Evaluation and Management of Refractory Asthma

Non-Pharmacological Treatments: Comorbidities & Bronchial Thermoplasty

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Disclosures

• Nothing to disclose
Objective

• Devise a nonpharmacologic management strategy for a patient with refractory asthma, including bronchial thermoplasty
Poor Asthma Control

COMPLIANCE

Inhaler Technique

ENVIRONMENTAL FACTORS

Frustration/chronic illness
Cost
Side effects
Social aspects

Difficulty checking for adherence

Incomplete training

Neurological problems

MSK problems
Case # 1

- 48 y/o woman with asthma, allergic rhinitis and arthritis, consults for *frequent exacerbations* (once a month x 3)
- *Wheezing daily* despite good compliance and technique
- Symptoms of allergic rhinitis are controlled
- Minimal GERD symptoms (once a month) after a heavy meal

**Testing:**
- **PFTs:** FEV1/FVC 65%, FEV1 69%, positive BDR, positive hyperinflation
- **CXR:** normal

**Medications:**
- Medium dose ICS/LABA
- Rescue SABA
- Nasal steroids
- Ibuprofen
Question # 1

In addition to increasing her ICS dose, what is the next step in management??

A. A trial of a proton pump inhibitor (PPI) once a day dosing for 8 weeks

B. A trial of a PPI twice a day dosing for 8 weeks

C. Refer the patient for pH monitoring (24 hour testing)

D. Refer the patient for an endoscopy to evaluate for GERD

E. Obtain an IgE level and testing for perennial allergens
ASTHMA

- OSA
- Obesity
- GERD
- Allergic Rhinitis
- Vocal cord dysfunction
- Anxiety
- Depression
- Smoking
- COPD
- Medications:
  - β blockers
  - ASA
  - ACE inhibitors
  - NSAIDS

- COPD
GERD

Esophageal Syndromes

- Typical reflux syndrome
- Reflux chest pain syndrome
- Reflux esophagitis
- Reflux stricture
- Barrett’s esophagus
- Adenocarcinoma

Extra-Esophageal Syndromes

- Reflux cough
- Reflux laryngitis
- Reflux asthma
- Reflux dental erosions
- Sinusitis
- Pulmonary fibrosis
- Pharyngitis
- Recurrent otitis media

Symptomatic Syndromes

- Reflux esophagitis
- Reflux stricture
- Barrett’s esophagus
- Adenocarcinoma

Established Association

Proposed Association
**ASTHMA**

- Vagal response
- ↑ abdominal pressure / ↑ negative thoracic pressure

**GERD**

- Micro aspiration
- Asthma medications

- Hyperinflation
- Lower esophageal sphincter
GERD and Asthma

• 55% of difficult to control asthmatics may have GERD
• 35% of asthmatic patients with documented GERD by pH monitoring did not have typical symptoms
• Clinical suspicion
  – Worsening of asthma symptoms after a meal
  – Heartburn or regurgitation before the onset of asthma symptoms
GERD and Asthma

- Littner et al.
- 24 weeks of lansoprazole BID in moderate to severe asthmatics and positive GERD symptoms. (n=173)
- Daily asthma symptoms, albuterol use, and PFTs did not improve.

GERD and Asthma

• Kiljander et al.
• 16 weeks of esomeprazole BID in moderate to severe asthmatics (n=624).
• Classified in 3 strata:
  1. (-) GERD and (+) nocturnal symptoms
  2. (+) GERD and (-) nocturnal symptoms
  3. (+) GERD and (+) nocturnal symptoms

• PPI was associated with benefits in PEF only in the group that had: (+) GERD and (+) nocturnal symptoms.
• Only 40% of the patients were using LABA. These subgroup had the greatest ↑ in PEF.
• No difference in exacerbations.
GERD and Asthma

- Kiljander et al.
- 26 weeks of esomeprazole once day vs. BID vs. placebo in asthmatics using ICS/LABA + GERD symptoms (n=828).
- No difference in asthma control or symptom scores.
- Modest improvement in quality of life and FEV1 in the PPI groups (more significant with BID dosing).

GERD and Asthma

• Mastronarde JG, et al. (Study of Acid Reflux and Asthma)

  – 24 weeks of esomeprazole BID in inadequately controlled asthmatics despite ICS and minimal or no GERD symptoms (n=393).
  – ~80% were using ICS + LABA
  – No difference in asthma control, PFTs, symptom scores, nocturnal awakenings or quality of life.
  – No subgroup had benefits with a PPI.
GERD and Asthma

- DiMango E, et al.
- Evaluated the baseline characteristics of the Study of Acid Reflux and Asthma (patients with pH recordings)
- 53% of the patients had reflux
- 38% had proximal reflux
- There was no difference in need for SABA, nocturnal awakenings, dose of ICS, use of LABA, PFTs, or methacholine reactivity between individuals with and without proximal or distal GERD

GERD and Asthma

**TAKE HOME POINTS:**

1. Asthmatics with GERD symptoms should be treated with a PPI, especially if they nocturnal asthma symptoms.

2. Severe asthmatics with GERD symptoms appear to have greater benefits with PPI treatment.

3. PPIs have no benefit in patients with poorly controlled asthma with minimal or no symptoms of GERD.

4. Ambulatory pH monitoring is not usually warranted unless there are atypical symptoms.
Allergic Rhinitis and Asthma

• AR increases the risk of asthma 3-fold
• AR is present 75-80% in patients with severe asthma
• AR may substantial costs to asthma patients

Allergic Rhinitis

- Activation of systemic inflammatory pathways
- Post nasal drip into the airways
- Nasobronchial reflex
- ↓ filtration
- ↓ humidification
- ↓ warming

Asthma
# Impact of Treating AR in Asthma

<table>
<thead>
<tr>
<th>STUDY</th>
<th>ASTHMATIC PATIENTS</th>
<th>DESIGN</th>
<th>OBSERVATIONS / CONCLUSIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adam RJ 2002</td>
<td>1610</td>
<td>Retrospective</td>
<td>Nasal steroids and antihistamines were associated with reduced ED visits</td>
</tr>
<tr>
<td>Crystal-Peters J 2002</td>
<td>4944</td>
<td>Retrospective</td>
<td>Asthma ED visits/hospitalizations occurred less often in the treated group 6.6 vs 1.3%, p = 0.001</td>
</tr>
<tr>
<td>Corren J 2004</td>
<td>361 cases 1444 controls</td>
<td>Nested case-control</td>
<td>Treatment with nasal steroids or antihistamines showed a reduction in the risk of hospitalization for asthma</td>
</tr>
</tbody>
</table>
Diagnosis of allergic rhinitis

Intermittent symptoms
Mild
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or LTRA*

Moderate-severe
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or intranasal CS
or LTRA* (or chromone)

In persistent rhinitis
review the patient
after 2-4 wks
If failure: step-up
if improved: continue
for 1 month

Persistent symptoms
Moderate-severe
In preferred order
intranasal CS
H1 blocker or LTRA*

Review the patient
after 2-4 wks
Improved
Step-down
and continue
treatment
for >1 month
Failure
Review diagnosis
Check for asthma
especially in patients with severe
and/or persistent rhinitis
Blockage
add decongestant
or oral CS
(oral or saline)
Rhinorrhea
add ipratropium
Add or increase
intranasal CS
dose
Failure
referral to specialist

Allergen and irritant avoidance may be appropriate

If conjunctivitis
Add
oral H1-blocker
or intraocular H1-blocker
or intraocular cromone
(or saline)

Consider specific immunotherapy

Case # 2

- 42 y/o woman with asthma referred uncontrolled asthma. She has had several exacerbations in the past 6 months including a ICU stay/intubation. Compliant with medications.
- Treated for omalizumab for 6 months 300mg q 2 weeks.

**Testing:**
- **PFTs:** FEV1/FVC 60%, FEV1 63%, positive BDR.
- **CXR:** normal
- **CT chest:** bronchial thickening

**Medications:**
- High dose ICS/LABA
- Rescue SABA
- Montelukast
- Omalizumab
Question # 2

Regarding treatment with bronchial thermoplasty (BT) in this patient, you would recommend which of the following?

A. BT is not recommended because of the severity of her asthma

B. BT can be considered only after omalizumab therapy has been tried for at least 12 months

C. BT is could be considered, but long term safety is not yet known

D. **BT is indicated should be performed in this patient**

E. BT is considered experimental and should be only done in referral centers
Bronchial Thermoplasty (BT)

**Rationale:**
- **Airway remodeling**: smooth muscle hyperplasia/hypertrophy. BT, using radiofrequency energy, can decrease significantly the smooth muscle mass.
Bronchial Thermoplasty
Bronchial Thermoplasty: Efficacy


- Severe asthmatics received either BT or sham
- Excluded pts with > 3 exacerbations in the previous year or > 4 pulses of steroids
- 79% vs. 64% achieved changes in ADLQ scores (0.5 or >)
- 8.4% were hospitalized after BT

* 32% ↓ in severe exacerbation
+ 84% reduction in ER visits
Bronchial Thermoplasty: Safety


- 5 year follow up study from the AIR trail
- Absence of clinical complications
- Stable lung function over 5 years
Bronchial Thermoplasty: Safety


- 5 year follow up study from the AIR2 trail
- Sustainable effect after 5 years
Bronchial Thermoplasty: Safety


- 5 year follow up study from the AIR2 trail
- Sustainable effect after 5 years
Bronchial Thermoplasty

Pros:
- Evidence of reduction of symptoms
- Lasting effects (5 years)

Cons:
- High cost
- Early exacerbation rate despite pre-treatment with oral steroids
- Need for 3 bronchoscopies
Summary

- In severe/refractory asthma the following should be always assessed:
  - Compliance
  - Inhaler technique
  - Comorbidities (GERD, AR, obesity, OSA, smoking)

- BT appears to be effective and safe in patients with uncontrolled asthma despite high dose ICS and has lasting effects