Quality of life in severe bronchial diseases

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HQOL and severe bronchial diseases

- Definitions
- Why HQOL in bronchial diseases ?
- New avenues ?
- Use in a routine setting ?
Asthma

GINA Guidelines 2001

«Is a chronic inflammatory disorder of the airways. Chronically inflamed airways lead to an increase in airway hyperresponsiveness with recurrent episodes of wheezing, coughing and shortness of breath, widespread, variable, and often reversible airflow limitation.»
COPD

GOLD  R. Pauwells et al AJRCM 2001

« Is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases »
Severe Asthma?

Difficult Asthma
ERJ 1999

Refractory Asthma
AJRCCM 2000

GINA
National Guidelines
?????

ENFUMOSA BIOAIR /NHLBI Initiatives
Severe asthma

1- **Real asthma** responsive to bronchodilators or short course of oral corticosteroid (no other diagnosis, no compliance issue) lifelong non-smokers or less than 5pq/yrs stopped more than 5 yrs before.

2- Follow-up by a specialist for at least one year and compliance to treatment considered to be fair.

3- Asthma symptoms not controlled. At least one asthma exacerbation necessitating an hospitalization within the past year, daily symptoms requiring rescue medications.

4- High doses of inhaled corticosteroids (2000µg of BDP eq) and LAB2 (SMR or FMR), and SAB2 as required.

5- On top of this treatment, a dose of Prednisone is sometimes required to avoid recurrence of severe exacerbations.

6- Despite this treatment some patients remain uncontrolled.
Health outcomes in bronchial diseases

Physician view point

• **Clinical**: (daily symptoms, control, exacerbations, hospitalisations, ICU)
• **Functional**: (baseline airflow impairment, reversibility, BHR, Variability of PEFR)
• **Therapeutical**: (lowest quantity of drug to control, risk-benefit ratio, resistance)
• **Economical**: (productivity at work, at school !!, duration of sick leaves, lowest cost of disease)
Health outcomes in bronchial diseases

Physician view point : Future

• **Biomarkers** :
  • Blood markers: ECP?
  • Exhaled NO, Exhaled air condensates: mediators
  • Temperature of the airways
  • Sputum eosinophils and mediators
  • Urine mediators
  • **Morphological features** :
  • Imaging CT-scan, MRI.....
Health outcomes in bronchial diseases

Physician view point: Future, future

Proteomic analysis of BAL fluid

Diagnosis, Follow-up, best therapeutic strategies...
Health outcomes in chronic bronchial diseases

- Patient perspective:
  - Overall satisfaction
  - Symptom free days
  - Quality of life
Modifiable factors associated with dissatisfaction with asthma treatment

Markson et al, Arch Int Med 2001

30% patient dissatisfied with TTT
Bronchial diseases are **chronic diseases** that can place **considerable restrictions** on the physical, emotional and social aspects of the lives of patients. Many patients, including the most severe, **may not completely appreciate** the impact of the disease on their social life and claim they lead "normal" lives because normality may be based on adjustments and restrictions they have already incorporated into their lifestyles or alternatively because they mask their restriction wanting to "live like others".
HQOL and severe bronchial diseases

• Definitions
• Why HQOL in bronchial diseases?
• New avenues?
• Use in a routine setting?
Severity of a chronic disease

adapted from Stein et al Lancet 1987

- symptoms severity
- functional severity
- burden of illness

Structural Changes

? Quality of Life

Inflammation
What is Quality of life?

"Quality of life (QOL) is a concept including a large set of physical and psychological characteristics for assessing problems in the social context of life style."

Walker & Rosser 1987
Functional Limitation and FEV1 (SF-36)
Bousquet et al AJRCCM 1996
Predictors of overall HQOL by asthma severity
Moy et al AJRCCM 2001

253 and 359 asthmatic patients in 2 trials
AQLQ retrospective analysis
Lung function is not a predictor of HQOL

<table>
<thead>
<tr>
<th></th>
<th>Albuteron</th>
<th>ZiLeuton base</th>
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<tr>
<td>FEV1</td>
<td>0.08</td>
<td>NS</td>
<td>-0.09 NS</td>
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<td>AMPF</td>
<td>-0.0001</td>
<td>NS</td>
<td>0.0003 NS</td>
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<td>-0.0057 NS</td>
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<td>-0.2 0.03</td>
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<td>Wheez</td>
<td>-0.376</td>
<td>0.03</td>
<td>-0.169 NS</td>
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</table>
Quality of life and Bronchial Diseases

G Guyatt
E Juniper

Pharmacoeconomy
Education
Rehabilitation

ASTHMA
Assessment of usefulness


COPD
Therapeutical trials

Chronic Respiratory Insufficiency

P Jones
F Quirk

Ann Int Med 1980

Increase in publication numbers

Routine use? Marketing?
HQOL

Generic Questionnaires

- Population based
- Different chronic diseases
- Wide array of HRQL domains (side-effects)
- SIP, NHP, SF-36
- Not sensitive enough for a specific disease
- Lack of responsiveness for changes
NHP and Asthma Severity
Godard et al ERJ 2002

- Physical
- Pain
- Sleep
- Energy
- Isolations
- Emotions

Stade 1
Stade 2
Stade 3
Stade 4

Godard et al ERJ 2002
NHP and Asthma Severity
Comparison of non specific SF-36 QOL in asthma and rhinitis

J. Bousquet, JACI 1994 et AJRCCM 1994

SF-36 scores in asthma and rhinitis
HQOL in asthma and rhinitis
Leynaert et al AJRCCM 2000

SF-36 PCS

- Control
- Rhinitis
- Asthma

p<0.001
p<0.03
p<0.05

SF-36 MCS

NS
Quality-of-Life in asthma and COPD (SF-36)

Bousquet, Richard, Chicoye et al
HQOL
Disease-Specific Questionnaires

- Domain mostly relevant to the respiratory impairment
- Asthma, COPD, Lung failure.....
- Responsiveness to interventions (trials)
- **AQLQ, SGRQ, MaugeriFoundation**...
- No comparison with normal ?
- No comparison with other chronic conditions ?
## Quality of life: Specific Questionnaires
derived from Mapi research InstituteWeb site

<table>
<thead>
<tr>
<th>Name</th>
<th>Administration</th>
<th>Author</th>
<th>Disease</th>
<th>Nb items</th>
<th>Nb translation</th>
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<tr>
<td>AQLQ</td>
<td>Auto, Inter, Phone, enet ?</td>
<td>Juniper</td>
<td>Asthma adult</td>
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<td>SGRQ</td>
<td>Auto</td>
<td>P. Jones</td>
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<td>KASE-AQ</td>
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<td>J. A. Winder</td>
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<td>miniAQLQ</td>
<td>Auto</td>
<td>E. Juniper</td>
<td>Asthma</td>
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<td>16</td>
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<td>QLQ-asthma</td>
<td>Inter</td>
<td>DT. Brown</td>
<td>Asthma</td>
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<tr>
<td>BPQ</td>
<td>Auto</td>
<td>ME. Hyland et al</td>
<td>COPD</td>
<td>10/33</td>
<td>3</td>
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</table>
Properties of the questionnaires

- **Responsiveness**: ability to detect changes within patients even if they are small
- **Cross sectional and Longitudinal validities**: appropriate correlations and changes in established health status measures
- **Reliability**: High/ratio variance between patients vs variance within patients
Properties of the questionnaires

Clinical validity?
Threshold?
Doctors or Patients?
AQLQ: 0.5
SGRQ: 4
AQLQ Changes
Rutten van Molken et al ERJ 1995

Salbutamol Salmeterol

0.49 when threshold is 0.50

* p from <0.03 to
** ** ** < 0.001
SGRQ Changes
Jones et al ERJ, Am J Respir Dis 1994

very effective
moderately effective
slightly effective
no effect

139      164      97      108
## Quality of life
### Specific Questionnaires

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Disease</th>
<th>Reliability</th>
<th>Validity</th>
<th>Longitudinal validity</th>
<th>Clinica validity</th>
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</thead>
<tbody>
<tr>
<td>AQLQ</td>
<td>Asthma</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Mini-AQLQ</td>
<td>Asthma</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Living with asthma</td>
<td>Asthma</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes?</td>
<td>?</td>
</tr>
<tr>
<td>St Georges Respiratory illness QOL</td>
<td>AS + COPD</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Life activities Questionnaire</td>
<td>Asthma</td>
<td>?</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
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<tr>
<td>Asthma bother profile</td>
<td>Asthma</td>
<td>?</td>
<td>?</td>
<td>?</td>
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</tbody>
</table>
AQLQ according to asthma severity
Enfumosa Study, AJRCCM 2000

**QOL scores**

- **Mild ICS**
- **Severe ICS**
- **Severe OCS**

* * P < 0.0001

- **AQLQ Overall**
- **Activities**
- **Symptoms**
- **Emotions**
- **Environment**
AQLQ according to asthma severity
 Difficult Asthma network in Montpellier, 2001

- Mild
- Severe
- Difficult compliant
- Difficult non compliant

* P < 0.001

Activity | Symptoms | Emotions | Environment

- 6
- 5
- 4
- 3
- 2
- 1
- 0
Adult chronic asthma study

AQLQ

T Reiss et al, Arch Intern Med 1998

Score (change from baseline: m±sem)

Activity  Symptoms  Emotions  Environment

Domains

Montelukast

Placebo
Omalizumab Improves Quality of Life
Bulh et al ERJ 2002

![Graph showing the change in quality of life metrics (Activities, Emotions, Symptoms, Environmental Exposure, Overall) for Omalizumab (n=274) and Placebo (n=272) groups.]

- Activities: *P ≤ 0.003
- Emotions: *P ≤ 0.003
- Symptoms: *P ≤ 0.003
- Environmental Exposure: *P ≤ 0.003
- Overall: *P ≤ 0.003

Note: * denotes significance at the p=0.003 level.
Significant improvement in AQLQ over 1 year: Steroid naïve (S1)

Mean change from baseline

Week

GOAL Study
HQOL and severe bronchial diseases

- Definitions
- Why HQOL in bronchial diseases?
- New avenues?
- Use in a routine setting?
HRQOL is related to mortality in COPD
A. Domingo-Salvany et al AJRCCM 2002 follow-up to 4 years

OR: FEV1: 2.04; SGRQ: 1.02; PCS-36: 1.04 (cox model)
Changes induced by back titrating inhaled corticosteroids

P. Gibson  J All Clin Immunol 2000
HQOL and Sputum Eos and PMns
Difficult Asthma Network Montpellier 2001
n=69
Inhaled corticosteroids in COPD
Yes always?
(3 major studies)

Major outcomes?
• 1 - Improvement of daily symptoms (dyspnea)
• 2 - Improvement of lung function
• 3 - Decrease number of exacerbations
• 4 - Improvement of QOL
• 5 - decrease rate of lung function decline
**COPD QOL ISOLDE Study**

**BMJ 2000**

<table>
<thead>
<tr>
<th>SGRQ score</th>
<th>placebo</th>
<th>FP</th>
<th>p</th>
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<tbody>
<tr>
<td>Total</td>
<td>3.4</td>
<td>2.3</td>
<td>0.004</td>
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<tr>
<td>Symptoms</td>
<td>2.8</td>
<td>1.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Activities</td>
<td>3.5</td>
<td>2.1</td>
<td>0.0003</td>
</tr>
<tr>
<td>Impact</td>
<td>3.7</td>
<td>2.6</td>
<td>0.03</td>
</tr>
</tbody>
</table>

- QOL degradation faster in the Placebo group: 3.2 U/yr vs 2 U/yr (p=0.004)
Health status – St George: total score

Threshold of clinical significance

* p=0.008 vs Placebo
† p=0.039 vs FP

Calverley et al, Lancet 2003
Adjustment of therapy based on sputum eosinophilic content
RH Green et al; Lancet 2002
Exacerbations during one year

\[ p < 0.01 \]

is there a potential model for using HR-QOL?
HQOL and severe bronchial diseases

• Definitions
• Why HQOL in bronchial diseases?
• New avenues?
• Use in a routine setting?
HRQOL measurement in asthma and COPD in the real life?

- Time is short, How do you feel?
- «The patients can not fill the form in the waiting room by themselves»
- «I do not know how to interpret the results»
- Minimal clinically significant changes?
- Doctor’s or patient’s perception?
- No direct impact on disease management
Conclusions

- Clinical
- Asthma
- COPD
- HRQOL
- Perception
- Depression
- Lung function
- Therapies
- Costs
- Valued Life Activities
- Severity
- Control
- Mortality