Rhinosinusitis and Asthma Exacerbations

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Chronic rhinosinusitis

- **Rhinosinusitis (including nasal polyps) is defined as inflammation of the nose and the paranasal sinuses characterized by**
- **Symptoms**: nasal blockage/obstruction/congestion or nasal discharge, facial pain/pressure, reduction or loss of smell;
- **Endoscopic findings**: polyps and/or mucopurulent discharge and/or; oedema/mucosal obstruction
- **CT changes**: mucosal changes within the ostiomeatal complex and/or sinuses.
### Epidemiology of CRS

- **Based on symptoms**: 1% - 15.5%
  - „problems with sinuses”
- **Increasing with age**: 2.7% -> 6.6%
- **Gender**: F > M
- **Geographic differences**
  - 1.01% in North Korea
  - 9.9% Scotland
- **Co-morbid conditions**
  - Immunodeficiency, systemic diseases
  - COPD, Bronchiectasis
  - Bronchial asthma
A postal questionnaire was sent to a random sample of adults aged 15-75 years in 19 centres in Europe.

**Results:**
- the overall prevalence of CRS by EP3OS criteria was **10.9%** (range 6.9% in Germany to 27.1% in Coimbra)
- Poor correlation of CRS symptoms with objective evidence (endoscopy/CT scanning)
- Strong, and consistent association of CRS with smoking

Tomassen P et al. Allergy 2011, 66:556,
Association of CRS with asthma

- CRS coexisted in 34% patients with asthma  
  \((\text{Annesi–Maesano 1999})\)
- Abnormal sinus radiographs can be found in 53% of asthmatics  \((\text{Berman S 1974})\)
- Mucosal thickening in can be visualized in 74% of patients with asthma  \((\text{Pfister R 1994})\)
- Asthmatics with CRS are more likely to have NPs than nonasthmatics with CRS  \((57.6\% \text{ versus } 25\%)\)  \((\text{Pearlman AN 2009})\)
The Global Allergy and Asthma Network of Excellence (GA2LEN) conducted a postal questionnaire in representative samples of adults living in Europe to assess the presence of asthma and CRS defined by the EP3OS.

Results: Over 52,000 adults aged 18-75 years and living in 19 centres in 12 countries took part.

There was a strong association of asthma with CRS (adjusted OR: 3.47; 95% CI: 3.20-3.76) at all ages.

The association with asthma was stronger in those reporting both CRS and allergic rhinitis (adjusted OR: 11.85; 95% CI: 10.57-13.17).
Eosinophylic versus non-eosinophylic CRS in Japan

- **Clinical features**
  - Reduction/loss of smell in early stages
  - Recurrent rate of nasal polyps very high

- **Endonasal findings**
  - Bilateral polyps,

- **CT findings**
  - Ethmoid redominance (in early stages) vs maxillary predominance (in early stages)

- **Blood examination**
  - Eosinophilia

- **Therapy**
  - Macrolide therapy not effective effective

- **Coexistence of asthma**
  - More frequent

Chronic sinusitis is related to blood and sputum eosinophilia

- In 89 outpatients with severe asthma CT scans were scored. Lung function, NO in exhaled air, and blood and sputum eosinophils were measured.

**Results**

- CT scans showed abnormalities in 84% of patients.
- There was a significant correlation between CT scores and eosinophils
  - in peripheral blood ($R = 0.46$)
  - in induced sputum ($R = 0.40$)
- Level of exhaled NO ($R = 0.45$, $P < 0.01$)
Exacerbations (commonly referred to as asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, chest tightness, or a combination of these symptoms.”
Asthma Inside and Reality studies
Asthma exacerbations over last year

Rabe K. et al.: AIR study J Allergy Clin Immunol 2004
Kowalski M. L. et al.: Alergia Astma Immunologia 2004
Consequences of asthma exacerbations

Asthma exacerbation

Exacerbations promote inflammation leading to loss of control despite treatment

And/Or
There is a subpopulation of patients that are more prone to exacerbations despite treatment

Asthma exacerbation

• Long term consequences of frequent asthma exacerbations
  – Accelerated loss of lung function
  – Increased risk of near fatal or fatal events
Risk factors for asthma exacerbations

The number of ER visits is associated with:

- Older age
- Non-white race
- Lower socio-economic status
- Co-existing psychiatric diseases
- Markers of asthma severity

These factors may help to identify susceptible populations, but are not preventable.
A group of 136 patients with difficult to control asthma divided into 2 groups:
- One exacerbation per year
- Three or more per year

• Risk factors for asthma exacerbations
  • Psychological dysfunctioning OR=10.0
  • Recurrent respiratory infections OR=6.9
  • GER OR= 4.9
  • Severe CRS OR=3.7
  • Sleep apnea OR=3.4

- All patients had at least one of the above factors
- 52% showed three or more factors

Ten Brinke et al. 2005
More symptoms of CRS in multi-symptom asthma

- 18,087 responders in the West Sweden Asthma Study
- 2.1% (25% of asthmatics) had "Multi symptom asthma" -
  - medication and attacks of shortness of breath and recurrent wheeze and at least one out of any wheeze, dyspnoea, breathlessness-exertion, breathlessness-cold and breathlessness-exertion in cold.

- Symptoms of CRS occurred more frequently in subjects with multi-symptom asthma compared with fewer-symptom asthma and non-asthma

Lötvall J et al. Resp Res 2010
Asthma comorbidity and control

- 56 controlled (ACT>20) and 102 uncontrolled (ACT<20) asthmatics were assessed for the presence of comorbidities.

**Results**

- Comorbidities more frequent in uncontrolled group
  - Nasal polyps (8.8 vs 0%)
  - Gastrooesophageal reflux (22.8 vs 8.9%)
  - ABPA (9.8 vs 0%)

- Simultaneous presence of 3 or more comorbidity factors was significantly more frequent in patients with suboptimal control ($P=.01$).

Perez deLano Arch Bronchopn 2010
Severe asthma is defined by the level of current clinical control and risks as

“Uncontrolled asthma which can result in risk of
-frequent severe exacerbations (or death) and/or
-adverse reactions to medications and/or
- chronic morbidity (including impaired lung function or reduced lung growth in children.”
CRS/NP and asthma severity

- Presence of CRS is associated with more severe asthma *(Liou A et al. Chest 2003)*

- Presence of CRS is related to more severe asthma: higher medication use and lower FEV1 *(Aazami et al. Iran JACI 2009)*
Relation between severity of CRS and asthma severity

To evaluate chronic rhinosinusitis in patients with severe steroid-dependent asthma,

- **Patients and methods**
  - A clinical score and coronal CT scanning were compared in 35 patients with severe corticosteroid dependent asthma and 34 mild to moderate asthmatics.

- **Results**
  - The proportion of patients with symptoms of rhinosinusitis was similar in both groups of asthmatic subjects (74% vs 70%).
  - **All subjects** with steroid-dependent asthma versus 88% of subjects with mild-to-moderate asthma had abnormal CT scan results.
  - The clinical and **CT scan severity scores were higher** in the subjects with severe steroid-dependent asthma.

Bresciani M. JACI 2001,107,73
CRS and asthma severity

**Patients**
A total of 121 patients with chronic rhinosinusitis, NPs and/or asthma were evaluated (sinus CT scans and nasal endoscopy).

**Results**
- Patients with CRS/NP/asthma (as compared to CRS only) had:
  - More severe sinus disease on CT scan (P<0.001), greater bronchial obstruction (P<0.05),
  - The extent of sinus CT changes was greater in asthmatics and correlated with greater duration of asthma (P<0.0001), and age (P=0.039)

Staikūniene J. Medicina 2008, 44, 257
Mechanisms linking CRS/NP. with asthma

CRS and asthma share common:
- Histopathology
- Immunopathology
- Patomechanism?

- Aspiration
- Mouth breathing
- Neurogenic reflex
- Common triggers
  - Infectious agents
  - Allergens
  - Other environmental (e.g. tobacco smoke)
- One airway disease – involvement of bone marrow
Chapter: Treatment of asthma: 
Removal of infection and nasal surgery

‘In view of the fact, that so many patients who have bronchial asthma have an associated paranasal sinus infection, proper and adequate management of such infections becomes very important’

‘Asthmatic patients may show temporary improvement following surgery … however, such operations usually do not lead to permanent relief ..’
<table>
<thead>
<tr>
<th>Medical treatment</th>
<th>Surgical treatment</th>
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<tr>
<td>• Improvement in asthma symptoms</td>
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<tr>
<td>• Decrease in using bronchodilators</td>
<td>• Decrease in asthma medication (including OCS)</td>
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<tr>
<td>• Improvement in spirometry</td>
<td>• Improved pulmonary function</td>
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<tr>
<td>• Improvement in severity of asthma</td>
<td>• Decrease in BHR</td>
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**Slavin RG** 1982

**Rachalevsky GS** 1984

**Friedman R** 1994

**Tosca** 2003

**Lamblin C et al.** 2000

**Ikeda K** 1999

**Palmer JN** 2001

**Okayama M** 1998

**Enhage A** 2009
Effect on asthma exacerbations:

- Surgery reduced the number of hospitalizations for asthma from seven (in three preoperative 12 months) to two (post-operatively) (p<0.05)

- The medical treatment of CRS reduced hospital admissions from five to one (p<0.05)

- No difference between surgical and medical treatment

Ragab s et al. ERJ 2006,28,68
Severity of CRS and asthma in patients with AERD

Recurrence of nasal polyps after FESS

Higher asthma severity in AERD

• Higher medication requirements, including dependence on oral GCS (Szczeklik A. et al. 2000)
• More likely to have been intubated and to have a steroid burst in the previous three months (Mascia K et al. 2005)
• Frequent exacerbations (Koga T. Et al. 2006)
• Association with near fatal asthma (Plaza W. et al. 2002)

Patients with AERD had history of 10 times as many previous FESS procedures as had the patients without aspirin sensitivity

Patients
- 91 patients with CRS resistant to medical treatment
  - 50 ASA-tolerant
  - 41 ASA-sensitive
- Patients were subjected to ESS and followed at 6 and 12 months after surgery

Results
- Improvement in asthma outcomes
  - FEV1, ICS, OCS
  - Exacerbations
- Similar response in AIA and ATA (Awad et al. (Am J Rhinol 22, 197–203, 2008))
Aspirin desensitization in patients with AERD

- 1923 F. Vidal reported „desensitization” to aspirin
- 1976 C. R. Zeiss & R.F. Lockey described refractory period to aspirin
- 1981 D.D. Stevenson reported clinical benefits of prolonged treatment with aspirin after desensitization

- Daily oral ASA after desensitization (300-2400mg) in some patients may lead to:
  - Improvement in asthma symptoms
  - Improvement in rhinosinusitis symptoms
  - Decreased need for sinus surgery/polypectomy
Rapid effect of treatment with 600 mg/day of ASA on nasal and bronchial symptoms in ASA-sensitive asthmatics

Long–term treatment with aspirin after desensitization

172 patients desensitized
126 patients followed up for a year
650 mg ASA bid at home
Clinical assessment: 6 month and 1 year

In 87% of patients decrease in:

- Number of sinus infections and surgical procedures
- Symptom score (sens of smell)
- Medications use
- Global assessment of asthma activity
- Hospital admissions and ER visits

Berges-Gimeno JACI 2003,111,180-6
Conclusions

• Presence of CRS in a patient with asthma may increase asthma severity and decrease asthma control, leading to increased asthma exacerbations.

• Proper management of CRS may improve asthma control and reduce the risk of asthma exacerbation.
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