Pharmacotherapy in tobacco addiction

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Smoking kills



Source: How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General.

Why do people still smoke?

Nicotine is addictive

- Euphoria
- Increased alertness, concentration and memory
- Reduced anxiety
- Habitual addiction
- Smoking is "socially acceptable"
 - Friend groups
 - Socialization through smoking
 - Hookah cafés...

Effective interventions for smoking cessation

Intervention	Effectiveness
Increasing the financial cost through taxes and illicit supply prevention	~1% – 2% prevalence reduction for 10% price increase
Anti-tobacco marketing campaigns	Varies
Brief physician advice to smokers	~1% – 3% increase in cessation rate
Pharmacotherapy	~5% – 15% increase in quitting success
Behavioral support	~3% – 10% increase in quitting success
Printed self-help materials	~1% – 2% increase in quitting success
Peer-led school-based anti-smoking programs and social competence training	Varies

How does pharmacotherapy help?

Increased success rate

•Reduced relapse rate

•Can be used in adjunct to other interventions

How does pharmacotherapy work?

1. Easing withdrawal symptoms of nicotine

2. Blocking the effects of nicotine

Pharmacotherapies available for smoking cessation

1. Nicotinic agonists

- I. Nicotine
- 2. Nicotine partial agonists
 - I. Cytisine (cytisinicline)
 - II. Varenicline
- 3. Nicotine antagonists
 - I. Bupropion

4. Non-nicotinic drugs

- I. Clonidine
- II. Antidepressants III.Glucose
- 5. Future developments
 - I. Vaccine
 - II. Drugs in development

Nicotine replacement therapy

- <u>Replacement</u> of nicotine without the other harmful substances
- Dosing can differ from person to person based on their needs and level of addiction
- Different forms are available







Cytisine

- a.k.a. cytisinicline
- No prescription required
- Nicotine receptor partial agonist
- Can activate the nAChRs in the mesolimbic reward pathways at low doses
- Inhibits the sensory stimulation of nicotine and decreases withdrawal symptoms
- Most common side effects include nausea, changes in dreaming, constipation, flatulence and vomiting



Varenicline

- Prescription drug
- Nicotine receptor partial agonist
- Cytisine derivative with (possibly) higher efficacy and (possibly) fewer side effects
- Can activate the nAChRs in the mesolimbic reward pathways at low doses
- Inhibits the sensory stimulation of nicotine and decreases withdrawal symptoms
- Most common side effects include nausea, changes in dreaming, constipation, flatulence and vomiting



Bupropion

- Prescription drug
- Nicotine receptor antagonist
- Atypical antidepressant with dopaminergic and adrenergic actions
- Also antagonizes a central nicotinic receptor and blocks the reinforcing effects of nicotine
- Helps prevent weight gain due to smoking cessation
- Most common side effects include insomnia, headache and dry mouth



Clonidine

- α_2 adrenergic agonist
 - Indications include hypertension, chronic pain syndromes, substance abuse withdrawal and other neuropsychiatric conditions
- Suppresses the acute symptoms of nicotine withdrawal
 - Tension, irritability, anxiety, cravings and restlessness

Antidepressants

- Tricyclics, SSRIs and MAO inhibitors
- Show some improvements in cessation rate and reduction in relapse
- Results inconclusive, not recommended for this indication

Glucose

- Nicotine's hunger relieving effect may cause tobacco cravings when hungry
- Chewing glucose tablets can reduce the desire to smoke during abstinence
- Low cost, virtually no caveats
- No definitive study

The future of pharmacotherapy in tobacco addiction

Nicotine vaccine

- Stimulation of the immune system to produce nicotine specific antibodies
 - Prevents nicotine from crossing the blood-brain barrier
- •To date, five nicotine vaccines have been tested in clinical trials
 - None of them caused a reduction in tobacco use due to various shortcomings
- Further research and clinical trials are required

Rimonabant

- Inverse agonist of cannabinoid receptor 1
- Can modulate systems in the brain that are altered by nicotine
- Clinical trials show success regarding smoking cessation
- Causes significantly increased rate of psychiatric adverse effects

Reboxetine

- Noradrenaline transporter inhibitor and noncompetitive nAChR antagonist
- Animal studies show promising results





• Naltrexone

- Opioid receptor antagonist
- Nicotine reinforcement may be through endogenous opiate system
- Preliminary studies show reduction of relapse and the desire to smoke
- Associated with significant side effects, especially sedation
- Vigabatrin
 - Anti-epilepsy drug
 - Causes dopamine increase in reward centers and can stop the craving for nicoti in animal experiments





What about e-cigarettes?

Tobacco harm reduction

What is tobacco harm reduction?

- Minimizing harms and decreasing total mortality and morbidity, without completely eliminating tobacco and nicotine use
- Also a movement for social justice built on a belief in, and respect for, the rights of people who smoke
- Also helps reduce the environmental tobacco smoke exposure in non-smokers
- Does not take precedent over measures that aim abstinence or never using tobacco
- Tobacco abstinence or never using tobacco is the ideal outcome



Electronic cigarettes

Effects of vaping, compared to smoking

- Less weight gain after smoking cessation
- Increased exercise tolerance
- Reduced mortality

Mouth and airways -

- Reduced spitting
- Reduced sore throat
- Reduced cough

Lungs-

 Reduced shortness of breath

- Nicotine electronic cigarettes provide non-combustion inhalation through vaporization by heating
- Acts like nicotine replacement therapy
- Fewer harmful chemicals compared to tobacco combustion
- Simulates smoking, useful for harm reduction especially in habitual addiction
- A recent meta-analysis shows that nicotine e-cigarettes have a higher smoking quit rate compared to nicotine replacement therapy, non-nicotine e-cigarette or behavioral support / no support*

* Hartmann-Boyce J, et al., Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev. 2022

Source: Wikimedia Commons

Why do most people fail to quit smoking?

- The use of cigarettes and other tobacco products as a coping mechanism in life should not be underestimated
- Most people find it difficult to give up their addiction to smoking in their current predicament in life
- Nicotine is a highly addictive compound that has strong withdrawal symptoms that most smokers would rather avoid
- Smoking cessation causes other unwanted effects like weight gain
- Most smokers started smoking very early in life and don't comprehend a life without it

Best method is pharmacotherapy + willpower



Thank you for listening

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