Workshop Interattivo 1
BPCO
Perché un eccesso di evidenze non modifica i comportamenti?
Daniela Canini
Discussant: Gian Paolo Bonini, Alfredo Potena

Scenario Clinico (1)
• Il signor Giuseppe è un ex camionista di 61 anni, forte fumatore (30-40 sigarette/die), con pregressa diagnosi di BPCO, effettuata nel 1992 sulla base di dati clinico-anamnestici, radiologici e spirometrici
• Il paziente, inoltre, ha una storia di iperconsumo alcolico con struttura e funzione epatica perfettamente conservate
• Da quando è stata posta diagnosi di BPCO, il paziente ha praticato terapia con aminofilina retard + salbutamolo spray al bisogno

Scenario Clinico (2)
• Sin dal 1993 il paziente va incontro a diversi episodi di riacutizzazione della BPCO, che vengono trattati con antibiotici (chinolonici e/o cefalosporine iniettive) e cortisonici per via sistemica.
• Alcuni di questi episodi hanno richiesto l’ospedalizzazione
• In occasione di uno di tali ricoveri (1996) vengono aggiunti alla terapia cronica inalatoria un anticolinergico (pratropio) ed una combinazione di beclometasone e salbutamolo

CLINICAL QUESTIONS
?
1. BPCO. Perché un eccesso di evidenze non modifica i comportamenti?

A. Ritieni appropriata la scelta degli antibiotici (chinolonici e/o cefalosporine iniettive) per trattare gli episodi di riacutizzazione?
1. Sì
2. No

American College of Chest Physicians
American College of Physicians
American Society of Internal Medicine

Evidence Base for Management of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Ann Intern Med 2001;134.595-99

Antibiotics

• 11 RCTs have shown that antibiotic treatment is beneficial in selected patients with acute exacerbation of COPD.

• In particular, the studies showed that patients with more severe exacerbations (type 1) are more likely to experience benefit than those whose exacerbations are less severe.

• Typical administration periods ranged from 3 to 14 days, and tetracycline, amoxicillin, and trimethoprim-sulfamethoxazole were the most common antibiotics.

• Although suggestions for appropriate management can be made on the basis of available evidence, the supporting literature is scarce and further high-quality research is necessary.

• Such research will require an improved, generally acceptable, and transportable definition of acute exacerbation of COPD, as well as improved methods for observing and measuring outcomes.

• Although most of these RCTS were done before the emergence of multidrugresistant organisms, they show only a minimal benefit with antibiotic treatment in the more severe exacerbations.

• On the basis of these data and the emergence over time of more resistant organisms, particularly Streptococcus pneumoniae, it has become common practice to use more broad-spectrum antibiotics in acute exacerbations of COPD.

• To date, however, no RCTs have proved the superiority of the newer broad-spectrum antibiotics in such cases.

GOLD

Global Initiative for Chronic Obstructive Lung Disease
World Health Organization
National Heart Lung and Blood Institute
April 2001

2. There was significant heterogeneity between the RCTs.

3. Our systematic review shows that mucolytic drugs have a modest, but significant effect on exacerbation rates in people with chronic bronchitis and chronic obstructive pulmonary disease.

4. On the basis of the annualised exacerbation rate of 2.7 per patient per year in the control group, the number needed to treat for one subject to remain free of exacerbations for the study period would be 6.

**Scenario Clinico (3)**

- Nel 1999, a causa del sopraggiungere di una insufficienza respiratoria ipossiemica-ipercapnica stabile (pO2 54, pCO2 50) con FEV1 < 50%, viene posta indicazione all'O2-terapia domiciliare.
-
- Viene anche modificata la terapia farmacologica:
  - sostituisce lo spray combinato beclometasone-salbutamolo con l'uso sequenziale di formoterolo e fluticasone
  - sostituisce l'ipratropio con l'ossitropio
  - inizia terapia steroidea sistemica continuativa (prednisone 7,5 mg/die x os).

**CLINICAL QUESTIONS**

3. Bronchite cronica, asma, BPCO. Pratica clinica ed eccesso di linee guida?

C. Ritieni appropriata la prescrizione della ossigenoterapia domiciliare
1. Si
2. No

---

**What this study adds**

- Regular use of mucolytic drugs for at least two months significantly reduces exacerbations and days of illness compared with placebo in patients with chronic bronchitis and chronic obstructive pulmonary disease.
- Facilitates that the event may not be as severe, and the benefit may be greater in those with milder disease.
- Reductions are modest and treatment may not be cost effective.

- **GOLD - Global Initiative for Chronic Obstructive Lung Disease**

**Mucolytic (Mucokinetic, Mucoregulator) Agents**

(aminocaril, endocilin, carbocisteina, iodinato di glycerid)

Although a few patients with viscous sputum may benefit from mucolytics, the overall benefits seem to be very small. Therefore, the widespread use of these agents cannot be recommended on the basis of the present evidence (Evidence D).

**Crockett AJ, Moss JR, Cranston JM, Alpers JH.**

Domiciliary oxygen in chronic obstructive pulmonary disease

*The Cochrane Library, Issue 2, 2003*  
*Oxford: Update Software*
• We found limited evidence that domiciliary oxygen treatment improves survival in people with COPD and hypoxaemia.
• One RCT found that continuous treatment was more effective than nocturnal treatment.
• Domiciliary oxygen treatment seems to be more effective in people with severe hypoxaemia, than in people with moderate hypoxaemia or those who have arterial desaturation only at night.


GOLD - Global Initiative for Chronic Obstructive Lung Disease

The long-term administration of oxygen (>15 hours per day) to patients with chronic respiratory failure has been shown to increase survival (Evidence A). It can also have a beneficial impact on hemodynamics, hemato-
logic characteristics, exercise capacity, lung mechanics, and mental state.

Long-term oxygen therapy is generally introduced in Stage III (severe COPD) for patients who have:
- PaO2 at or below 55 mm Hg or SaO2 at or below 88%, with or without hypercapnia; or
- PaO2 between 55 and 60 mm Hg or SaO2 89%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive heart failure, or polycythemia (hematocrit > 55%).

CLINICAL QUESTIONS

D. In quale delle seguenti categorie collocheresti l’uso degli steroidi inalatori nella BPCO
1. Utile
2. Probabilmente utile
3. Da valutare caso per caso
4. Di efficacia sconosciuta
5. Probabilmente inutile
6. Inutile o dannoso

Chronic Obstructive Pulmonary Disease

Clinical Evidence
April 2003
Inhaled corticosteroids

Unlikely to be beneficial

- Short term RCTs found no evidence of benefit of inhaled corticosteroids.
- Large RCTs of at least 6 months have found that inhaled steroids increase FEV1 during the first 3–6 months of use, but found no subsequent effect on decline of lung function.
- Two studies also found a reduction in exacerbation frequency and an improvement in health status.

Clinical Evidence. April 2003

Oral Corticosteroids

- One systematic review of short term RCTs has found that steroids versus placebo significantly improves lung function.
- We found no RCT of the effects of long term treatment on lung function.
- We found evidence of potentially serious adverse effects, including osteoporosis and induction of diabetes.

Clinical Evidence. March 2003

CLINICAL QUESTIONS

E. Ritieni che il rapporto rischio/beneficio sull’uso long-term degli steroidi orali nella BPCO sia:
1. Verosimilmente favorevole
2. Verosimilmente sfavorevole

Clinical Evidence April 2003

GOLD - Global Initiative for Chronic Obstructive Lung Disease

- Regular treatment with inhaled glucocorticosteroids should only be prescribed for symptomatic COPD patients with a documented spirometric response to glucocorticosteroids or for those with an FEV1 < 50% predicted and repeated exacerbations requiring treatment with antibiotics and/or oral glucocorticosteroids (Evidence B).

Clinical Evidence. March 2003
McEvoy CE, Niewoehner DE.

Adverse effects of corticosteroid therapy for COPD: a critical review


GOLD - Global Initiative for Chronic Obstructive Lung Disease

Long-term treatment with oral glucocorticosteroids is not recommended in COPD (Evidence A). There is no evidence of long-term benefit from this treatment. Moreover, a side effect of long-term treatment with systemic glucocorticosteroids is steroid myopathy, which contributes to muscle weakness, decreased functionality, and respiratory failure in patients with advanced COPD.

Scenario Clinico (4)

- Nell'agosto del 2000, a seguito di un trauma banale, il signor Giuseppe riportava la frattura non mielica di L1.
- Tutti i tentativi di sospendere la terapia steroidea sistemica comportavano un peggioramento soggettivo del quadro respiratorio
- Il paziente, comunque, continua a fumare

Scenario Clinico (5)

- Nel febbraio 2002 ricovero per insufficienza respiratoria acuta in terapia intensiva, dove viene sottoposto a ventilazione meccanica invasiva.
- Il paziente viene dimesso dopo circa 20 giorni di degenza in discrete condizioni generali
- Attualmente, il paziente continua a fumare (di nascosto)

CLINICAL QUESTIONS

F. In occasione delle riesacerbazioni di BPCO, riteni appropriata la ventilazione meccanica non-invasiva?
1. Sì
2. No
Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of COPD

Cochrane systematic review and meta-analysis

The Cochrane Library, Issue 2, 2003
Oxford: Update Software

Table 1 Effects of non-invasive positive pressure ventilation as an adjunct to usual medical care, compared with usual medical care alone: overall results of the review for dichotomous outcome measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Total number of patients</th>
<th>Relative risk (95% CI)</th>
<th>Number needed to treat (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>23 (19/4)</td>
<td>520</td>
<td>0.81 (0.74 to 0.89)</td>
<td>8.9 (6.9 to 11.5)</td>
</tr>
<tr>
<td>Infection</td>
<td>14 (3/11)</td>
<td>207</td>
<td>0.67 (0.55 to 0.83)</td>
<td>5 (4 to 7)</td>
</tr>
<tr>
<td>Complications</td>
<td>11 (1)</td>
<td>143</td>
<td>0.63 (0.53 to 0.76)</td>
<td>3 (2 to 4)</td>
</tr>
</tbody>
</table>

Table 2 Effects of non-invasive positive pressure ventilation as an adjunct to usual medical care, compared with usual medical care alone: overall results of the review for continuous outcome measure

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Total number of patients</th>
<th>Weighted mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay in hospital (days)</td>
<td>13 (11/2)</td>
<td>156</td>
<td>3.36 (2.10 to 4.62)</td>
</tr>
<tr>
<td>Length of ventilation (days)</td>
<td>7 (6/1)</td>
<td>100</td>
<td>2.29 (0.06 to 4.52)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (15/4)</td>
<td>243</td>
<td>-0.78 (-4.07 to 2.50)</td>
</tr>
</tbody>
</table>

What this study adds

Evidence from good quality, randomised controlled trials shows that NPPV is an effective treatment for acute exacerbations of COPD.

NPPV should be considered early in the course of respiratory failure and before severe acidosis ensues, to avoid the need for endotracheal intubation and reduce mortality in patients with COPD.

GOLD - Global Initiative for Chronic Obstructive Lung Disease

* Non-invasive intermittent positive pressure ventilation (iNPPV) in acute exacerbations improves blood gases and pH, reduces in hospital mortality, decreases the need for invasive mechanical ventilation and intubation, and decreases the length of hospital stay (Evidence A).
### Table 16: Selection and Exclusion Criteria for NIPPV™

**Selection criteria at least 2 should be present:**
- Moderate to severe dyspnea with use of accessory muscles and paradoxical abdominal motion.
- Moderate to severe acidosis (pH < 7.35, P CO₂ > 60 mm Hg).
- Respiratory frequency > 25 breaths per minute.

**Exclusion criteria (may be present):**
- Respiratory arrest.
- Cardiorespiratory instability (hypotension, arrhythmias, myocardial infarction).
- Comatose, impaired mental status, uncooperative patient.
- High aspiration risk, vomiting or oropharyngeal secretions.
- Recent head or gastrointestinal surgery.
- Cranial or thoracic trauma, head neck or spinal abnormalities.
- Extreme obesity.