

Chronic Obstructive Airway Disease-Acute Exacerbation

Controversies & Update

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Definition

- Sustained worsening of pt's symptoms
- From usual stable state
- Beyond normal day to day variation
- Acute onset
- Often necessitates a change in medication

Anthonisen et al

- Based on three cardinal symptoms
worsening of dyspnea,
↑sputum purulence,
↑sputum volume

Type 1(severe): all 3

Type 2(moderate): 2 of these

Type 3(mild): 1 of these + 1 of following

Unexplained fever, URTI in past 5
days, ↑wheeze, ↑cough, ↑RR/HR 20% above
baseline

Consequences

- A retrospective audit of 1400 pts in UK has shown
 - 34% were readmitted
 - 14% had died within 3 month of an exacerbation
- Median time of recovery
 - symptoms: 7 d
 - PEFr: 6 d
- Incomplete recovery of lung function following an exacerbation
 - recovery of PEFr not complete
 - 25% at 35 d
 - 7% at 90 d

Patients experiencing frequent exacerbations (>2.92/yr) have more rapid decline in lung function (FEV₁ fall 40 ml/yr vs 32 ml/yr).

↑ed level of IL-6 & IL-8 is found in patients with frequent exacerbations

Factors associated with ↑ risk of readmission

- ≥ 3 admissions in the previous yr
- FEV₁ % predicted
- PaO₂
- Lower level of physical activity
- Need for an anticholinergic bronchodilator

Mechanism of Exacerbation

• Increased breathlessness

Airway narrowing

mucosal damage, increased irritability/ bronchospasm
inflammatory cell infiltration into airway tissues

airway edema
increased airway secretion and viscosity/ mucus plugging

V/Q mismatch

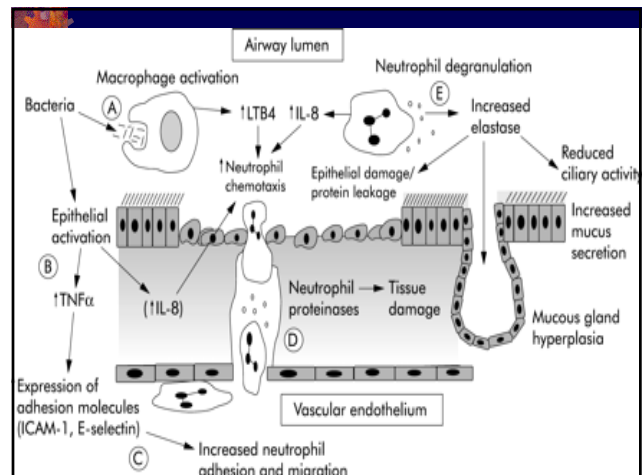
Increased metabolic/catabolic rate

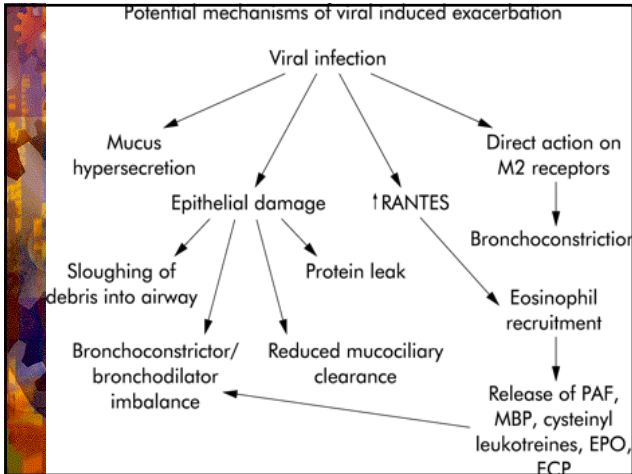
• Increased sputum production

mucosal gland hypertrophy
goblet cell hyperplasia
goblet cell degranulation

• New or increased sputum purulence

eosinophil recruitment
neutrophil recruitment





- ## Causes
- **Infections: Viral** Rhinoviruses
Influenza
Parainfluenza
Coronavirus
Adenovirus
RSV
 - **Bacterial** *C pneumoniae*
H influenzae
S pneumoniae
M catarrhalis
Staph aureus
P aeruginosa

- ## Non infective causes
- Nitrogen dioxide
 - Particulates
 - Sulphur dioxide
 - Ozone
 - Unidentified causes in 30%

- ## Mimickers
- Pneumonia
 - Pneumothrax
 - LVF/pulmonary edema
 - Pulmonary embolus (30%)
 - Lung cancer
 - Upper airway obstruction
 - Pleural effusion
 - Recurrent aspiration



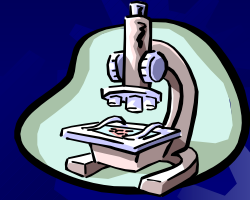
Hospital or Home?



Patients with following features should be admitted

- Cyanosis
- Worsening pedal edema
- Impaired level of consciousness
- Already receiving LTOT
- $\text{pH} < 7.35$
- $\text{PaO}_2 < 49$
- CXR changes

Investigations



- ABG
- ECG
- CXR
- Haemogram
- SERFT

- Sputum c/s: limited value
- Theophylline level
- Blood c/s: if fever
- Lung function: not practical
PEF < 100, FEV1 < 1 indicates severe exacerbation

Systemic Corticosteroids



3 systematic reviews: *McCory et al*, *Wood-Baker et al*, *Singh et al*

- Significant effect in favor of steroids over placebo in terms of **FEV1 for at least 72 h**
- Improvement in **oxygenation**
- **Shorter duration of hospitalization**
- No effect on mortality
- Patients on corticosteroids were 2.7 times more likely to have an adverse drug reaction
- Most common adverse event was asymptomatic hyperglycemia

- Prednisolone 30 mg should be used for 7-14 days. (no advantage of continuing steroids beyond 14 days). **SCOPE trial**
- Steroids should be started as early as possible to get the maximum benefit
- Osteoporosis prophylaxis should be considered

Inhaled steroids

- Inhaled steroids have a role in pts with FEV₁<50%, who are getting 2 or more exacerbations requiring treatment with antibiotics or oral steroids in 12 month period (*SOLDE trial, BMJ 2000*)
- In patients with mild COPD there is no difference in exacerbation rate (*Vestbo et al, Lancet 1999*)
- **EUROSCOP** study did not show any beneficial effect of inhaled steroids on prevention of exacerbations
- **Lung Health Study II** showed decrease in exacerbation by 40-50%

Antibiotics

- Meta-analysis by *Saint et al JAMA 1995*
Found a small but statistically significant effect favoring antibiotics in AE
- **Anthonisen et al** showed a relationship of better outcomes with antibiotic treatment in severe and moderately severe exacerbations. **Mild exacerbations did not show any benefit**
- Oral ofloxacin reduced the need for additional courses of antibiotics and decreased duration of MV and hospital stay

Antibiotics used in different RCTs

- Jagerson et al 1992: Amoxicillin
- Sach's et al 1995 : amoxicillin or cotrimoxazole
- Anthonisen et al 1987: TMP-SMX, Amoxy, Doxy
- Pines et al 1972: Tetracycline/ chloramphenicol

Brochodilators in acute exbn

- Short acting beta₂ agonists
most commonly used
improve dyspnea and fatigue
- Short acting anticholinergics
COPD → ↑resting tone of cholinergic bronchoconstrictor nerves
- Combination of SABA+ Short acting anticholinergic
mean peak FEV₁, significantly greater than either component alone on day 1, 2, 5, 7 and 85

(*Auerbach et al Chest 1997*)

Role of LABA in AECOAD

- No proven benefit when given **during** exacerbation.
- Formoterol has a short onset of action similar to salbutamol, so can be used theoretically.
- When used in stable COAD may ↓ frequency of exacerbation
(*Calverley 2003 N=1465, Rossi 2002 N=854, Mahler 1999 N=411*)

Long acting anticholinergic Tiotropium

- Role in AE not clear
- When used in stable COAD ↓ frequency of AE compared to placebo
Casbury2002, Donohue2002, Brusaco 2003
- **Better than ipratropium in preventing AE**
Vicken 2002
- Same as salmeterol in preventing AE
Brusaco 2003

Delivery system

- Hand held inhalers with spacer are equally effective as nebuliser
 - for lower dosed inhalers are better
 - nebuliser can deliver larger doses easily
- Nebulisers are
 - effort independent
 - do not require supervision by staff
 - have further beneficial effect due to it's physical properties (inhaled droplets alter mucus viscosity)
- Meta-analysis has shown small but insignificant effect in favor of wet nebulisation.
Tuner et al. Ann int med 1997

Theophylline

- In addition to bronchodilation, ↑ respiratory drive, overcomes some of the respiratory depression present during AE, improves diaphragm contractility, and is antiinflammatory
- In 3 RCTs no significant difference in pulmonary function or symptom scores was seen when theophylline was used in AE compared to placebo
- I/V theophylline should only be used when there is inadequate response to inhaled bronchodilators
- Monitoring of theophylline levels should be done within 24 hrs

Respiratory stimulants

- Doxapram is effective but not as effective as NIV so should be used only when NIV is not available (Greenstone et al systemic review 4 RCTs)
- Oral Almitrine has also been used

Oxygen therapy

- Oxygen therapy relieves pulmonary vasoconstriction
- Relieves right heart strain
- Lessens myocardial ischemia
- Better oxygenation of CNS
- Enhanced lung defences
- Better mucociliary transport

Oxygen therapy

- During AE PaO₂ falls 55-60 to 25-50 mmHg
- Oxygen should be given to keep SaO₂>90% but <93%
- Oxygen therapy may lead to hypercapnia and acidosis
 - *Degaute et al* gave 28% O₂ for 1 hour, avg PaCO₂ increased from 59 to 63 mmHg
 - similar studies by *Plant et al*, *Smith et al*, *Elbridge et al*
- Radial a. punctures are more painful for ABG
- Aerialized ear lobe samples may not accurately reflect PaO₂ but are acceptable for PaCO₂

Pitkin et al Thorax 1994

Non Invasive Ventilation

Selection criteria

- Moderate to severe dyspnea with use of accessory muscles of respiration and paradoxical abdominal motion
- pH<7.35, PaCO₂>45
- RR>25/min

Exclusion criteria

- respiratory arrest
- cardiovascular instability,
- somnolence, impaired mental status, uncooperative pt
- high aspiration risk, viscous or copious secretions
- facial injury, deformity

NIV as compared to usual medical care

- ↓ mortality RR 0.41
- ↓ need for intubation RR 0.42
- improvement in pH(mean=0.03), PaCO₂ and RR in 1st hr
- fewer complications VAP(RR 0.32)
- shorter hospital stay (diff= -3.24d)
- NIV service will avoid 6 deaths and 3-9 admissions to ICU per annum

Peter et al ,NIV in ARF: a meta-analysis. Cr Care Med 2002

Mechanism of action of NIV

- reduction in inspiratory muscle work and avoidance of respiratory muscle fatigue
- respiratory rate falls as tidal volume is augmented
- bilevel ventilation has been shown to reduce diaphragmatic pressure swings
- prompt improvements in gas exchange occurs within the first hour. Improvement in oxygenation is related to the patient's ability to tolerate a higher FIO₂ without further hypoventilating
- improves respiratory system compliance by reversing microatelectasis

Treatment failure in NIV

Paco₂ remains elevated

Consider a COMPLICATION pneumothorax, aspiration pneumonia,

Adjust FIO₂ to maintain SpO₂ between 85% and 90%

- Is there excessive leakage?
- Check mask fit
- If using nasal mask, consider chin strap or full-face mask
- Increase IPAP

Paco₂ improves but Pao₂ remains low

- Increase FIO₂
- Consider increasing EPAP

Invasive Ventilation

- RR>35/min
- PaO₂<40 mmHg, or PaO₂/FIO₂<200
- pH<7.25 and PaCO₂> 60
- Respiratory arrest
- Cardiovascular complications
- Impaired mental status
- NIV failure

Ventilatory strategy

- correcting the respiratory acidosis while avoiding further hyperinflation
- RF for autoPEEP development are OLD AGE and high V_E requirement
- combination of slow MV with a prolonged expiratory time and a limited tidal volume. A degree of permissive hypercapnia is well tolerated
- First 12–24 hours of MV, **paralysis** is required. This reduces chest and abdominal wall contributions to **↓respiratory system compliance** and prevents **patient ventilator dyssynchrony**, which will impair alveolar ventilation and result in high airway pressures

- PCV preferred as high airway pressures are avoided

The inspiratory flow pattern, resembles normal breathing, tends to equalise ventilation between lung units rather than overinflating, the less obstructed lung units

- If volume controlled: A/C
- RR of 10–14 breaths/minute
- TV: low TV 6-8 ml/kg; easier to exhale
- Higher inspiratory flow >100 lpm
- $P_{plat} < 30$
- Longer pd of exhalation (I: E) ratio of 1:2.5 or 3.0.
- Small amount of ePEEP: narrows pressure diff b/w alveolus and cent airways and ↓ mus effort

Respiratory Physiotherapy

- Little research in this area : *McCrory 2001, Bellone et al*
- Bellone et al used Positive Expiratory Pressure mask in AECOAD and mild acidosis who were requiring NIV
- Sputum production was higher in PEP mask+assisted coughing group(10g) vs assisted coughing alone(5 g)
- Weaning time from NIV was also shorter(5d vs7d)
- *Brown et al*: short term mechanical vibration increased sputum production at 60 min but not at 24 hr

Expectorants & Mucolytics

- Based on five RCTs it is concluded that these agents do not shorten the course of treatment in AE
- Possibly they produce some symptomatic relief
- Agents used were **DOMIODOL** vs control, **BROMHEXINE** vs placebo, **AMBROXOL** vs control, **S-CARBOXYMETHYLCYSTEINE** vs bromhexine, **POTASSIUM IODIDE** vs chloramphenicol

DVT and SU prophylaxis

- Patients with AECOAD are at high risk of DVT and PTE
 - 30% in one study
 - 50% in autopsy series
- SU prophylaxis should be given as a part of standard care

Monitoring recovery

- Clinical
 - Pulse oximetry for non hypercapnic, non acidotic
 - Intermittent ABG analysis till stability
 - Daily monitoring of FEV1 or PEF is not required because the changes are small

Discharge

- Inhaled beta2 agonist requirement <4h
- Patient should be able to walk across the room
- Should be able to eat and sleep without dyspnea
- Clinically stable for 12-24 hrs
- Stable ABG for 12-24 hrs
- ? spirometry

How to prevent exacerbation

- **STOP SMOKING**
- Manage "Stable" COAD effectively
- LABA
- Tiotropium
- Inhaled steroids
- Influenza vaccination in chronic lung disease results in fewer OPD visits, ↓hospitalization and mortality. *Nicol et al. Ann Int Med 1999*
- Pneumococcal vacc

