AECOPD: Management and Prevention

Neil MacIntyre MD
Duke University Medical Center
Durham NC

AECOPD: Management and Prevention
• AECOPD: Definitions and impact
• Acute management of AECOPD
• Preventing AECOPD

COPD Exacerbations

Macrophages

TNF-α

CXCL8

CXCL5

IL-6

Neutrophils

Oxidative stress

AMPLIFICATION OF INFLAMMATION IN COPD

Inflammation

Neutrophils

Macrophages

Cytokines

Mediators

Proteases

Non-smokers
Normal smokers
Mild COPD
Severe COPD
Exacerbation

Global Strategy for Diagnosis, Management and Prevention of COPD

An exacerbation of COPD is:

“an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”
Impact on symptoms and lung function

Negative impact on quality of life

Accelerated lung function decline

Increased Mortality

Increased economic costs

**Consequences Of COPD Exacerbations**

- Increased economic costs
- Accelerated lung function decline
- Increased Mortality
- Negative impact on quality of life

**Recurrence of Exacerbations**

- 27% of first exacerbations associated with second exacerbation in 8 weeks
- 34% of 1,221 hospitalized patients in UK readmitted within 3 months (range 5–55%)

**COPD: Direct Cost**

- Nursing Home Care*
- Home Health Care*
- Physician Services
- Hospital Care
- Prescription Drugs

**AECOPD: Management and Prevention**

- AECOPD: Definitions and impact
- Acute management of AECOPD
- Preventing AECOPD

**Arterial blood gas measurements:** PaO₂ < 60 mm Hg with or without PaCO₂ > 48 mm Hg on RA indicates respiratory failure.

**Chest radiographs:** may aid in the diagnosis of coexisting cardiac problems.

**ECG:** may aid in the diagnosis of coexisting cardiac problems.

**Whole blood count:** identify polycythemia, anemia or bleeding.

**Purulent sputum** indication to begin empirical antibiotics

**Biochemical tests:** detect electrolyte disturbances, diabetes, and poor nutrition.

**Spirometric tests:** not recommended during an exacerbation.

**Contrasted CT:** consider in pts at risk with severe hypoxemia.
Oxygen: titrate to improve the patient’s hypoxemia with a target saturation of 88-92%.

Bronchodilators: Short-acting inhaled beta2-agonists with or without short-acting anticholinergics are preferred.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV1) and arterial hypoxemia (PaO2), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 30-40 mg prednisolone per day for 10-14 days is recommended.

Antibiotics should be given to patients with:
- Three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence.
- Who require mechanical ventilation.

**Meta-analysis of the Benefits of Antibiotics in AECOPD**

<table>
<thead>
<tr>
<th>Study</th>
<th>Favors Placebo</th>
<th>Favors Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elmes et al. 1957</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Berry et al. 1960</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Fear and Edwards. 1962</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Elmes et al. 1965</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Petersen et al. 1967</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Pines et al. 1972</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Nicotra et al. 1982</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Anthonisen et al. 1987</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Jorgensen et al. 1992</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
<tr>
<td>Overall</td>
<td><img src="image1" alt="Placebo" /></td>
<td><img src="image2" alt="Antibiotic" /></td>
</tr>
</tbody>
</table>

Effect size: 0.46 (95% CI: 0.34-0.58)
Acute Respiratory Failure in COPD

- Narrowed airways increases inspiratory work
- Narrowed airways increases air trapping and decreases muscle force generation capability

*Net result is hypercapneic respiratory failure*

Noninvasive ventilation (NIV) for patients hospitalized for acute exacerbations of COPD:

- Improves respiratory acidosis, decreases respiratory rate, severity of dyspnea, complications and length of hospital stay.
- Decreases mortality and needs for intubation.

NPPV in Acute Exacerbations of COPD:

Risk of “Treatment Failure” (Mortality, Intubation, Intolerance)

<table>
<thead>
<tr>
<th>Study</th>
<th>NPPV</th>
<th>Usual medical care</th>
<th>Risk ratio (fixed 95% CI)</th>
<th>Weight</th>
<th>Risk ratio (fixed 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antwe et al 1998</td>
<td>2/29</td>
<td>12/29</td>
<td>11.2 0.00 (0.07 to 1.37)</td>
<td>1</td>
<td>0.5 (0.00 to 10.32)</td>
</tr>
<tr>
<td>Barlow et al 1993</td>
<td>4/14</td>
<td>0/16</td>
<td>12.1 0.10 (0.12 to 0.96)</td>
<td>0.5</td>
<td>0.10 (0.00 to 10.32)</td>
</tr>
<tr>
<td>Brett et al 1990</td>
<td>1/9</td>
<td>1/20</td>
<td>31.1 0.16 (0.21 to 0.58)</td>
<td>0.5</td>
<td>0.17 (0.02 to 1.32)</td>
</tr>
<tr>
<td>Boland et al 1996</td>
<td>1/15</td>
<td>0/15</td>
<td>1.5 0.00 (0.00 to 3.23)</td>
<td>0.5</td>
<td>0.00 (0.00 to 3.23)</td>
</tr>
<tr>
<td>Kilic et al 1990</td>
<td>7/17</td>
<td>7/17</td>
<td>6.9 0.54 (0.00 to 1.93)</td>
<td>0.5</td>
<td>0.56 (0.00 to 2.30)</td>
</tr>
<tr>
<td>Morning et al 1999</td>
<td>3/18</td>
<td>8/18</td>
<td>3.9 0.39 (0.00 to 1.37)</td>
<td>0.5</td>
<td>0.38 (0.00 to 1.37)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>85/468</td>
<td>100/361</td>
<td>0.5 (0.38 to 0.37)</td>
<td>1</td>
<td>0.5 (0.38 to 0.37)</td>
</tr>
</tbody>
</table>

Risk for hospitalization (AECOPD): MPPC better than usual medical care (P=0.001).


AECOPD: Management and Prevention

- AECOPD: Definitions and impact
- Acute management of AECOPD
- Preventing AECOPD

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Non-pharmacologic

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Smoking cessation (can include pharmacologic treatment) + Pulmonary rehabilitation</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
</tbody>
</table>

Prevention of COPD Exacerbations: Pneumococcal and Influenza Vaccinations

- Pneumococcal vaccination
  - COPD hospitalization
  - All-cause mortality
- Pneumococcal + influenza vaccination
  - COPD hospitalization
  - All-cause mortality

Smoking Cessation

- “First thing you have to do to get out of hole is stop digging”
- Nicotine is incredibly addictive – spontaneous quit rates <5%/year
- What can help?
  - Nicotine replacement
  - Welbutrin
  - Varenicline
  - Formal programs (ALA, ACS)

LAMAs and Exacerbations and Hospitalizations vs Ipratropium


LABA+ ICS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean number of exacerbations/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1.13</td>
</tr>
<tr>
<td>SALM</td>
<td>0.97*</td>
</tr>
<tr>
<td>FP</td>
<td>0.93*</td>
</tr>
<tr>
<td>SFC</td>
<td>0.85**</td>
</tr>
</tbody>
</table>

Probability of being exacerbation free vs days on treatment
Probability of being hospitalization free vs days on treatment

LABA vs LAMA

Global Strategy for Diagnosis, Management and Prevention of COPD

Preventing AECOPD

- The phosphodiesterase-4 inhibitor roflumilast may be useful to reduce exacerbations for patients with FEV₁ < 50% of predicted, chronic bronchitis, and frequent exacerbations.
Pharmacotherapy Management (PCE)

- 2 rates are reported:
  1. Patients dispensed a systemic corticosteroid within 14 days of event
  2. Patients dispensed a bronchodilator within 30 days of event

PCE Performance 2008–2012

Pharmacotherapy: Corticosteroids (HMO)

Commercial | Medicaid | Medicare

PCE Performance 2008–2012

Pharmacotherapy: Bronchodilators (HMO)

Commercial | Medicaid | Medicare

Pulmonary rehabilitation

- Education
  - chronic management
  - acute management
- Exercise
  - deconditioning common
  - may need bronchodilators/O2
- Psycho-social support

Follow-Up Can Improve Patient Outcomes

Follow-up with a PCE or pulmonologist reduced 20-day ED visits and hospital readmissions
Can Patients Be Given an “Action Plan” to Self Manage AECOPD?

- Yes....But....
- Conflicting data from 2 large VA trials
  - First showed remarkable reduction in need for hospitalizations etc if patients educated to start antibiotics promptly at symptom onset
  - Second showed worse outcomes using a similar strategy
- Take home message: Self management offers advantage of prompt therapy but patients need to know when to call for help

AECOPD: Management and Prevention

- AECOPD: Definitions and impact
- Acute management of AECOPD
- Preventing AECOPD