BREATHE EASY: OBSTRUCTIVE LUNG DISEASE IN THE ICU

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CHRONIC OBSTRUCTIVE PULMONARY DISEASE

What is chronic obstructive pulmonary disease (COPD)
- Persistent airflow limitation
- Progressive chronic inflammatory process
- Preventable → noxious particles or gases
- Parenchymal lung damage
- Dyspnea
- Chronic cough and sputum production

DISCLOSURE

I do not have any significant financial interest or other relationship with the companies who make/provide these products/services

OBJECTIVES

- Discuss the impact of obstructive lung disease on the health care system
- Evaluate the literature on the treatment of critically ill obstructive lung disease patients
- Analyze the discrepancies between the literature and common practice
- Review emerging therapies and techniques in the care of obstructive lung disease patients

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

- Spirometry required for diagnosis
  - Forced expiratory volume in one sec (FEV₁)/ Forced vital capacity (FVC) < 0.70
- Further classified after diagnosis

GOLD 1 Mild FEV₁ > 80% predicted
GOLD 2 Moderate 50% < FEV₁ < 80% predicted
GOLD 3 Severe 30% < FEV₁ < 50% predicted
GOLD 4 Very severe FEV₁ < 30% predicted

BASELINE RESPIRATORY MALFUNCTION

- Depletion of alveolar surface area
- Decrease in elastic properties
- Loss of respiratory capabilities
- Hyperinflation
- Intrinsic peak end expiratory pressure (iPEEP)


WHAT IS PEAK END EXPIRATORY PRESSURE?
- Peak end expiratory pressure (PEEP)
  - The pressure that must be overcome to passively exhale
  - Commonly employed in mechanical ventilation
  - Improves oxygenation via recruitment
  - Extrinsic → artificially applied
  - Intrinsic → restrictive properties

ACUTE EXACERBATION OF COPD
- Classification systems
  - Mild: Increased need for medication which he/she can manage on their own in a normal environment
  - Moderate: When the patient has an increased need for medication and feels the need to seek additional medical assistance
  - Severe: Patient/carer recognizes obvious and/or rapid deterioration in condition, requiring hospitalization
- Anthonisen classification
  - Type I (severe): Increased sputum purulence, increase in sputum volume, worsening dyspnea
  - Type II (moderate): Has two of the three above listed symptoms
  - Type III (mild): One of the above symptoms + fever, wheezing, increased cough or increased respiratory rate or heart rate

PATHOPHYSIOLOGY OF ACUTE EXACERBATION
- Infections are the most common cause

<table>
<thead>
<tr>
<th>Causes</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>80</td>
</tr>
<tr>
<td>Bacteria (H. influenzae)</td>
<td>40-50</td>
</tr>
<tr>
<td>Viruses (Rhinovirus)</td>
<td>30</td>
</tr>
<tr>
<td>Atypical</td>
<td>5-10</td>
</tr>
<tr>
<td>Other</td>
<td>20%</td>
</tr>
<tr>
<td>Air pollutants</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td></td>
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<tr>
<td>Non-pulmonary infections</td>
<td></td>
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</tbody>
</table>

RESPIRATORY FAILURE
- Inability to adequately gas exchange
  - Hypercapnia (pCO₂ > 50 mmHg)
  - Hypoxia (pO₂ < 60 mmHg)
In the US COPD affects 16 million adults
• More than 2.4% of all acute medical admissions
• In 2000 was responsible for:
  • 1.5 million ED visits and 726,000 hospitalizations
  • 119,000 deaths
• COPD patients experience 2 AECOPD/yr
  • 10% will require hospitalization
  • Average length of stay 7 days

In the US COPD affects 16 million adults

In 2000 was responsible for:

COPD patients experience 2 AECOPD/yr

Impact of AECOPD

Impact of AECOPD

Global initiative for chronic obstructive lung disease guidelines (GOLD)
• Short acting bronchodilators (Evidence C)
  • β2-agonists +/- anticholinergics
    • although there are no controlled trials... they are usually the preferred treatment
• Corticosteroids (Evidence A)
• Antibiotics (Evidence B)
  • 5-10 days

Therapeutic Options

Therapeutic Options

OBstructive Lung Disease in the ICU

OBstructive Lung Disease in the ICU

Impact of bronchodilators
• In conjunction with mechanical ventilation

Steroids
• Too little, too late?
• Risk vs. benefit

Patient selection

Antibiotic use?
• Is patient selection the issue not severity of illness?
Bronchodilators should not work in COPD!
- No controlled studies to date on clinical outcomes
- Attempt to reduce dynamic hyperinflation
  - ↓ airway pressure = ↓ resistance (iPEEP) → ↑ exhalation
  - Roughly 15-25% reduction in iPEEP
- Extrinsic PEEP (ePEEP) utilized after intubation
  - Synergistic effect with ePEEP
  - Roughly 15-25% reduction in iPEEP

Extrinsic PEEP (ePEEP) utilized after intubation
- Dilation of bronchus
  - Bronchodilators
  - ePEEP
  - ePEEP ~85% of iPEEP
  - Dilation promotes outflow
  - ePEEP > bronchodilators

Evaluating the impact of salbutamol +/- ePEEP
- 10 MV COPD patients
- Outcomes
  - Δ iPEEP
  - Airway resistance
  - Hemodynamics
  - Oxygenation

Impact of fenoterol + ePEEP
- 10 severe COPD MV patients
- Admitted for AECOPD (n=5) and LRTI/edema (n=5)
- iPEEP consistently lower with ePEEP
- Relative reduction greater with zero PEEP
- Airway resistance was not different
- Failed to improve V/Q mismatch

Expiratory Flow limitation
- 40% of population became non-flow limited
- In the setting of ePEEP may promote expiratory flow
- Potential to induce hyperinflation
- ePEEP fixed at a percentage of iPEEP
- β-agonist initiated after ePEEP → iPEEP < ePEEP
BRONCHODILATORS IN THE ICU

- Literature extremely difficult to interpret
  - Administration technique
  - Ventilator modes
  - Placement in inspiratory limb
  - Humidification
  - Bronchodilator utilized
  - Formulation of bronchodilator

ADMINISTRATION TECHNIQUE

- Meter dose inhaler (MDI) vs. nebulizer?

ADMINISTRATION TECHNIQUES

- Administration distance
  - 30 cm appears to be most effective
  - During inspiration > continuous

MDI VS. NEBULIZER

Bench - models of mechanical ventilation
Administration to mechanically ventilated patients

ADMINISTRATION TECHNIQUES

- Humidification should be avoided
  - Drug delivery reduced about 40%
  - Most data from bench models

BRONCHODILATOR DOSING

- Three stage experiment COPD patients (n=19)
  - Dose response of albuterol during MV
  - Experiment 1 → resistance variation/no albuterol
  - Experiment 2 → resistance after albuterol
    - Doubling dose every 15 mins
    - Cumulative dose of 28 puffs
  - Experiment 3 → duration of effect
**BRONCHODILATOR DOSING**

- Dhand et al. lower doses more frequently
  - 4 puffs every 1-2 hrs (2.5 mg nebulizer)
- Manthous et al. doses up to 100 puffs
- 5 puffs produced 70% of maximal effect
- Similar findings by Nair et al. (n=86)
  - RCT assessing optimal albuterol dose
  - Non-MV patients
  - 2.5 mg similar efficacy, ↓ ADR compared to 5 mg

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**THE CONS OF BRONCHODILATORS**

- Potentially worsen hyperinflation
- Reduction in iPEEP < ePEEP
- Tachycardia
- Minimal impact → dose dependent
- Pneumonia
- MDI vs. nebulizer

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**VENTILATOR MECHANICS AND BRONCHODILATORS**

- Impact of ventilator settings on drug delivery
  - Bench-models suggest manipulation significantly alters
  - Mouloudi et al research series
  - Tidal volume → larger better?
  - Inspiratory hold → time for deposition?
  - Inspiratory rate → slower rate ↑ drug in lung?
  - Respiratory efforts → disrupt drug delivery?

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**BRONCHODILATORS IN THE ICU**

- Should only be utilized in select patients
  - Hyperinflated or reactive airways
  - Should be utilized in conjunction with ePEEP
  - Initiated before ePEEP initiated
  - Technique
    - Non-humidified, 30 cm upstream on inspiratory limb
  - Manipulation of ventilator not warranted
  - Doses of 4-6 puffs (2.5 mg) at shorter intervals
CORTICOSTEROIDS IN THE ICU

- Minimal data supporting use in ventilated patients
  - Prevent need for ventilation
  - NEVER associated with decrease in mortality
  - Doses commonly utilized significantly higher
  - Dose based on acuity of illness
  - Optimal dose unknown
  - Minimal benefit → significant risk?

CORTICOSTEROIDS IN THE ICU

- 217 AECOPD patients requiring MV
  - Received 1 mg/kg prednisone for 10 days or until discharge
  - Bronchodilators +/- antibiotics
  - Mean 8 days of prednisone
  - Endpoints
    - ICU mortality
    - Length of MV and ICU stay
    - NIV failure

CORTICOSTEROIDS IN THE ICU

- 83 COPD patients requiring MV
  - Methylprednisolone 0.5 mg/kg Q6 hrs or placebo
  - Salbutamol + Ipratropium +/- antibiotics
  - Endpoints
    - Duration of MV
    - Failure of non-invasive ventilation(NIV)
    - Length of ICU stay
    - Mortality
    - Complications

CORTICOSTEROIDS IN THE ICU

- No difference in outcomes
  - Similar occurrences
  - Larger population, smaller doses of steroids
  - Significantly less NIV failure

CORTICOSTEROIDS IN THE ICU

- Improved success rates of NIV
- Concern for limitations
  - Significant exclusion criteria
  - Unblinding

CORTICOSTEROIDS IN THE ICU

- 217 AECOPD patients requiring MV
  - Retrospective review of AECOPD and the impact of steroid dose
    - "Low dose" <240 mg/day
    - "High dose" > 240 mg/day
    - 17,239 patients from 473 hospitals included
    - 11,083 high dose
    - 6,156 low dose
    - Critically ill patients
      - 47% ventilated
      - 96% received antibiotics, 89% bronchodilators
CORTICOSTEROIDS IN THE ICU

- Significantly less in low dose group
  - Total cost (p<0.01)
  - Length of invasive ventilation (p<0.05) and NIV (p<0.01)
  - 28-d ICU free days (<0.01)

Kiser TH. Am J Respir Crit Care Med 2014;189(9):1052-1064

EOSINOPHIL GUIDED STEROIDS

- Significantly reduce the patients receiving steroids
  - Improved outcomes
    - Eosinophil positive → “steroid responsive”
    - Eosinophil negative → steroid worsen
    - Higher C-reactive protein (CRP) → suggestive of respiratory infection?
    - Antibiotics
  - Not studied in critical illness

ARE WE CHOOSING THE RIGHT PATIENT?

- Improved outcomes?
- Eosinophilic airway inflammation
  - Primarily seen in asthma
  - Present in AECOPD
  - Sputum eosinophilia associate with steroid response
- Bafadhel et al. looked to test this hypothesis


EOSINOPHIL GUIDED STEROIDS

- 166 AECOPD randomized to biomarker guided steroids
  - Eosinophils counted in peripheral-blood
  - Eosinophil positive → prednisolone
  - Eosinophil negative → placebo

- Largest benefit likely in NIV
- Utility may be limited after invasive ventilation
  - ↑ infection
  - ↑ myopathy, weakness
- Therapy may be guided by eosinophil counts
  - > 2% in peripheral counts
  - Lower doses better than higher doses

Abroug F. Eur Respir J 2014;43:717-724
Kiser TH. Am J Respir Crit Care Med 2014;189(9):1052-1064
Data remains controversial
- Identification of population
- Anthonisen classification still widely utilized
- Subjective classification results in overutilization
- Benefit in MV patients
- Procalcitonin (PCT)?

Antibiotics in AECOPD
- A prospective study evaluating the correlation of CRP and PCT
  - 319 pneumonia, asthma, and AECOPD patients
- Both significantly higher in pneumonia
  - Compared to AECOPD or asthma exacerbations

Disease state | % that would have received abs on CRP | % that would have received abs on PCT | % of Patients receiving abs
---|---|---|---
Pneumonia | 91 | 73 | 100
AECOPD | 18 | 7 | 76
Asthma exacerbation | 7 | 4 | 67

Antibiotics in AECOPD
- Utility of antibiotics remains controversial
- Antibiotics should be utilized judiciously
  - PCT
  - CRP
- Elevations in PCT correlated with more severe illness
- Biomarker based approach appears to be safe
  - Assist in differentiating colonization

Antibiotics in AECOPD
- PCT guided antibiotic use (n=226)
  - Standard of care vs. PCT guided therapy
  - 50% of patients met all three Anthonisen criteria
- Evaluated long term outcomes and antibiotic use
  - Rates of re-hospitalization
  - Additional antibiotics
  - Lung function at discharge

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