Nicotine Addiction and Pharmacological Aids for Tobacco Treatment

Linda A. Thomas, MS
Tobacco Consultation Service
University of Michigan Health System
Webinar Objectives

- Describe nicotine addiction
- Identify PHS identified first-line pharmacological aids available for tobacco treatment including dosing guidelines and the pros and cons of each
- Describe strategies of combination pharmacological therapies
What is Nicotine?

- The most common cause of drug addiction in the world
- Naturally occurring in the tobacco plant
- A colorless alkaloid that turns brown when burned
- Nicotine is absorbed through the mucosa, skin, and lungs

National Institute on Drug Abuse Research Report, 1998
Nicotine

- In pure state - clear, oily toxin
- Binds in brain and muscles
- Nicotine poisoning symptoms:
  - Nausea, salivation, abdominal pain, vomiting, sweating, dizziness, mental confusion, rapid heart beat
  - Convulsions, respiratory failure due to paralysis of respiratory muscles
Absorption is pH dependent

- In acidic media
  - Ionized $\Rightarrow$ poorly absorbed across membranes
- In alkaline media
  - Nonionized $\Rightarrow$ well absorbed across membranes

At physiologic pH (7.3–7.5), nicotine is readily absorbed.

Beverages can alter pH, affect absorption.
Nicotine Absorption

- Nicotine is “distilled” from burning tobacco and carried in tar droplets.
- Nicotine is rapidly absorbed across respiratory epithelium.
  - pH of the lung is 7.4
  - Surface area of alveoli is large
  - Capillary system in lung is extensive.
Nicotine Metabolism

- Metabolized in liver to cotinine
- Nicotine half-life is 2 hours, cotinine is 20 hours
- Toxic levels 40-60mg
- Some individuals have more rapid metabolisms, leading to more cigarettes smoked per day and potentially earlier addiction as a teenager
- For example: males > females
  Caucasian > African American

Effects of Selected Neurotransmitters & Hormones

NICOTINE

- Dopamine ⇒ Pleasure, Appetite Suppressor
- Norepinephrine ⇒ Arousal, Stimulation
- Acetylcholine ⇒ Memory, Cognitive Enhancement
- Vasopressin ⇒ Blood Pressure
- Serotonin ⇒ Mood Modulation, Appetite Suppressor
- GABA ⇒ Reduction of Anxiety & Tension, relaxation

Nicotine stimulates dopamine release.

Pleasurable feelings

Repeat administration

Tolerance develops

Nicotine addiction is *not* just a bad habit.

Discontinuation leads to withdrawal symptoms.
Nicotine enters the brain and stimulates nicotine receptors, leading to dopamine release. This process is part of the dopamine reward pathway. Key areas involved include the prefrontal cortex, nucleus accumbens, and ventral tegmental area.
Negative Effects

- Increases both blood level of glucose and insulin production
- Enhances platelet aggregation which can lead to thrombotic events
- Increased risk for cancer of various body organs
- Increases bowel tone and activity, saliva and bronchial secretions, heart rate, blood pressure, and may also increase sweating, nausea, and bouts of diarrhea
- Decreased blood flow especially to extremities and skin
Nicotine Withdraw

- Withdraw begins within 2 hours after the last cigarette peaks at 48-72 hours
- Symptoms of withdraw:
  - Cravings
  - Anxiety
  - Restlessness
  - Irritability
  - Depressed mood
  - Difficulty concentrating
  - Increased appetite
  - Stomach cramps
  - Coughing
  - Constipation
  - Mouth sores
Summary

- Tobacco products are effective delivery systems for the drug nicotine.
- Nicotine is a highly addictive drug that induces a constellation of pharmacologic effects.
- Nicotine activates the dopamine reward pathway in the brain, which reinforces continued tobacco use.
- Tobacco users who are dependent on nicotine self-regulate tobacco intake to maintain pleasurable effects and prevent withdrawal.
Mini Quiz

1. True or False – Drinking water prior to using a piece of nicotine gum will not effect nicotine absorption?

2. True or False – Exposure to nicotine increase blood sugar level but decreases insulin levels?
Mini Quiz Answers

1. False – Any introduction of something into the mouth starts the digestive process which creates an acidic environment.

2. False – Nicotine increases both blood sugar and insulin production.
Nicotine in Tobacco Products

1 cigarette = 1-2 mg (12 – 14 mg)

1 can spit tobacco = approx. 60 - 80 mg
1 average size dip = approx. 3 - 5 mg

1.5 ounce stogie = 12 - 24 mg the same as a one pack cigarettes
Some up to 50 mg for one cigar
NRT: Rationale for Use

- Reduces physical withdrawal from nicotine
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

IMPROVES SUCCESS RATES
Best Treatment Practices in Nicotine Addiction

- Use of nicotine replacement therapy and/or bupropion
- Cognitive-behavioral intervention
- High level of motivation
- Implementation of exercise program
Clinical Practice Guidelines: 2000

Treating Tobacco Use and Dependence

- **First-line Medications**
  - Bupropion SR
  - Varenicline
  - Nicotine Replacement

- **Second-line Medications**
  - Clonidine
  - Nortriptyline

  - Nicotine Gum
  - Nicotine Lozenge
  - Nicotine Inhaler
  - Nicotine Nasal Spray
  - Nicotine Patch
Typical Smoking Pattern

Nicotine level before bedtime

1-1.5 hours

First 2 hours
<table>
<thead>
<tr>
<th>NRT: Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Any one who smokes &gt; 10 cigarettes a day</td>
</tr>
<tr>
<td>• Anyone who reports withdrawal symptoms during a previous quit attempt</td>
</tr>
<tr>
<td>• Each quit attempt is different; if NRT didn’t help before, it’s OK to try it again; motivation may have shifted</td>
</tr>
<tr>
<td>• All NRTs are better than placebo</td>
</tr>
</tbody>
</table>
Effects of NRT

- Reduces withdrawal symptoms and craving
- Allows patient time to relearn life w/o tobacco
- May provide positive effects of nicotine – desirable mood, improved attention
- Replaces oral/handling aspects of habit
- Can keep patient away from smoking due to fear of smoking and using NRT
NRT: Contraindications

- Post MI
- Uncontrolled arrhythmias
- Severe or worsening angina
- Accelerated or severe hypertension
- Severe PV
- Poorly controlled insulin dependent Diabetes
- Active peptic ulcer
- Renal Insufficiency
NRT: Contraindications

- Hepatic insufficiency
- Uncontrolled Hyperthyroidism
- Pregnancy - Few studies have addressed the safety of NRT, varenicline or bupropion in pregnancy
- Children and adolescents
NRT: PRECAUTIONS

- Patients with underlying cardiovascular disease
  - Recent myocardial infarction
  - Life-threatening arrhythmias
  - Severe or worsening angina

- Patients with other underlying conditions
  - Active temporomandibular joint disease (gum only)
  - Lactation
  - Peptic Ulcer Disease
Fant et al., 1999; Schneider et al., 2001; Choi et al., 2003).
Nicotine Gum/Lozenge

- Nicotine absorbed in mucosa
- 2mg and 4mg doses
  - Insert recommendations < 24 cigarettes 2mg; >24 cigarettes 4mg
- Each piece is good for 20-30 minutes
- Chew gum until “peppery” taste; “park” between gum and cheek until peppery taste is gone, repeat process
Nicotine Gum/Lozenge

Pros:

- Easily imitate individual’s nicotine loading pattern
- Nicotine reaches brain 5-10 minutes
- Can be prescribed on regular schedule and/or PRN use
- Flexibility of use
Nicotine Gum/Lozenge

Cons:

- Not user friendly; must follow instructions
- For gum - Difficult with dental work & gum chewers
- For Lozenge – Chalky build-up in patients with dry mouth
- Makes saliva; GI problems
- Restrictions with eating and drinking
- OTC, expensive
- Difficulties getting off the gum/lozenge
Nicotine Patch

- Six dosages: 21mg, 14mg, 7mg
- Both OTC
- 24 hour doses
- Place on non-hairy area above the waist
- Passive dosing
- Can be used while swimming or showering
Nicotine Patch Delivery

Application

2 hours

8 - 10 hours

8 - 10 hours
Typical Smoking Pattern

Nicotine level before bedtime

First 2 hours

1 - 1.5 hours
Nicotine Patch

Pros:

• User friendly, just stick and go
• Once a day dosage & different dosages

Cons:

• Steady state dosing
• Passive aid
• \(\approx 2\) hrs to reach therapeutic level
• Skin reactions
• Sleep disturbance if worn at night
• Can cause “dull” pain if applied on “boney” area
Nicotine Spray

- Nicotine absorbed through nasal mucosa
- 1 spray to each nostril after exhale - SHOULD NOT BE INHALED
- Each bottle contains 100 doses (200 sprays)
- Recommend to not be used more than 5 times an hour or 40 times in 24 hours
Nicotine Spray

Pros:
- Fastest absorption (< 5 minutes)
- Rx
- Flexibility

Cons:
- First week difficult; burning eyes, throat, nasal discharge, sneezing
- Poor compliance or problems getting off
- Expensive without insurance
Nicotine Inhaler

- Absorbed in mucosa
- Mouthpiece with 10mg cartridge
- User “sucks” on mouthpiece to deliver nicotine – use like a straw
- Each cartridge good for 80 puffs or 20 minutes
- Minimum use 6 cartridges, maximum 16 cartridges per day
Nicotine Inhaler

Pros:
- Flexible dosing
- Hand to mouth behavior
- Relative quick delivery, 5-10 minutes

Cons:
- Frequent use to achieve adequate dosing
- Throat irritation
- Prescription medication, expensive; not always covered by insurance plans
Bupropion: Mechanism of Action

- Atypical antidepressant thought to affect levels of various brain neurotransmitters
  - Dopamine
  - Norepinephrine

- Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal
bupropion hydrochloride

- Similar effects on brain as nicotine (60% people)
- Rx
- Begin 7-10 days before quit date
- 3-6 days 150mg; 150mg bid
- Contraindications: Seizure disorder, active eating disorder, recent MI, unstable angina, MAOs, abrupt cessation of alcohol or sedatives
bupropion hydrochloride

Pros:

• Easy to use
• Can be used in combination with NRT
• Effective with large number of people
• Covered by most insurance plans
• Cheap without insurance as generic

Cons:

• Most common side effects: Sleep disorder, dry mouth, sense of discomfort
Combination Nicotine Therapy

- Use of a “passive” and “ad libitum” NRT product
  - Increases long-term abstinence rates than did use of only one NRT
  - More studies are being completed on combination therapy
Varenicline

- Oral tablet delivery
- Non-nicotine tobacco cessation aid
- Partial agonist/antagonist
  - Increases the brain’s response to nicotine
  - Blocks the brain’s natural response to nicotine
- Release of dopamine but blocks response to nicotine
  - Lower dose but longer lasting
Varenicline

- Prescription required
- Monotherapy
- Begin treatment 7-10 days before quit date
- Dosing: 0.5 mg daily for three days, then 0.5 mg BID for four days, then 1 mg BID
Varenicline

Pros:

- Easy to use
- Alternative to bupropion and NRT
- Non-nicotine medication – surgery, MI patients, plastics
- Initial research looks promising
- Covered by most insurance plans

Cons:

- Most common side effects: Nausea, insomnia, and unusual dreams
- Expensive without insurance ($355/3 months)
Varenicline

- FDA Boxed Warning –
  All patients being treated with Chantix should be observed for neuropsychiatric symptoms including changes in behavior, hostility, agitation, depressed mood and suicide-related events including ideation, behavior, attempted suicide.
Summary

- Consider pharmacological interventions for all smokers making quit attempts
- Gather history
- Get involved in the process of choosing meds
- Nicotine patch is the recommended first aid – bupropion next
- Use guidelines for dose and tapering
- Consider combination therapy for those who have failed NRT/bupropion alone
- Counseling and pharmacotherapy have additive effects
Questions

Linda Thomas, MS, CTTS-M
Tobacco Consultation Service
University of Michigan Health System
734-998-6222
lathomas@umich.edu
quitsmoking@med.umich.edu
Training Evaluation

http://www.zoomerang.com/Survey/?p=WEB229KBRC3GJ2