birth weight infants (<1500g), BPD remains a major complication of premature birth.

• BPD tends to improve with advancing age, it can lead to lifelong consequences.
1. Upper airway disease

- Children born preterm may be more likely to have obstructive sleep apnea compared with term, may persist into adulthood.

- Deficit of intelligence quotient and possible neuronal injury.
PARTICIPANTS: 398,961 children, aged 2.5 to 6 years.

RESULTS:
2- Central airway disease

Children with BPD are at increased risk of developing central airway collapse or obstruction, including:

- **Glottic and subglottic damage**
- **Acquired tracheobronchomalacia**
- **Tracheal & bronchial stenosis and granuloma formation**
a. Glottic and subglottic damage:

- Reported after endotracheal intubation.
- Risk factor: intubated for many weeks, required more intubations, use inappropriately large endotracheal tubes.
- Postextubation stridor is common sign of moderate to severe subglottic stenosis. This child may have chronic symptoms or exhibit symptoms only during acute upper respiratory tract infections.
b. Acquired tracheobronchomalacia:

- Common in infant with classic BPD treated with prolonged positive pressure ventilation.
- Associated with barotrauma, chronic or recurrent infection, chronic aspiration, and endotracheal intubation.
- Improve with age, as the tracheal cartilage matures.
- Symptoms: reflex apnea or chronic wheezing (don’t improve or worsen with bronchodilator); increase with crying or exertion.
b. Acquired tracheobronchomalacia:

- Infants with classic BPD, tracheomalacia was found in 45% and bronchomalacia was found in 34%.

(Cohn RC, Kercsmar C. Am J Dis Child. 1988;142(11):1225)
Study of 974 neonates with BPD
Tracheobronchomalacia: 353 (36.2%)
Without Tracheobronchomalacia: 621 (63.8%)

Results: Neonates with TBM and BPD had more comorbidities, such as gastroesophageal reflux and pneumonia, and more commonly required surgeries, such as tracheostomy and gastrostomy, than those without TBM
c. *Tracheal and bronchial stenosis and granuloma formation:*

- Result of trauma from artificial airways and suctioning techniques.
- Cause long-term pulmonary problems: acquired lobar emphysema, persistent lobar atelectasis.
3- Sleep Hypoxemia

- Infants with BPD are more experience hypoventilation and hypoxemic episodes during sleep; may be clinically silent.
- Common during rapid eye movement (REM) sleep
- Due to reduction of intercostal and upper airway muscle tone, inadequate autonomic response mechanisms and hypoxemia-induced airway narrowing.
- Hypoxemic episodes during sleep can also affect older children, associated with growth delay.
4- Pulmonary Function

• Decrease FEV₁ and FEV₁/FVC, consistent with airflow limitation and small airway obstruction.

• Airflow limitation may be consequence of dysanaptic growth: length and diameter of the airways grow less rapidly than the lung parenchyma.
Effect of preterm birth on later FEV$_1$: a systematic review and meta-analysis

Sarah J Kotecha,¹ Martin O Edwards,¹ W John Watkins,¹ A John Henderson,³ Shantini Paranjothy,² Frank D Dunstan,² Sailesh Kotecha¹


Study characteristics: 59 studies; ages ranged from 5 to 23 years; preterm-born subjects were born between 24 and 36 weeks gestation.

Results:
The mean differences for %FEV$_1$ compared with term-born controls:

- preterm-born group without BPD: $-7.2\%$ ($-8.7\%$ to $-5.6\%$)
- preterm-born group with BPD$_{28}$: $-16.2\%$ ($-19.9\%$ to $-12.4\%$)
- preterm-born group with BPD$_{36}$: $-18.9\%$ ($-21.1\%$ to $-16.7\%$)

Pooled %FEV$_1$ estimate:

- preterm-born group without BPD: $91.0\%$ ($88.8\%$ to $93.1\%$)
- preterm-born group with BPD$_{28}$: $83.7\%$ ($80.2\%$ to $87.2\%$)
- preterm-born group with BPD$_{36}$: $79.1\%$ ($76.9\%$ to $81.3\%$)

BPD$_{28}$ supplemental oxygen dependency at 28 days
BPD$_{36}$ supplemental oxygen dependency 36 weeks postmenstrual age
5- Asthma-like Symptoms:

- Recurrent wheezing episodes: common in children with BPD, beginning in the preschool years and continuing into adulthood.

- “The prevalence of asthma was higher in children and adolescents with a history of prematurity and BPD compared with those who did not develop BPD.”

- **Results:** Children born EP had significantly more chest deformities and respiratory symptoms than classmates, with twice as many (25% vs. 13%; P < 0.01) having a current diagnosis of asthma. 56% of children born EP had abnormal baseline spirometry and 27% had a positive bronchodilator response.

*Extremely Preterm: born at or less than 25 completed weeks of gestation*
5- Asthma-like Symptoms:

- BPD and asthma differ in underlying pathophysiology:
  - BPD: fixed obstruction + neutrophilic inflammation
  - Asthma: reversible obstruction + eosinophilic inflammation

- If spirometry suggests obstructive lung disease, a trial of standard asthma-management techniques is appropriate

- May respond to bronchodilator and inhaled corticosteroids, but the effect is less consistent than in children with asthma.
METHODS:
44 children with BPD with a mean gestational age of 25.6 weeks measured of lung function V(max)FRC and FRC at 6, 12, and 24 months after initial discharge from the neonatal care unit.

RESULTS:
Response to bronchodilator was significant in approximately 1/3 patients, similar to the findings of Robin et al, who reported 35% of their patients to have significant response to bronchodilator.

Mean FRC was significantly higher in children who were using bronchodilators and inhaled steroids but showed no correlation with clinical symptoms. Bronchodilator response was initially present in 30% of the patients and declined to 20% at the end of the study.

6- Respiratory Infection

• 50% BPD require rehospitalization during the first two years of life due to a respiratory illness.
• Pathogen is usually viruses (RSV, Rhino virus,…)
• Respiratory infections, including RSV, can cause particularly severe illness, can be life-threatening.
• Respiratory Infections may interfere with postnatal lung growth and adversely affect lung function in later life.
6- Respiratory Infection

- BPD hospitalized with an RSV infection within the first 2 years of life have increased health care costs and worse lung function at school age.

- BPD may require additional immunizations and immunoprophylaxis for RSV (Palivizumab).

- Rhinovirus predominately causes upper airway symptoms in healthy individuals, but causes severe lower respiratory tract disease can occur in children with BPD.
7- Pulmonary Artery Hypertension

- An important complication associated with BPD.
- PAH was diagnosed prior to hospital discharge in 18% of ELBW infants.
  
- BPD infants with PAH more require supplemental respiratory support, have longer initial hospitalizations, and higher medical costs.
- Resolves with age and catch-up lung growth
- Mortality rates in BPD infants with PAH: 14% - 38% in retrospective studies
  
  (An HS, Bae EJ, Kim GB. *Korean Circ J.* 2010 Mar;40(3):131-6)

and 12% in one prospective study.

Risk factor for PAH:

1. Extremely Low Gestational Age (GA < 28 weeks)
2. Very Low Birth Weight (<1500 g)
3. Small for gestational age birth weight
4. Oligohydramnios
5. Prolonged mechanical ventilation
6. Prolonged oxygen therapy
Pathogenesis for PAH:

- **Abnormal pulmonary vascular bed**: reduce size and complexity of pulmonary vascular bed, and increased reactivity of the arteries.

- **Oxygen toxicity and barotrauma**: interfere with alveolar development, reducing the number of alveoli and intra-acinar arteries → impaired production of nitric oxide and vascular endothelial growth factor (VEGF).

- **Alveolar hypoxia**: cause vasoconstriction and injury endothelial cell, hypertrophy of pulmonary arterial wall.

- **Cardiac dysfunction**: Left ventricular diastolic dysfunction.
Candidates for screening PAH:

1. VLBW (<1500 g) with BPD
2. ELBW (<1000 g) with or without BPD
3. Infants unable to wean from supplemental oxygen and/or positive pressure ventilation by 2 months of age
4. VLBW infants with poor weight gain
5. Infants born small for gestational age
CONCLUSION

• BPD can lead to lifelong consequences:
  - Upper and lower airway disease
  - Altered pulmonary function
  - Pulmonary artery hypertension

• To minimize lung injury:
  - Avoid recurrent respiratory infections
  - Minimize feeding-related aspiration
  - Optimize nutrition

particularly during the first two years of life.
CONCLUSION

• Recurrent wheezing is common in children with BPD, but pathophysiology differs from asthma. If spirometry suggests obstructive lung disease, a trial of standard asthma-management techniques is appropriate.

• Severe BPD may develop PAH. Infants need for supplemental oxygen at the time of hospital discharge should be evaluated for PAH.
References

• Sharon McGrath-Morrow, Joseph M Collaco. Complications and long-term pulmonary outcomes of bronchopulmonary dysplasia. Uptodate 2017


THANK YOU FOR ATTENTION