Update on Medications for Tobacco Cessation

Marc Fishman MD
Johns Hopkins University Dept of Psychiatry
Maryland Treatment Centers
Baltimore MD

MDQuit
Best Practices Conference
Jan 2013
Nicotine Addiction – the bad news

• “Smoking is the leading preventable cause of disease and death in the US”

Report of Surgeon General on the Health Effects of Smoking, 2004

• 23% of the US population, 58M people

• 440,000 premature deaths per year

• Avg 10 yr decrease life span

• 50% will die of smoking related illness
Nicotine Addiction – the good news (quitting)

• Substantial recovery of pulmonary symptoms and infections after 9 months
• Risk of MI decreased 50% after 1 yr
• 2 years after MI, mortality decreased 36%
• Risk of most cancers decreased 50% after 5 yrs
• Risk of lung CA decreased 50% after 10 yrs
• Almost all disease risk back to background after 15 yrs
Nicotine Addiction – the bad news (quitting)

• <6% quit attempts successful
• 50% quit attempts fail in the 1st week
• Only 1/3 quit attempters have ever sought assistance
Conceptual Issues

• Should medications be used in the treatment of addiction?
  – Is this a philosophical question?
  – Is this a scientific question?
  – Is this a practical question?
Rationale for medication

- Reduce craving
- Impact the physiology of dependence
- Protect against lapses, which should be expected
- Reduce high rates of relapse
- Improve treatment retention
- Improve outcomes of current psychosocial treatments
Anti-addiction medications - potential effects

- Block the effects of action
- Reduce reward
- Prevent withdrawal
- Act as non-impairing substitute
- Enhance negative consequences
- Prevent relapse after abstinence
Reward Circuits

Drugs of Abuse Engage Systems in the Motivation Pathways of the Brain
Vocabulary

- Agonist - drug that activates a receptor
- Antagonist - drug that blocks a receptor
- Partial agonist/antagonist - drug that does some of both
Drugs of Abuse Cause a Release of Dopamine

SOURCE: Di Chiara et al
Drugs of Abuse Cause a Release of Dopamine

**AMPHETAMINE**
- **Accumbens**
- DA, DOPAC, HVA

**COCAIN**E
- **Accumbens**
- DA, DOPAC, HVA

**NICOTINE**
- **Accumbens**
- **Caudate**

**MORPHINE**
- **Dose (mg/kg)**
  - 0.5
  - 1.0
  - 2.5
  - 10

SOURCE: Di Chiara, and Imperato
Vocabulary

• Craving - subjective sense of hunger for substance
• Triggers – salience of environmental cues, associated with behaviors (conscious or unconscious)
• Reinforcement - response that increases likelihood of behavior
• Positive reinforcement - positive stimulus (reward craving) that increases likelihood of behavior
• Negative reinforcement - removal of noxious stimulus (relief craving) that increases likelihood of behavior
• Punishment - noxious stimulus that decreases likelihood of behavior
Multiple Mechanisms of Action

• Agonists
• Antagonists
• Modulators of reinforcement pathways
• Aversive agents
• Modulators of metabolism
• Immunization
• Modulators of sustaining or re-instatement pathways
• Others?
Conceptual underpinnings

- Use as many effective tools as are available
- One size does not fit all: as many doors as possible
- A full continuum of care: multiple services with flexible responses
- Institutional affiliation promotes engagement
- Expectation of relapsing/remitting course
- Expectation of variable and shifting treatment readiness
- Recovery as a gradual process, not an overnight event -- expectation of incremental progress
Medications for Nicotine Dependence

Nicotine replacement therapy

Bupropion

Varenaciline
Current treatments

Effectiveness of Non-Pharmacologic Treatments

% Quit at 12-months

No Therapy: 5%
Brief Advice: 10%
Behavior Therapy: 25%

Lerman, Patterson, & Berrittini, 2005.
Nicotine replacement therapy (NRT)

- Patches
- Gum
- Nasal spray
- Inhaler
- Lozenge
- [E-cigarettes??]
Use of medications – the basics

• Step #1: enhance motivation
• Repeat step #1 endlessly until action stage
• When in action stage, establish a plan
• Set a quit date
• Self-directed cutting down until then
• Prescribe craving medication now, with plan to start 1-3 weeks before quit date
• Start NRT on quit date
Use of medications – the advanced course

• The more monitoring the better
• Add-on counseling if available (group, individual, telephone, on-line)
• Establish the *personal* link to health outcomes
• Frequent visits and debriefing
• Encourage successes (even small)
• Encourage multiple quit attempts
Barriers to effectiveness and adoption

- Cost
- Knowledge and training
- Prejudice and misunderstanding
- Lack of medical involvement in treatment
- Lack of delivery system models
- Limited potency of medications
- Side effects
- Problems with adherence and compliance
Role of medical professionals

- Screening
- Assessment
- Brief intervention
- Extended intervention
- Referral
Role of medical professionals

- Problem: doctors have no time
- Solution: the 3 questions approach
  - How much do you smoke?
  - Would you like to try to quit or cut down?
  - Why or why not?
Role of medical professionals

• Problem: even if they say yes I don’t know what to do (I’d rather not know)
• Solution: you’ve already done something (advancing motivation is an effective intervention)
Barriers to greater medical role

• Only half of smokers receive quit advice from physicians – WHY?
• Frustration at low success rates (lower in real world than in research)
• Time pressures in medical settings
• Concerns about medication side effects
Use of medications – the advanced course 2

• Start NRT 1-3 wks before quit date
• Combine long acting NRT (patch) with short acting NRT (gum, lozenge, spray, inhaler)
• Consider *combining* bupropion + varenicline + NRT
Varenicline & Bupropion SR Combination Therapy for Smoking Cessation

7-day point-prevalence smoking abstinence rates

Gonzales et al., 2006; Jorenby et al., 2006

Varenicline + Bupropion
- 71% 58%

Varenicline
- 50% 33%

Bupropion
- 36% 25%

3 months
6 months

Medications and substance use: linear pharmacological model

MEDICATION

REDUCED CRAVING and REWARD

REDUCED USE
Medications and stages of change: Potential positive feedback loop

- Improved motivation and reinforcement of adherence
- Reduced use
- Improved self-efficacy
- Cycle of advancing stage of change
- Reduced craving
- Reduced use
- Reduced reinforcement
Use of medications – Innovative delivery techniques

• Practice Quit Attempts (PQA) – attempting to not smoke for a few hours or days, without pressure to quit for good

• NRT sampling as a possible facilitator

• NRT sampling increases conversion of PQA’s into more serious quit attempts and might increase success

• A potential technique for advancing stage of change: contemplation $\rightarrow$ preparation?
Smoking during pregnancy

Percentage of U.S. Mothers Who Smoked During Pregnancy

Pregnancy

• Unfortunately safety and efficacy not well studied in pregnancy
• Clinical consensus – use bupropion + NRT (safer than smoking)
Co-Morbidity
Scope of the problem

Rates of smoking:

- Background population 25%
- Alcohol addiction 90%
- Drug addiction 90%
- Schizophrenia 85%
- Depression 80%
Co-Morbidity
Treatment approaches

• Target these populations for tobacco cessation
• Treat the co-morbidity!
Is everything on the menu?

“And if you like comfort food, I would recommend the Xanax stuffed pork-loin.”
Psychiatric co-morbidity
Special considerations

• Psychiatric side effects in general population, and higher rates in patients with psychiatric co-morbidity
  – Risk of depression/anxiety with varenicline
  – Risk of irritability or agitation with bupropion
  – Risk of mania with bupropion in bipolar disorder

• Worsening of depression with quit attempt should be addressed
Addiction co-morbidity

• Conflict in the field:
  – Tobacco use worsens addiction treatment outcomes, vs
  – “I can’t deal with that now… one thing at a time…”
Weight gain

• Avg 4 lbs with smoking cessation
• But 1 in 10 have larger gain of ≥ 25 lbs
Youth

• Unfortunately treatment trials in adolescents disappointing
• Adolescents are complicated and hard to treat (*I know – you’re shocked ….*)
Genetics

- Variations in the genes for nicotine receptors predict severity and treatment response
- One high risk variant (1/3 European descent population) correlate with more smoking, later quit age, lower rates of quitting, poorer response to treatment
- Some evidence that medication eliminates this risk, and this variant accounts for most of medication effect
Practical Treatment Approaches

- 95% is just showing up
Medication Treatment
Collaborative Team Approach

• Illness education and role induction
• Family (or other support network) involvement and commitment
• Cross discipline monitoring
  – Presence of symptoms
  – Medication compliance
  – Treatment response
  – Side effects
  – Social influences
• Expectations and arrangements for continuing care
Pharmacological Treatment

• Question:
  – Which is better - medications or counseling?

• Answer:
  – Yes
A sprint or a marathon?

**Early:** I agree I was huffing and puffing with my smoking out of control, but I’ve cut down to less than a pack a day.

**Later:** I’ve been trying to quit, and the medication my doctor gave me has really been helping. But those last 10 cigarettes are a bear…

**Even Later:** I’ve quit a few times…I even got up to 6 months. But something always seems to happen … sometimes when I get stressed I just can’t resist the first cigarette, and then it’s off to the races again. Maybe I’ll try those meds again? (sigh)
The future?

• Nicotine vaccine
• Nicotine metabolism enhancers
• Other reinforcement modulators
  – N-Acetyl Cysteine
  – Others
• NK-1 (substance P; neurokinin) antagonists for stress-induced relapse
We’ve come a long way