Pharmacotherapy for Treating Tobacco Dependence

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Rationale for Pharmacological Therapy

- Success rate doubles
- Manage negative mood states
- Provides opportunity to alter behavior without withdrawal
- Reduce withdrawal symptoms
First-Line Pharmacologic Therapy

- Non-Nicotine Therapy
  - Bupropion (prescription only)
  - Chantix (prescription only)

- Nicotine Replacement Therapy
  - Nicotine patch (OTC)
  - Nicotine gum (OTC)
  - Nicotine lozenge (OTC)
  - Nicotine nasal spray (prescription only)
  - Nicotine inhaler (prescription only)
Factors for Consideration

- Contraindications
- Patient preference
- Previous patient experience
- Patient characteristics
Optimizing Pharmacotherapy

• Goals of treatment
  • Withdrawal symptom relief
  • Control of cravings/urges
  • Abstinence

• Modification of medication doses may be necessary to achieve these targets
  • Higher doses
  • Multi-drug regimens
  • Longer course of treatment
Withdrawal Symptoms

- Depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Shakiness
- Increased appetite or weight gain

Patch Dosing

• 40 cpd or greater = 42 mg/day
• 21-39 cpd = 28-35 mg/day
• 10-20 cpd = 14-21 mg/day
• 10 cpd or less = 14 mg/day

* If a dose >42 mg/day may be indicated, contact the patient’s prescriber
Patch Dosing Schedule

- Use initial dose for 4-6 weeks
- After 4-6 weeks of smoking abstinence, taper 7-14mg steps every 2-4 wks
- Length of therapy varies based on patient response
- Withdrawal symptoms while tapering are mild to nonexistent
- Advise using overnight
Nicotine Patch – Person smoked 30 cpd

Patient A
• 28 mg x 4 weeks
• 21 mg x 4 weeks
• 14 mg x 3 weeks
• 7 mg x 2 weeks

Patient B
• 28 mg x 6 weeks
• 21 mg x 4 weeks
• 14 mg x 4 weeks
• 7 mg x 4 weeks
Combination NRT rationale

Combine long-acting patch with *ad libitum* short-acting medication (gum, lozenge, inhaler, nasal spray)

• Encourages patient to be in control of cravings and withdrawal symptoms, while keeping a consistent baseline

• Improves compliance with treatment plan

• Achieves higher drug concentrations

• Allows further dose adjustments

• Replace tactile stimulus by mimicking smoking
Medication:

Without Medication

With Medication

Intensity

TIME

Stop Date
Immediate-release NRTs

- Nicotine gum, lozenge and inhaler
  - Buccal mucosal absorption
  - Affected by pH
  - Technique important with NG, NL
  - Peak absorption in 15-20 min.

- Nicotine nasal spray peak absorption in 5-10 min.
Smoking produces much higher nicotine levels and much more rapidly than NRT

Nicotine Lozenge and Gum Dosing

- Based on time to first cigarette
  - < 30 minutes = 4 mg
  - > 30 minutes = 2 mg

Based on cpd
  - >20 cpd = 4 mg
  - <20 cpd = 2 mg

- Monotherapy:
  - 1-2 pieces every 1-2 hours
  - Minimum of 9 lozenge/day or 10-12 gum/day
  - Taper over 12 weeks (or as tolerated)

- Consider in Combination with other NRT
  (Use 2 mg lozenge or gum)
Nicotine Nasal Spray

- 1 dose = 1 spray in each nostril
- Starting dose: 1 dose 1-2 times/hr, Up to 5 times/hr or 40 times/day
- Most average 14-15 doses/day initially
- Length of Rx: 12 weeks but can be shorter
- Can taper or stop abruptly, as tolerated
Nicotine Nasal Spray

- Side Effects -
  - moderate to severe nasal irritation (81-94%)
  - nasal congestion
  - transient change in sense of smell/taste

- Dependency profile between other NRT and cigarettes

- Contraindication - severe reactive airway disease
Nicotine “Inhaler”

Dose Instruction

- Puff on inhaler several times a minute
- Each cartridge will last about 30 minutes of active puffing
- 1 cartridge = as much nicotine as 2-3 cigarettes
- Monotherapy: At least 6 cartridges each day, up to 16/day
- Can be used alone or in combination with other NRT
Nicotine Inhaler: Side Effects

- local irritation throat/mouth (40%)
- coughing (32%)
- rhinitis (23%)

“puff” not “inhale”
Combination NRT Compared With Single Agent NRT

- Nicotine patch + short-acting NRT
  - Patch provides steady baseline
  - NG, NL NNS, NI respond to urges
- Withdrawal may be improved
- Overall abstinence rates at 6 mos. better
  - OR 1.35 (95% CI 1.11-1.63)*

*Cochrane Database of Systematic Reviews 2009
How to use Combination Rx

• Use NP at dose adjusted for CPD

• Assess patient preference for immediate-release NRT

• Use IR NRT scheduled or ad lib
  • Every 1-2 hours while awake
  • In response to urges to smoke

• Taper per individualized plan
Bupropion SR

Wellbutrin
Zyban
Bupropion SR prescribing

- Set target quit date 1 week from start of medication
- Begin with 150 mg daily for 3 days
- Increase to 150 mg twice daily at least 8 hrs apart
- Evening dose before 6PM
- Treat for 8-52 weeks
Common adverse events reported in 40 controlled clinical trials of bupropion SR

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<th>AE</th>
<th>Mean %</th>
<th>Range</th>
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<tr>
<td>Dry mouth</td>
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<td>(6 to 62)</td>
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<td>Headache</td>
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<tr>
<td>Diarrhea</td>
<td>17.5</td>
<td>(6 to 50)</td>
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Serious adverse effect with bupropion SR

- Seizure rate about 1/1000 treated
  - 7/6409 subjects on active therapy in RCT’s
  - Post marketing studies show seizures in people with known predisposition
  - Contraindications: known seizure (ever); structural brain abnormality; serious closed head injury
Bupropion: Seizure Screen

- **Known seizure history:** epilepsy, febrile seizure, withdrawal seizure
- **Structural brain lesion:** tumor, stroke, previous brain surgery
- **Drugs that lower seizure threshold:** phenothiazines, benzodiazepines, theophylline, ethanol
- **Anorexia/Bulimia**
- **Significant head trauma:** prolonged LOC, skull fracture, intracranial bleeding
Varenicline

Chantix
Varenicline Dosing

• Taken with full glass of water after eating
• Start one week prior to Target Quit Date
  • Days 1-3: 0.5 mg once daily
  • Days 4-7: 0.5 mg twice a day (morning and evening)
  • Day 8 and for 11 weeks: 1.0 mg twice daily

• If abstinent at 12 weeks, continue twice daily for an additional 12 weeks
### Common Adverse Events in Clinical Trials (%)

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Conclusions

- **NRT**
  - Patch dosing matched to CPD is safe and effective
  - Combined NRT’s are efficacious
  - Length of therapy guided by patient response (longer may be better)
  - Safe in smokers with CHD
Conclusions

• Bupropion

• Safe and effective in most populations at 300mg per day

• Increased efficacy combined with NP

• Can be safely combined with SSRI’s

• Attenuates post-cessation weight gain
Conclusions

• Varenicline

• Varenicline is efficacious for the treatment of tobacco dependence

• Side effects have been generally mild and well-tolerated

• Trend in increased cessation with duration of use
E-Cigarette

A battery-powered device that provides inhaled doses of vaporized nicotine solution. It is used as an alternative to smoking tobacco product.
“Vaping”
• E-cigarette cartridges labeled as “no nicotine”
  • Low levels of nicotine present in all cartridges tested, except one.
• 3 different E-cigarette cartridges with same label
  • Markedly different amount of nicotine with each puff
• One high-nicotine cartridge delivered 2 x as much nicotine as the nicotine inhaler
ENDS

• “E-cigarettes”- electronic nicotine delivery systems
• Deliver nicotine solution by heating and vaporizing for inhalation
• Safety concerns have been raised
• No evidence to support use as a treatment to help smokers stop smoking
• Legal status in the US– regulated as tobacco
  • FDA yet to reveal regulations
Case Study - “Karla”

- 42 year old divorced female
- Patient reports the following:
  - COPD-bronchitis
  - Type II diabetes
  - Seizure disorder
  - Hearing impaired
- Smoked for past 25 years, 2 1/2 ppd
- Reports several quit attempts
  - Hypnotized once and quit for 9 days
  - Longest abstinence was 3 weeks with patch
- Motivation: health concerns, role model for children, tired of the ‘control’ of the addiction
Case Study
“Travis”

• 52-year old divorced male

• Medical History
  • Chronic back pain
  • Migraine headaches
  • Arthritis

• 35 yr hx of smoking, 20 cpd

• In recovery from alcohol for past 3 months

• No “serious” quit attempts

• Wife and sponsor are both smokers
Case Study “Colleen”

• 33-year old married female

• Patient reports following:
  • Recurring skin rash

• 15 yr hx of smoking, 20 cpd, but down to 10 cpd for past week

• Quit 6 years ago “cold turkey” for 10 months (pregnancy was motivation)

• Relapsed after birth of child

• Several serious quit attempts in the past 4 years – never abstinent for more than 1 day.
References

**Treating Tobacco Dependence in a Medical Setting**, Richard D. Hurt, Jon O. Ebbert, J. Taylor Hays, and David D. McFadden *CA Cancer J Clin* 2009; 59;314-326; *originally published online Aug 25 2009*

**Treatment of Tobacco Dependence**, Michael V. Burke, EDD; Jon O. Ebbert, MD, MSC; and J. Taylor Hays, MD Mayo Clinic Proceedings 2004;83(4):479-484