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
Air Trapping

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 expiration signifies that lung volume is above functional residual capacity and indicates 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)

FIG 3. Three-dimensional molecular conformation of (S)-albuterol and (R)-albuterol (also called levalbuterol).
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%
PEF, % Predicted

* - p for heliox < 0.001 compared with baseline
# - p for oxygen < 0.05 compared with baseline
θ - p for heliox < 0.01 compared with 20 minutes

Time from Initiation of Treatment
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, AJRCCM. 1999
2. Devabhaktuni VG. 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

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
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 expiration signifies that lung volume is above functional residual capacity and indicates dynamic hyperinflation.
Auto-PEEP
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 H20

Papiris S Crit Care 2002
Non-invasive ventilation?

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

Soroksky, A Chest 2003
Ram FSF Cochrane Database Syst Rev 2005
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 PCO$_2$ (>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
Auto-PEEP

![Diagram showing pressure levels in the mouth and alveoli with Auto-PEEP = +6.]
Auto-PEEP
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