Optimizing Asthma Treatment Through Behavior Modification

Harold S Nelson, MD
Professor of Medicine
National Jewish Health &
University of Colorado School of Medicine
Denver, Colorado, USA
Learning Objectives

• Upon completion of this session the attendee should be aware of:
  - The effect of smoking on asthma
  - An approach to smoking cessation
  - The association of obesity with asthma
  - The effect of weight loss in obese asthmatics

• No conflicts of interest.
Tobacco Smoking
Extent of the Problem

- Globally tobacco smoking is estimated to cause 5 million deaths per year.
- The average smoker dies 13 to 14 years earlier than non-smokers.
- If a smoker quits, all cause mortality approaches that of people who never smoked by 10-15 years of abstinence.

Tobacco smoking is reported to be as common in asthmatics as in the general population.
Tobacco Smoking and Asthma
Extent of the Problem

- Asthmatics who smoke have been shown to have
  - Increased symptoms
  - Increased emergency department visits
  - Impaired response to both inhaled and oral corticosteroids.

Spears M et al Eur Respir J 2009;33:1010-7
Tobacco Smoking Effects on Asthma (Pulmonary Function)

- Copenhagen heart Study: Annual decline in FEV1 in asthmatics:
  No ICS 43.5 mL (smokers 57.9 mL)
  ICS 22.8 mL (smokers 30.8 mL)

- In 4000 U.S. citizens age 18-30 years and followed 10 years: Decline in FEV1 was 8.5% never smokers, 10.1% with diagnosis of asthma, 11.1% in smokers, and 17.8% in asthmatics who smoked.

Lange P et al Thorax 2006;61:100-4
Apostol GC et al AJRCCM 2002;160:166-72
Tobacco Smoking Effects on Asthma (Response to corticosteroids.)

- In the GOAL study the odds ratio for not achieving “well controlled” status on FP or FSC was 2.76 for current smokers compared to never smokers.

Pedersen S et al. JACI 2007;120:1036-42.
Tobacco Smoking Effects on Asthma (Response to corticosteroids.)

- 36 smokers and 59 non-smokers with mild asthma received inhaled beclomethasone either 400 mcg/day or 2000 mcg/day for 12 weeks.
- The change in AM PEF:

<table>
<thead>
<tr>
<th></th>
<th>Non-smoker</th>
<th>Current smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDP 400 mcg/d</td>
<td>+ 19 L/min</td>
<td>- 7 L/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>( p = 0.02 )</td>
</tr>
<tr>
<td>BDP 2000 mcg/d</td>
<td>+ 18 L/min</td>
<td>+ 11 L/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>( p = \text{NS} )</td>
</tr>
</tbody>
</table>

Tomlinson JEM et al. Thorax 2005;60:282-7
Tobacco Smoking Effects on Response to corticosteroids: Can it be improved?

- The anti-inflammatory action of corticosteroids is mediated in part by recruitment of histone deacetylase (a nuclear enzyme involved in switching off activated inflammatory genes).
- Cigarette smoke decreases HAD activity.
- There is some evidence this can be restored by low dose theophylline.

“Relapse is expected and a short-term treatment approach will not meet the needs of most patients seeking treatment.

Successful treatment should take a long-term view of the therapeutic relationship between clinician and patient.”

The treatment should incorporate encouragement, counseling, and pharmacotherapy.”

Tobacco Addiction Therapy Program

1) Assess current tobacco use at every office visit (The new “Vital Sign”)
2) Advise stopping
3) Determine willingness to quit now
4) Establish a plan:
   - Establish a “quit date”
   - Problem solving (examples: removing all tobacco from home and work, planning for high risk situations, development of coping strategies)
5) Prescription of medication
6) Schedule follow-up to provide continued support.

Tobacco Addiction Pharmacotherapy

Available medications:

1) Histamine replacement: Gum, lozenge, nasal spray, inhaled spray, patch. Designed to relieve withdrawal symptoms.

2) Bupropion SR: Blocks the reuptake of dopamine, serotonin and norepinephrine.

3) Varenicline: Partial agonist/antagonist at the a4b2 nicotine receptor. Elicits some dopamine release leading to less craving in smokers and completes with nicotine for receptor binding curbing the pleasure of subsequent nicotine delivery.

4) Nortriptyline: A selective norepinephrine uptake inhibitor.

### Tobacco Addiction Pharmacotherapy

#### Medication Effectiveness (review of 83 controlled studies)

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Abstinence rate 6 months</th>
<th>OR versus Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varenicline</td>
<td>33.2%</td>
<td>3.1</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>26.7%</td>
<td>2.3</td>
</tr>
<tr>
<td>Nicotine gum &gt; 14 weeks</td>
<td>26.1%</td>
<td>2.2</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>24.8%</td>
<td>2.1</td>
</tr>
<tr>
<td>Bupropion SR</td>
<td>24.2%</td>
<td>2.0</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>23.4%</td>
<td>1.9</td>
</tr>
</tbody>
</table>

## Tobacco Addiction Pharmacotherapy

Medication Effectiveness (review of 83 controlled studies)

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Abstinence rate 6 months</th>
<th>OR versus Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline</td>
<td>22.5%</td>
<td>1.8</td>
</tr>
<tr>
<td>Nicotine gum 6-14 weeks</td>
<td>19.0%</td>
<td>1.5</td>
</tr>
<tr>
<td>Patch + gum</td>
<td>36.5%</td>
<td>3.6</td>
</tr>
<tr>
<td>Patch + Bup SR</td>
<td>28.0%</td>
<td>2.5</td>
</tr>
<tr>
<td>Patch + Nortrip</td>
<td>27.3%</td>
<td>2.3</td>
</tr>
<tr>
<td>Patch + Inhaler</td>
<td>25.8%</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Comparative Effectiveness of 5 Smoking Cessation Pharmacotherapies in Primary Care Clinics.

- A “real life” smoking cessation study conducted in 12 primary care clinics in Wisconsin, USA.
- Screening and recruitment by medical staff.
- Participating subjects were referred to a telephone quit line for cessation counseling.

Smith SS Arch Intern Med 2009;169:2148-55
Comparative Effectiveness of 5 Smoking Cessation Pharmacotherapies in Primary Care Clinics.

- 22.5% of the clinic patients were current smokers
- 7,128 eligible smokers were identified and approached.
- 1346 (19%) agreed to participate and were randomized to pharmacotherapy.

Smith SS Arch Intern med 2009;169:2148-55
Comparative Effectiveness of 5 Smoking Cessation Pharmacotherapies in Primary Care Clinics.

6-month abstinence rates were:
- Bupropion SR 16.8%
- Nicotine patch 17.7%
- Nicotine lozenge 19.9%
- Patch + lozenge (prn) 26.9%
- Bupropion + lozenge 29.9%

Smith SS Arch Intern med 2009;169:2148-55
Persistence of Smoking Cessation with Mono- and Combined-Treatment

Smith SS Arch Intern med 2009;169:2148-55
Comparative Effectiveness of 5 Smoking Cessation Pharmacotherapies in Primary Care Clinics.

Conclude: Among the 20% who are willing to try many smokers can be effectively treated by combination of quite line counseling and combination drug therapy.

Smith SS Arch Intern med 2009;169:2148-55
### Association of Obesity and Asthma

The simultaneous epidemics of asthma and obesity in the United States:

<table>
<thead>
<tr>
<th>Year</th>
<th>Asthma</th>
<th>Obesity (adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td></td>
<td>15.0%</td>
</tr>
<tr>
<td>1980</td>
<td>3.1%</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>7.3%</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>No change</td>
<td>32.9%</td>
</tr>
</tbody>
</table>

Litonjua & Gold. JACI 2008;121:1075-8
Overweight, Obesity and Incident Asthma

DA Beuther, LR Sutherland. AJRCCM 2007;175:661-6

- Identified prospective studies evaluating BMI and incident asthma in adults.
- Annualized asthma incidence for:
  - Normal weight, BMI < 25
  - Overweight, BMI 25-29.9
  - Obese, BMI ≥ 30
- 7 studies (n = 333,102) met criteria.
Association of Obesity and Asthma

- Obese asthmatics have poorer asthma control and decreased response to corticosteroids.
  - In 3,095 subjects with physician diagnosed asthma, obese reported more symptoms, missed workdays, greater use of rescue and controller medication.
    \[\text{Thorax 2008;63:14-20.}\]

- In 1113 adults with asthma, obese more likely to reported poor Q of L (2.8), poor asthma control (2.7) and asthma-related hospitalization (4.6)
  \[\text{Schatz M et al JACI 2008;122:507-11}\]
Association of Obesity and Asthma

Possible mechanisms by which obesity might effect asthma:

1) Pro-inflammatory effects of adipose tissue (IL-6 and leptin)
2) Limitation by chest wall and abdominal fat (Decreased FRC)
3) Lack of deep breathing
4) Gastroesophageal reflux
5) Obstructive sleep apnea

Shore SA. JACI 2008;121:1087-93
Airway Inflammation in Obese and Nonobese Patients with Difficult-to-treat Asthma

Van Veen et al Allergy 2008;63:570-4

- 136 nonsmoking asthmatic adults
- Symptomatic despite high dose inhaled corticosteroids and LABAs.
- 32% on oral corticosteroids
- Mean age 44.6 years.
Characteristics of Obese and Nonobese Patients with Difficult-to-treat Asthma

<table>
<thead>
<tr>
<th></th>
<th>Non-obese</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>75.8 %</td>
<td>85.9 % (p = .05)</td>
</tr>
<tr>
<td>FRC/TLC</td>
<td>117.7%</td>
<td>100.3% (p &lt; .01)</td>
</tr>
<tr>
<td>Sp Eosin</td>
<td>2.0 %</td>
<td>0.5% (p = .03)</td>
</tr>
<tr>
<td>eNO</td>
<td>11.1 ppb</td>
<td>7.2 ppb (p = .03)</td>
</tr>
<tr>
<td>GER</td>
<td>44.9 %</td>
<td>65.5% (p = .05)</td>
</tr>
<tr>
<td>OSA</td>
<td>9.3%</td>
<td>24.1% (p = .05)</td>
</tr>
</tbody>
</table>

Van Veen et al Allergy 2008;63:570-4
Effect of Weight Loss on Asthma

- 15 studies were identified assessing the effect of weight loss on asthma (1966 - 2007).
- All studies were small (6-40 subjects) and of variable duration (8 week to 14 years)
- All studies reported improvement in at least one asthma outcome with weight loss.

Effect of Weight Loss on Asthma

- 12 obese asthmatic women had bariatric surgery and 10 were non-operated controls.
- Evaluation after one year revealed:
  - Mean BMI 45.2 to 34.8 versus no change in control
  - ACT score 18.7 to 22.2 versus no change in control
  - FVC increased 8.4% but decreased in control
  - NSD in FeNO in either group.

Effect of Weight Loss on Asthma

- 10 obese asthmatics were maintained for 8 weeks on a regimen of ad lib eating or < 20% their normal caloric intake on alternate days.
- Average weight loss 8.5 Kg
- Mini-AQLQ increased 2.1
- ACQ decreased 1.3
- AM PEF increased 47 L/min
- Oxidative stress and markers of inflammation declined.

Optimizing Asthma Treatment Through Behavior Modification

Cessation of smoking, and reduction in weight in appropriate patients with asthma offer not only better overall health, but also improvement in asthma symptoms and pulmonary function.