Comorbidities of asthma & its impact on control

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Pathological Changes of Bronchial Asthma

- Vasodilation
- Mucous plug
- Desquamation of epithelium
- Hyperplasia of mucous glands
- Smooth muscle & hypertrophy hyperplasia
- Thickened BM
- Edematous submucosa
- Cellular infiltration

- Wheezing, chest tightness, breathlessness, coughing
Comorbidities of asthma
(Diseases co-existing with asthma)
Misdiagnosis

Misinterpretation of symptoms

Aggravation of one or both diseases
Strongly associated with:
- Allergic rhinitis
- Gastroesophageal reflux disease (GERD)
- Infections
- Psychological disturbances

Weakly associated with:
- Cardiovascular &
- Hypertensive diseases
Cardiovascular comorbidities

Adjusted odds ratios and 95% confidence intervals of comorbidities in asthma. Total is adjusted for age and sex. Males and females are adjusted for age.
Adjusted odds ratios and 95% confidence intervals of comorbidities in asthma. Total is adjusted for age and sex. Males and females are adjusted for age.
Effect of Comorbid diseases on severity of asthma

http://erj.ersjournals.com/content/33/4/897.long
Relationship between asthma & Comorbid diseases
Mediator release
Neural reflexes
Increased inflammatory cells
Increased mouth breathing

http://erj.ersjournals.com/content/33/4/897.long
Frequent physician’s visit & hospital admission increased drug related expenses

http://erj.ersjournals.com/content/33/4/897.long
Asthma & GERD

- Acid reflexly cause Bronchospasm
- Increased intrathoracic pressure & theophylline causes relaxation of spincter.

http://erj.ersjournals.com/content/33/4/897.long
Asthma & GERD

Cough, chest & throat tightness in both conditions
Possible mechanisms to explain the high prevalence of gastroesophageal reflux and gastroesophageal reflux disease (GERD) in asthma. *Adapted from Harding et al. (49)
Incedence of GERD, Oesophagitis and Hiatus hernia in asthma patient

http://erj.ersjournals.com/content/33/4/897.long
OSA in asthma patient $[n=154+659]$

Mechanical factors, increased inflammatory cells

http://dx.doi.org/10.1155/2013/251567
Obesity & asthma

- GERD
- Mechanical Factor
- Increased cytokines
- Decreased response to steroid

30% misdiagnosis of asthma
Asthma and psychiatric disorders

- Depressive Disorders
- Anxiety Disorders

Comorbidity
Asthma – Psychiatric Disorders

31% - 38%

- Triggers asthma symptoms
- Affects symptom perception
- Influences drug compliance

Chronic sinusitis and asthma

Radiological evidence of chr. sinusitis

http://erj.ersjournals.com/content/33/4/897.long
Smoking

- Increase risk of asthma
- Decreased response to steroid
Asthma in pregnancy

- Symptoms improve in pregnancy
- Increased chance of development of GERD related asthma.
Control of asthma

- What is control?
- How it is controlled?
- How much can be controlled?
- Why not controlled?
- How to achieve maximum control?
Treat asthma aggressively initially to help the patient achieve quick control, then gradually cut back to the fewest medications and lowest effective doses required to maintain control.
# Defining asthma control

<table>
<thead>
<tr>
<th></th>
<th>CONTROLLED (All of the following)</th>
<th>PARTIALLY CONTROLLED (Any measure present in any week)</th>
<th>UNCONTROLLED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime Symptoms</td>
<td>None (twice or less weekly)</td>
<td>More than twice weekly</td>
<td></td>
</tr>
<tr>
<td>Limitation of activity</td>
<td>None</td>
<td>Any</td>
<td>3 or more features of partly controlled asthma present in any week.</td>
</tr>
<tr>
<td>Nocturnal Symptoms</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Reliever medication</td>
<td>None (twice or less weekly)</td>
<td>More than twice weekly</td>
<td></td>
</tr>
<tr>
<td>Lung function.</td>
<td>Normal</td>
<td>&lt;80% personal best or predicted</td>
<td></td>
</tr>
<tr>
<td>Exacerbation</td>
<td>None</td>
<td>Any in past year</td>
<td>Any in past week</td>
</tr>
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</table>

## ACTION

<table>
<thead>
<tr>
<th></th>
<th>MAINTAIN CONTROL &amp; FIND LOWEST CONTROLLING STEP</th>
<th>CONSIDER STEPPING UP TO GAIN CONTROL</th>
<th>STEP UP UNTIL CONTROLLED &amp; TREAT ANY EXACERBATION</th>
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</table>
Diagnose asthma

Assess asthma severity

Initiate medication & demonstrate use
Asthma management

Step 1: SABA PRN

Step 2: Low-dose ICS
Alternative: cromolyn, LTRA, nedocromil, or theophylline

Step 3: Low-dose ICS + LABA or medium-dose ICS
Alternative: low-dose ICS + LTRA, theophylline, or zileuton

Step 4: Medium-dose ICS + LABA
Alternative: medium-dose ICS + LTRA, theophylline, or zileuton

Step 5: High-dose ICS + LABA and consideromalizumab if allergies are present

Step 6: High-dose ICS + LABA + oral corticosteroids and consideromalizumab if allergies are present
How much can be controlled?
Asthma control rate

3000 asthma outpatient, 36 general hospitals, 10 large Chinese cities, from April 2007 to March 2008

http://dx.doi.org/10.1155/2013/549252
Asthma control rate
2323 adult patients & 884 children patients

http://dx.doi.org/10.1155/2013/549252
Work loss or school absence

http://dx.doi.org/10.1155/2013/549252
Asthma control, weighted prevalence, n=2238

- 58% Uncontrolled
- 42% Controlled

http://dx.doi.org/10.1155/2013/549252
Why can not be controlled?

Impact of co-morbidities
Impact of rhinitis on asthma control, (n=1027)
Impact of rhinitis on asthma control, (n=1027)
Impact of rhinitis on asthma control, (n=256), School children, 2007

Uncontrolled asthma

**Figure 2:** Odds tendency to inadequate control of asthma in 256 asthmatic children, by age group. *P* value for odds homogeneity test: A = 0.007, B = 0.097, and C ≤ 0.001; *P* value to the score test with tendency of odds: A ≤ 0.001, B = 0.008, and C ≤ 0.001. The dotted line describes a predicted trend (see text).
PSYCHIATRIC DISORDERS IN ASTHMA
-CONSEQUENCES-

Comorbidity with Depression and anxiety

Psychopathology in patients With sever asthma

Asthma Control

Helth Costs

Goldney RD et al. 2003
Lavoie et al 2006; Deshmukh T et al 2008
Ten Brinke et al. 2001
Psychological disturbances & asthma
The Impact of Adenotonsillectomy on Asthma in Children
n=465, Dept. of paed. New Jersey Medical school

Figure 1. Measures of Asthma Control
Effect of continuous positive airway pressure (CPAP) on asthma with OSA patients

| Functional and clinical characteristics of the subjects at baseline (pre-) and after 6 weeks of treatment (post-) with continuous positive airway pressure (CPAP) |
|---|---|
| Pre-CPAP | Post-CPAP |
| FEV1 % pred | 82.2 ± 13.6 | 80.4 ± 13.6 |
| FEV1/FVC % | 77.3 ± 8.3 | 76.3 ± 10.1 |
| PC_{20} mg·mL^{-1} | 2.2 (1.3–3.5) | 2.5 (1.4–4.5) |
| AHI | 48.1 ± 23.6 | 2.6 ± 2.5*** |
| QOLAs | 5.0 ± 1.2 | 5.8 ± 0.9*** |
| QOLAp | 4.1 ± 1.4 | 6.0 ± 1.0*** |

Data are presented as mean ± SD or geometric means (95% confidence interval), i.e. average of three individual geometric means before and after CPAP. FEV1: forced expiratory volume in one second; % pred: % predicted; FVC: forced vital capacity; PC_{20}: provocative methacholine concentration causing a 20% fall in FEV1; AHI: apnoea/hypopnoea index; QOLAs: quality of life specific to asthma; QOLAp: quality of life specific to obstructive sleep apnoea. ***: p ≤ 0.001.
Comorbid factors associated with recurrent severe exacerbations. Patients with more than three severe exacerbations per year (&) had significantly more prevalent psychosocial dysfunctioning, severe sinus disease, gastric reflux or recurrent respiratory infections compared with patients with only one severe exacerbation (h). Error bars represent SE. NS: nonsignificant. *: p<0.05.
Comorbidity ratios
Uncontrolled/controlled ratios

Uncontrolled/controlled patients

None  One  Two  Three or more

Comorbidity factors
How to achieve maximum control?
Asthma
Well-controlled

Yes

Maintain or step-down therapy

No

Detailed asthma assessment

Review medicine technique & adherence;
assess side effects;
review environmental control

comorbidities
Poor asthma control

Comorbidities

- Severe nasal rhinal disease
- GERD
- Rec. resp. tract infection
- Psychological disturbance
- OSA

13 comorbid factors considered to be responsible, n=136

*Eur Respir J 2005; 26: 812-818
Asthma assessment

- Spirometry
- Peak flow
- CXR
- Allergy testing
- Provocative testing
- Challenge test
Uncontrolled Asthma

Step 5 Therapy:
- High-dose ICS + LABA

Step 6 Therapy:
- High-dose ICS + LABA
  - plus
  - Oral glucocorticoids

Gastroesophageal Reflux
- Anti-reflux therapy (H2 blocker, PPI, Nissen)

Aeroallergen Sensitivity?
- Aggressive Treatment of rhinitis with antihistamines and nasal corticosteroids.

Persistent IgE Elevation?
- Consider omalizumab

Persistent Eosinophilia?
- Consider anti-IL-5 therapy (mepolizumab/reclizumab)

Chronic Infection (sinusitis/bronchitis)
- Consider antimicrobial therapy

Consider alternative diagnoses (ABPA, vocal cord dysfunction, bronchiectasis from primary immunodeficiency, CF, etc)
Assessment and management of some asthma-related comorbidities cont.
Assessment and management of some asthma-related comorbidities cont.
Thank you
### Assessment and management of some asthma-related comorbidities.†

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Potentially useful tests</th>
<th>Management: possible treatment options</th>
</tr>
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<tbody>
<tr>
<td><strong>Rhinitis</strong></td>
<td></td>
<td></td>
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<tr>
<td>– Allergic</td>
<td>Allergy skin prick test</td>
<td>Avoid relevant allergen exposure</td>
</tr>
<tr>
<td></td>
<td>Serum-specific IgE</td>
<td>New generation oral H₁, antihistamine</td>
</tr>
<tr>
<td>– Nonallergic</td>
<td></td>
<td>Intranasal corticosteroids</td>
</tr>
<tr>
<td>– Associated with nasal polyps</td>
<td>ENT examination</td>
<td>LTRAs</td>
</tr>
<tr>
<td>– CRS and sinusitis</td>
<td>Sinus radiography/CT scan</td>
<td>Immunotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intranasal corticosteroids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nasal saline irrigations</td>
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<tr>
<td></td>
<td></td>
<td>Nasal anticholinergics</td>
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<tr>
<td></td>
<td></td>
<td>Oral corticosteroids</td>
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<tr>
<td></td>
<td></td>
<td>Surgical treatment</td>
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<tr>
<td><strong>GERD</strong></td>
<td>Proton-pump inhibitor treatment trial</td>
<td>Management of lifestyle</td>
</tr>
<tr>
<td></td>
<td>24-h esophageal measurement</td>
<td>Acid-suppressive therapy</td>
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<tr>
<td></td>
<td>Imaging techniques</td>
<td>– Proton-pump inhibitor</td>
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<tr>
<td></td>
<td></td>
<td>– H₂ blocker</td>
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<tr>
<td></td>
<td></td>
<td>Surgical intervention</td>
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</tbody>
</table>
Assessment and management of some asthma-related comorbidities cont.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Assessment/Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>BMI and other obesity measures, Detection of metabolic syndrome</td>
</tr>
<tr>
<td></td>
<td>Weight loss measures, Diet and exercise, Bariatric surgery (morbid obesity)</td>
</tr>
<tr>
<td>OSA</td>
<td>Polysomnography, Oxymetry</td>
</tr>
<tr>
<td></td>
<td>CPAP plus other methods, Weight loss when relevant</td>
</tr>
<tr>
<td>Psychopathologies</td>
<td>Psychological evaluation</td>
</tr>
<tr>
<td></td>
<td>Psychotherapy, Referral to psychologist/psychiatrist</td>
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<tr>
<td>Dysfunctional breathing</td>
<td>Nijmegen questionnaire [203]</td>
</tr>
<tr>
<td></td>
<td>Psychotherapy, Breathing retraining</td>
</tr>
<tr>
<td>VCD</td>
<td>Visualization of the pharynx, Laryngoscopy</td>
</tr>
<tr>
<td></td>
<td>ENT referral, Speech therapy, and so on</td>
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</tbody>
</table>
Assessment and management of some asthma-related comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnosis/Management</th>
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<tbody>
<tr>
<td>Hormonal and metabolic disorders</td>
<td>Hormones measurements, Referral to endocrinology and metabolism specialist, Treatment of the specific disorder</td>
</tr>
<tr>
<td>COPD and smoking</td>
<td>Pulmonary function tests, Smoking cessation program, Bronchodilators, Inhaled corticosteroids, Readaptation-exercise program, Other measures and Rx</td>
</tr>
<tr>
<td>Infections</td>
<td>Specific serologies, Various identification measures, Precipitins for Aspergillus/fungal cultures/Aspergillus serology, Specific treatment according to the agent, if available and considered clinically significant, Systemic corticosteroids if allergic reaction to agent (e.g., ABPA)</td>
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