Quittin’ Time: Trends in Treating Nicotine Dependence

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MPA CONTINUING EDUCATION SYMPOSIUM
AUGUST 23, 2016

Learning Objectives

• Describe the safety and efficacy of combining first line medications for tobacco cessation
• Discuss the role of precessation nicotine replacement therapy
• Review the current evidence regarding the black box warning for varenicline
• Recommend a duration of treatment for a patient who is quitting smoking

Tobacco Use in the U.S.

U.S. Adult Smoking Rate by Percent

Healthy People 2020 Goal

2016 2020 2021

0 2 4 6 8 10 12 14 16 18 20
Trends in Youth Tobacco Use

- FDA rule to regulate e-cigarettes as tobacco products beginning August 2016
- FDA regulation bans sale to kids
- Flavors still allowed
  - Unlike cigarettes, both cigars and electronic cigarettes are allowed to have flavors under current regulation

Percent of High School Students Using E-Cigarette in Last 30 Days

- 2011: 1.5%
- 2012: 16%
- 2013: 13.4%
- 2014: 4.5%
- 2015: 2.8%

967% Increase

Campaign for Tobacco-Free Kids, CDC/FDA National Youth Tobacco Survey
Let’s Meet Our Patient…

- Mitch is a 56 year old man with hypertension and a history of depression that is currently treated with fluoxetine. He smokes 15 to 20 cigarettes per day. When asked about his interest in quitting smoking he says, “I know I should, but I’ve tried everything. Nothing works.”
- He used a nicotine patch for 5 days but stopped it because he still wanted a cigarette. While taking bupropion for a month he reduced to 5 cigarettes daily but never achieved abstinence. He has heard that varenicline might be dangerous.
- He asks you what you think about him using an electronic cigarette.

Let’s Meet Our Patient

- Which of the following would be the most appropriate intervention for Mitch to help him quit smoking?
  
  A. Nicotine 21 mg patch and bupropion SR
  B. Nicotine 21 mg patch started 2 weeks prior to quit date
  C. Varenicline starter pack
  D. Electronic cigarette

Medications for Nicotine Dependence

**Nicotine Replacement Therapy (NRT)**
- Nicotine patch
- Nicotine gum
- Nicotine lozenge
- Nicotine nasal spray
- Nicotine inhaler

**Non-Nicot ine Therapy**
- Bupropion SR
- Varenicline

Electronic cigarettes?
Combination Therapy

Which medications for tobacco cessation can be combined?

- Nicotine patch plus "ad libitum" short-acting NRT
  - Nicotine gum
  - Nicotine lozenge (not studied, but can be used)
  - Nicotine inhaler
  - Nicotine nasal spray
Combination Therapy

- Combining bupropion and varenicline
  - Evidence supports combination is safe and effective
    - Prospective studies demonstrated increased odds of quitting in combination group versus varenicline alone
    - Retrospective study showed higher abstinence rate with combination at 52 weeks versus varenicline alone (55% vs 32.1%, p < 0.001)
    - Possibly more effective in males and patients with higher baseline nicotine dependence


Combination Therapy

- Combining NRT with varenicline
  - Hypothesized that varenicline may not saturate all nicotinic receptors in the brain in heavier smokers
  - Studies to date combined nicotine patch with varenicline
    - 2 studies started patch on target quit date, 1 had patients start patch 2 weeks prior to target quit date
    - Varenicline started 1 week before target quit date in all studies


Combination Therapy

- Combination nicotine patch and varenicline

<table>
<thead>
<tr>
<th>ODDS RATIO</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Early outcome (1-12 week CA)</td>
<td>1.5 (1.14, 1.97)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Late outcome (2-24 week CA)</td>
<td>1.62 (1.38, 2.23)</td>
<td>-</td>
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CA = continuous abstinence

Precessation Treatment

- Smokers **willing** to make a quit attempt
  - Nicotine patch initiated 2 weeks prior to target quit date
  - Studies have demonstrated higher quit rates in pre-quit group compared to standard treatment
  - Guidelines do not recommend strategy routinely due to lack of sufficient evidence

Precessation Treatment

- Smokers **unwilling** to quit completely
  - Meta-analysis demonstrated use of precessation NRT more than doubled likelihood of abstinence at 12 months
  - Unclear if results are relevant to broader population of smokers unwilling to quit
  - Reduce to quit versus completely uninterested

Precessation Treatment

- Recommend patients be counseled on symptoms of nicotine overdose (nausea, dizziness) if precessation treatment utilized
  - **Caution** with routinely asking patients about cutting back on smoking versus complete cessation as this may suggest reduction offers health benefits
Varenicline Black Box Warning

Black Box Warning

- Depression
- Mood disturbances
- Hostility

Nicotine Withdrawal

- Depressed mood
- Anxiety
- Irritability

Varenicline Black Box Warning

- Effect of varenicline versus placebo on neuropsychiatric adverse events in patients with and without a history of psychiatric illness
- Retrospective analysis of 17 placebo controlled randomized controlled trials

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds Ratio (95% CI)</th>
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<tr>
<td>Suicidal thoughts and behavior</td>
<td>0.57 (0.23, 1.38)</td>
</tr>
<tr>
<td>Depression</td>
<td>1.01 (0.68, 1.52)</td>
</tr>
<tr>
<td>Aggression/agitation</td>
<td>1.27 (0.85, 1.92)</td>
</tr>
<tr>
<td>Nausea (positive control)</td>
<td>3.69 (3.03, 4.38)</td>
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Varenicline Black Box Warning

- Prospective, randomized, double-blind, active and placebo controlled, multi-center study
- Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES)
- Drug companies (Pfizer, Glaxo) commissioned by FDA to complete study
- Compared varenicline, bupropion, nicotine patch, and placebo
- Primary outcome
  - Composite of 16 neuropsychiatric symptoms

Varenicline Black Box Warning

- Anxiety
- Suicidal ideation
- Schizophrenia
- Paranoia
- Panic
- Mania
- Homicidal ideation
- Agitation
- Delusions
- Psychosis
- Feeling abnormal

Varenicline Black Box Warning

- Percent Composite Neuropsychiatric Endpoint

Varenicline Black Box Warning

- Next steps?
- Should warning also be removed from bupropion labeling?
Update on Electronic Cigarettes for Cessation

- United Kingdom Royal College of Physicians recently published “Nicotine without smoke: Tobacco harm reduction”

“...in the interests of public health, it is important to promote the use of e-cigarettes, NRT, and other non-tobacco nicotine products as widely as possible as a substitute for smoking in the UK.”


Update on Electronic Cigarettes for Cessation

- Lingerling concerns in the U.S.
  - Youth initiation
  - Product regulation

Let’s Check Back with Our Patient

- After a discussion with Mitch, he decided to use varenicline alone for his quit attempt. Initially he had a few slips, but has now been quit for the last 4 weeks.
- When he comes to pick up a refill of his medication at the pharmacy, he asks you how long he is going to need to be on the varenicline?
- How would you respond?
Duration of Treatment

- Nicotine dependence as a chronic disease
- Nicotine addiction represents one of the most challenging addictions to break
  - Average number of quit attempts to quit successfully = 30 (range 6-142)
- Premature discontinuation of tobacco cessation medications often results in relapse

References

References


Self-Assessment Questions

- Which of the following combinations have demonstrated safety and efficacy in treating tobacco dependence?
  - A. Nicotine patch and nicotine gum
  - B. Nicotine patch and bupropion
  - C. Varenicline and nicotine patch
  - D. All of the above

- Which of the following is TRUE regarding pre-cessation use of nicotine replacement?
  - A. The goal must still be complete cessation
  - B. It is associated with an increased risk of heart attacks
  - C. This approach works best in patients who are unwilling to quit
  - D. Patients must be completely abstinent from smoking before they can use nicotine replacement therapy
Self-Assessment Questions

According to recent evidence, varenicline has been associated with an increased risk of which of the following compared to placebo?

A. Nausea
B. Aggression
C. Suicidal thoughts
D. Depression

Self-Assessment Questions

Mr. Green is a 44 year-old male who has smoked 1 pack of cigarettes per day for the last 30 years. He has a history of multiple quit attempts and has tried the nicotine patch and nicotine gum on separate occasions. His longest quit attempt in the past lasted for 7 days. He is interested in quitting smoking again and was prescribed varenicline. When he stops to pick the medication up from the pharmacy he asks how long he will need to take varenicline. Which one of the following represents an appropriate duration of treatment for this patient?

A. 4 weeks
B. 8 weeks
C. 12 weeks
D. As long as it takes!