Pharmacotherapy of Tobacco Use and Dependence

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Overview

✧ Identify the risks of tobacco use

✧ Describe highlights from the 2008 Clinical Practice Guidelines for Treating Tobacco Use and Dependence

✧ Compare the efficacy and mechanism of action of the tobacco cessation treatments

✧ Identify common barriers/concerns associated with the use of tobacco cessation treatments
Risks of Tobacco Use
Tobacco Use and Dependence

- Tobacco use and cessation needs to be approached as a **CHRONIC** disease not an acute condition.
Prevalence of Cigarette Smoking

✧ Nearly 1 in 5 adults smoke either every day or some days
  ➢ Cigarette smoking has declined by almost 50% since 1965 reflecting public health efforts

✧ Tobacco use leads to > 400,000 PREVENTABLE deaths annually

✧ 50,000 annual deaths attributed to second hand smoke

State-Specific Prevalence of Smoking among Adults, 2004

- California: 14.8%
- Nevada: 23.2%
- Utah: 10.5%
- Texas: 20.6%
- New York: 18.9%
- Illinois: 22.2%
- Kentucky: 27.6%

Smoking in New York

✧ **18.9%** Adult smokers
  ➤ ↓ from 23.2% in 2001

✧ **Annual Deaths:** 25,500

✧ **New Yorkers living with tobacco-related diseases:** 510,000

Cancers
- Acute myeloid leukemia
- Bladder and kidney
- Cervical
- Esophageal
- Gastric
- Laryngeal
- Lung
- Oral cavity and pharyngeal
- Pancreatic

Pulmonary diseases
- Acute (e.g., pneumonia)
- Chronic (e.g., COPD)

Cardiovascular diseases
- Abdominal aortic aneurysm
- Coronary heart disease
- Cerebrovascular disease
- Peripheral arterial disease

Reproductive effects
- Reduced fertility in women
- Poor pregnancy outcomes (e.g., low birth weight, preterm delivery)
- Infant mortality

Other: cataract, osteoporosis, periodontitis, poor surgical outcomes
Quitting: Health Benefits

Circulation improves, walking becomes easier
Lung function increases up to 30%

Excess risk of CHD decreases to half that of a continuing smoker

Lung cancer death rate drops to half that of a continuing smoker
Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decrease

2 weeks to 3 months
1 to 9 months
1 year
5 years
10 years
after 15 years

Lung cilia regain normal function
Ability to clear lungs of mucus increases
Coughing, fatigue, shortness of breath decrease
Risk of stroke is reduced to that of people who have never smoked
Risk of CHD is similar to that of people who have never smoked

Time Since Quit Date
2006 Report of the Surgeon General: Key Conclusions

- **SHS causes premature death and disease in nonsmokers**

- **Children:**
  - Increased risk for sudden infant death syndrome (SIDS), acute respiratory infections, ear problems, and more severe asthma
  - Respiratory symptoms and slowed lung growth

- **Adults:**
  - Immediate adverse effects on cardiovascular system
  - Increased risk for coronary heart disease and lung cancer
Cigarette Smoking Statistics

✧ 70% of smokers want to quit
  ➢ 81% of smokers have tried to quit once
  ➢ 44% try to quit each year
  ➢ On average, smokers will try 9-10 attempts before quitting

✧ 7% of smokers trying to quit are able to remain smoke-free at 1 year

2008 Clinical Practice Guideline Update
2008 Clinical Practice Guideline Update

✧ Target **ALL** patients
  - Brief and intensive interventions work

✧ Tobacco cessation treatments are effective and encouraged unless contraindications or special populations
  - 7 First line agents
  - Combination treatments

✧ Counseling *and* the use of medications are more effective than either intervention alone

✧ Specific considerations when counseling special populations

Special populations

- Pregnant patients
- Light smokers
- Adolescents
- Smokeless tobacco users

Recommendation

- To utilize counseling cessation interventions rather than medications to assist in the quit process

Tobacco Cessation Treatments
Targets of Tobacco Cessation

**Environment/Habit**
- Coping strategies
- Modifying daily routines
- Social interactions

**Psychological**
- Healthy alternatives
  - Stress
  - Weight control
  - Pleasure/relaxation

**Physical Addiction**
- Alleviation of withdrawal symptoms
- Use of Medications
- Additional focus on behavioral changes
Targets of Tobacco Cessation

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Tobacco Cessation Treatments

- Nicotine Replacement Therapies (NRTs)
  - Nicotine Gum
  - Nicotine Patch
  - Nicotine Lozenge
  - Nicotine Nasal spray
  - Nicotine Inhaler

- Bupropion SR (Zyban®)

- Varenicline (Chantix®)
Tobacco Cessation Treatments

- **Nicotine Replacement Therapies (NRTs)**
  - Nicotine Gum
  - Nicotine Patch
  - Nicotine Lozenge
  - Nicotine Nasal spray
  - Nicotine Inhaler

- **Bupropion SR**
  - (Zyban®)

- **Varenicline**
  - (Chantix®)
Nicotine Replacement Therapies: Mechanism of Action

- Reduces withdrawal symptoms
- Allows patient to focus on the behavioral and psychological aspects of tobacco use

Source: www.rxforchange.ucsf.edu
# Nicotine Replacement Therapies: Efficacy

<table>
<thead>
<tr>
<th>Nicotine Replacement Therapies</th>
<th>Estimated Abstinence Rate at 6 months vs. Placebo</th>
<th>Estimated Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patch</td>
<td>23.4%</td>
<td>1.9 (1.7- 2.2)</td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>19%</td>
<td>1.5 (1.2- 1.7)</td>
</tr>
<tr>
<td>Nicotine lozenge</td>
<td>23.6- 24.2%</td>
<td>2.0 (1.4- 2.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 (1.9- 4.0)</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>24.8%</td>
<td>2.1 (1.5- 2.9)</td>
</tr>
<tr>
<td>Nicotine spray</td>
<td>26.7%</td>
<td>2.3 (1.7- 3.0)</td>
</tr>
</tbody>
</table>

Tobacco Cessation Treatments

- Nicotine Replacement Therapies (NRTs)
  - Nicotine Gum
  - Nicotine Patch
  - Nicotine Lozenge
  - Nicotine Nasal spray
  - Nicotine Inhaler

- Bupropion SR (Zyban®)

- Varenicline (Chantix®)
Bupropion: Mechanism of Action

- **Atypical antidepressant**
  - Dopamine
  - Norepinephrine

- **Clinical effects**
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal

Available online from URL: http://us.gsk.com/products/assets/us_zyban.pdf Accessed 2008 June 1;
www.rxforchange.ucsf.edu
## Bupropion: Efficacy

<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Estimated Abstinence Rate at 6 months vs. Placebo</th>
<th>Estimated Odds Ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>24.2%</td>
<td>2.0 (1.8-2.2)</td>
</tr>
</tbody>
</table>

Tobacco Cessation Treatments

✧ Nicotine Replacement Therapies (NRTs)
  ➢ Nicotine Gum
  ➢ Nicotine Patch
  ➢ Nicotine Lozenge
  ➢ Nicotine Nasal spray
  ➢ Nicotine Inhaler

✧ Bupropion SR (Zyban®)

✧ Varenicline (Chantix®)
Varenicline: Mechanism of Action

✦ Nicotinic receptor partial agonist
  - Stimulates low-level agonist activity
  - Competitively inhibits binding of nicotine

✦ Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal

## Varenicline: Efficacy

<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Estimated Abstinence Rate at 6 months vs. Placebo</th>
<th>Estimated Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varenicline</td>
<td>33.2%</td>
<td>3.1 (2.5 - 3.8)</td>
</tr>
</tbody>
</table>

## Varenicline: Efficacy (cont.)

### Table 1. Randomized, Controlled, Safety and Efficacy Studies of Varenicline

<table>
<thead>
<tr>
<th>Varenicline Dosage and Duration</th>
<th>Method to Confirm or Record Abstinence Rate</th>
<th>Abstinence Rates (%) for Weeks 9-52</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mg b.i.d. x 12 wks</td>
<td>Carbon monoxide</td>
<td>Varenicline: 21.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 16.1 (p=0.057)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo: 8.4 (p&lt;0.001)</td>
</tr>
<tr>
<td>1.0 mg b.i.d. x 12 wks</td>
<td>Carbon monoxide</td>
<td>Varenicline: 23.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 14.6 (p=0.004)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo: 10.3 (p&lt;0.001)</td>
</tr>
<tr>
<td>0.3 mg q.d. x 6 wks</td>
<td>Patient diary</td>
<td>Varenicline: 28.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 17.1 (p=0.03)</td>
</tr>
<tr>
<td>1.0 mg q.d. x 6 wks</td>
<td></td>
<td>Placebo: 17.1 (p&lt;0.001)</td>
</tr>
<tr>
<td>1.0 mg b.i.d. x 6 wks</td>
<td></td>
<td>Varenicline: 37.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 17.1 (p&lt;0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo: 17.1 (p&lt;0.001)</td>
</tr>
<tr>
<td>0.5 mg b.i.d. x 12 wks</td>
<td>Carbon monoxide</td>
<td>Varenicline: 18.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 3.9 (p&lt;0.001)</td>
</tr>
<tr>
<td>1.0 mg b.i.d. x 12 wks</td>
<td></td>
<td>Placebo: 3.9 (p&lt;0.001)</td>
</tr>
<tr>
<td>1.0 mg b.i.d. x 24 wks</td>
<td>Carbon monoxide</td>
<td>Varenicline: 43.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bupropion SR: 36.9 (p=0.02)</td>
</tr>
</tbody>
</table>

Common Barriers/Concerns
Common Barriers/Concerns

- Use of combination treatments
- Long term use of tobacco treatments
- Smoking cessation and other medications
- Varenicline - Recent labeling changes
- Use of NRTs as “pre-treatment” prior to the quit date
Use of Combination Treatments
## Use of Combination Treatments

<table>
<thead>
<tr>
<th>Pharmacotherapy Combinations</th>
<th>Estimated Abstinence Rate at 6 months vs. Placebo</th>
<th>Estimated Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patch + gum or nasal spray</td>
<td>36.5%</td>
<td>3.6 (2.5- 5.2)</td>
</tr>
<tr>
<td>Nicotine patch + Bupropion</td>
<td>28.9%</td>
<td>2.5 (1.9- 3.4)</td>
</tr>
<tr>
<td>Nicotine patch + Inhaler</td>
<td>25.8%</td>
<td>2.2 (1.3- 3.6)</td>
</tr>
</tbody>
</table>

Long Term Use of Tobacco Treatments
Long-Term ($\geq 6$ month) Quit Rates for Cessation Medications

Source: www.rxforchange.ucsf.edu; Silagy et al. (2004). Cochrane Database Syst Rev
Smoking Cessation and Medication Levels
Smoking Cessation and Medication Levels

* Smoking is an inducer of CYP450 1A2 that can affect medication levels for drugs metabolized by CYP 1A2
  - Clozapine
  - Olanzapine
  - Chlorpromazine
  - Haloperidol

* No effect on medications not metabolized by 1A2
  - Risperidone
  - Aripiprazole
  - Ziprasidone
  - Quetiapine

Varenicline Labeling Changes
Varenicline Labeling Changes

 предпочг Update to Varenicline
  Monitor patients for behavior or mood changes
  Use caution when driving or operating machinery

 предпочг Recent news

Use of NRTs Prior to Quitting
Use of NRTs Prior to Quitting

- Schuurmans et. al.
  - Primary outcome
  - Results

- Rose et. al.
  - Primary outcome
  - Results

- 2008 Clinical Guideline Recommendation

Summary

✧ Tobacco use and cessation needs to be approached as a chronic disease

✧ Targets of Cessation
  ➢ Physical dependence
  ➢ Habit
  ➢ Psychological dependence

✧ Seven first line options available

✧ Highlighted key barriers/concerns with tobacco cessation treatments
Resources

✧ New York State Quit Line
  - 1-866-NY-QUITS (1-866-697-8487) (English & Spanish)
  - http://www.nysmokefree.com/

✧ Department of Health and Human Services
  - http://www.surgeongeneral.gov/tobacco/

✧ National Cancer Institute
  - http://www.smokefree.gov/hp-hcsit.html
Questions?