Asthma and COPD in the ICU

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Acute Exacerbations of Asthma

Asthma exacerbations Pathophysiology

- Occlusion of the bronchial lumen by mucus, cells, thickened/contracted smooth muscle, bronchial wall inflammation and edema.

- Leads to:
  - low V/Q ratios
  - increased work of breathing
  - dynamic hyperinflation
Asthma exacerbations
Patterns of deterioration

• "Type 1" - Slow deterioration
  – inspissated mucus and inflammatory cells
  – slow to respond to therapy
• "Type 2" - Rapid deterioration
  – may not have mucus inspissation,
  – rapid response to therapy
  – much less common (~15% of exacerbations)

Woodruff PG Acad Emerg Med 1998
Barr RG Eur Resp J 2000

Asthma exacerbations
Initial therapy

• Oxygen

• Aerosolized albuterol, 2.5mg q 15 mins or continuously

• Methylprednisolone IV for ICU pt
Asthma exacerbations
Other therapies

- The NAEPP recommends against
  - Methylxanthines
  - Mucolytics
  - Chest Physical therapy
  - Antibiotics (unless pt has fever, purulent sputum or pneumonia)

Asthma exacerbations
Other therapies

- Levalbuterol
- Aerosolized ipratropium
- Heliox
- Magnesium
- Leukotriene blockade
- Inhalational anesthetics

Levalbuterol: background

Albuterol is racemic (equimolar mixture of stereoisomers)
Levalbuterol: rationale

• (R)-albuterol is the active drug
  – bronchodilator and bronchoprotective

• (S)-albuterol may not be simply inert
  – intensifies bronchoconstriction?
  – induces hypersensitivity?
  – promotes activation of eosinophils?

Levalbuterol: weakness in rationale

• Structure of the β-receptor/ligand interaction predicts that only (R)-albuterol should bind

• On direct comparison:
  – R- and RS-albuterol have similar dose-related effects on FEV1, HR, K+ in laboratory setting
  – Neither S-albuterol nor placebo have any effects

Lotvall JACI 2001

Levalbuterol: non-supportive adverse effects data

• RCT (crossover) in 20 ICU pts showed no difference in effects of levalbuterol (1.25mg/dose) vs albuterol (2.5mg) on HR

• "In the clinical trials, a slightly greater number of serious adverse events and clinically significant ECG changes were reported in patients who received Xopenex 1.25mg as compared to the other active treatment groups."

Lam Am J Health-Syst Pharm 2003
CDER and Xopenex® package insert
Conflicting Reviews

**PRO**


**CON**

- Levalbuterol nebulizer solution: is it worth five times the cost of albuterol? Asmus MJ. Pharmacotherapy 2000;20(2)123-9

Ipratropium: clinical studies

- Meta-analysis of ipratropium in emergency management of adults with acute asthma
  - Ipratropium provides an additional 7.3% improvement in FEV1 (approximately 100 ml)
  - Associated with a decreased risk of hospitalization (RR=0.73, 95% CI 0.53-0.99)
  - Not associated with any additional adverse effects


Heliox: background

- Helium: low MW => density 4-fold less than air
- Lower Reynolds number => laminar flow
- Heliox: a mixture of helium and oxygen available with helium concentrations ranging from 60-80%
Heliox: clinical studies

- 2 systematic reviews/meta-analyses:
  - Slight benefit in first hour of use
  - Insufficient data on harder clinical outcomes such as intubation, ICU admission rates, duration of hospitalization, or mortality

Ho AM Chest 2003
Rodrigo GJ Chest 2003

Mechanical ventilation with Heliox

- Heliox has been used with:
  - Conventional ventilators
  - High frequency ventilators
  - Noninvasive ventilators

- Problems encountered
  - Tidal volume discrepancy
  - FiO2 discrepancy
  - Malfunction

- Solution
  - Directly monitor the actual VT and actual FiO2 (see ref 4)

1. Tassaux D, AJRCM. 1999
2. Deshmane GU, Crit Care Med 2000
4. Venkataraman ST, Resp Care 2006
**Intravenous magnesium**

- 2 RCTs in adults demonstrate improved lung function in subjects with severe obstruction (FEV1 < 25% predicted) when used as adjunct to albuterol and steroids
- Adult dose: 2 gms IV MgSO$_4$ in 50ml NS infused over 10-15 mins

Silverman RA, Chest 2002
Bloch H, Chest 1995

**Leukotriene blockade: IV montelukast**

- RCT in 201 adults with moderate to severe acute asthma in the ED
- Three arm study:
  - 7 mg IV montelukast
  - 14 mg IV montelukast
  - Placebo
- * Not currently available


**IV montelukast**

Other therapies: inhalational anesthetics

- Laboratory studies and case reports for:
  - Isoflurane
  - Sevoflurane
  - Halothane
  - Enflurane
- Excellent bronchodilators
- Anesthesia ventilators have improved ICU applicability
- Occupational exposure an issue

Parnass SM Anesth Analg 1987
Revich LR Pulm Pharmacol Ther 2001
Maltais F Chest 1994
Mutlu GM Crit Care Med 2002

Asthma exacerbations
Other therapies: review

- Levalbuterol value uncertain
- Aerosolized ipratropium YES
- Heliox may have short term value
- Magnesium YES, if severe
- Leukotriene blockade a possible option
- Inhalational anesthetics little data, difficult to use
Asthma exacerbations
Ventilator management

- Controlled modes
- Typically, high FiO2 is not required
- Permissive hypercapnia - well tolerated
- Increase expiratory time – slow respiratory rate

### Air Trapping

![Air Trapping Diagram](image)

*Fig. 3. Flow-time waveform showing persistence of flow at end-expiration in a patient with intrinsic positive end-expiratory pressure (auto-PEEP). In most patients with obstructive lung disease, failure to reach zero flow at the end of a relaxed expiratory signal signifies that lung volume is above functional residual capacity and indicates dynamic hyperinflation.*

### Auto-PEEP

![Auto-PEEP Diagram](image)
Initial ventilator management

Suggested initial settings:

- VE 8-10L/min
- TV 6-10ml/kg
- RR 10-15 breaths/min
- I/E ≥ 1:3
- PEEP 0
- Pplat <35cm H2O

Non-invasive ventilation?

- Good experience with COPD
- Less experience in asthma (only one RCT, in ED setting, with sham device)

Acute Exacerbations of COPD
COPD exacerbations
Pathophysiology
• Occlusion of the bronchiolar lumen by mucus, cells, thickened/contracted smooth muscle, bronchial wall inflammation and edema.
• Leads to:
  – low V/Q ratios
  – increased work of breathing
  – dynamic hyperinflation

Differences from Asthma
• Have chronic small airway disease and emphysema
• Are older, weaker, have more comorbid conditions
• More likely to have bacterial infection

COPD Exacerbations
Therapeutic options
• Oxygen
• Bronchodilators
  – Aerosolized albuterol
  – Ipratropium?
  – Methylxanthines?
  – Long acting bronchodilators?
• Corticosteroids for (<14 day total course)
• Antibiotics
• Non-invasive ventilation
• Invasive ventilation
COPD Exacerbations
Antibiotics

• Indications
  – increased dyspnea, sputum volume and purulence
  – mechanical ventilation (any type)

• Organisms
  – S. pneumoniae, H. influenzae and M. catarrhalis

• Risk factors for P. aeruginosa infection
  – recent hospitalization
  – Frequent antibiotics
  – severe COPD exacerbations
  – prior P. aeruginosa

COPD Exacerbations
Non-invasive Ventilation

• Indications
  – Accessory muscle use/abdominal paradox
  – Acidosis (pH<7.35) and PCO₂ (>45mmHg)
  – RR>25

• Contraindications
  – Resp arrest, CV instability
  – Impaired mental status
  – Aspiration risk, recent facial, GE surgery
  – Facial trauma/abnormality
  – Extreme obesity

COPD Exacerbations
Mechanical Ventilation (intubated)

• Air-trapping: use a slow respiratory rate

• Auto-PEEP: consider matching extrinsic to intrinsic PEEP if the patient appears to have difficulty triggering the ventilator
COPD Exacerbations

Therapeutic options

- Oxygen
- Bronchodilators
  - Aerosolized albuterol
  - Ipratropium? YES
  - Methylxanthines? PROBABLY NOT
  - Long acting bronchodilators? UNCERTAIN
- Corticosteroids <14 DAY COURSE
- Antibiotics ESPECIALLY in ICU, CONSIDER PSEUDOMONAS
- Non-invasive ventilation YES, USE EARLY
- Invasive ventilation
Finally…in both asthma and COPD

• Remember SQ heparin if bed-bound