Neurobiology and Treatment of Opioid Dependence

Nebraska MAT Training

September 29, 2011
Top 5 primary illegal drugs for persons age 18-29 entering treatment, %

Heroin or Prescription Opioids are the primary drug of abuse for more than 1 in 4 persons age 18-30 seeking treatment.
18-29 year olds are the largest group represented among persons seeking treatment for heroin or opioid abuse, nearly 40%.
Prior treatment episodes for persons starting treatment for heroin dependence, 2009

SAMHSA (2009) Treatment Episodes Data Set.
History of MAT for heroin dependence

- 1806 Scientists isolate morphine from opium
- 1820 Scientists isolate codeine from opium
- 1853 Introduction of the hypodermic syringe
- 1898 introduction of heroin
- Late 1800s marketing of opioid based “patent” medicines
History of MAT for heroin dependence

1919 The Harrison Act and its interpretation
1929 Congress establishes “narcotics hospitals”
at Lexington and Fort Worth
- over 90% relapse rate
1964 Mary Nyswander and Vincent Dole
experiment with methadone
Primary virtues of Methadone

- Long-acting so that with a daily dose, a steady state of active opioids can be achieved
- Eliminates or severely reduces opioid craving
- At proper doses, it can create an opioid blockade through cross-tolerance
- People with opioid addiction can focus on the rest of their lives
2002 Buprenorphine (Suboxone®/Subutex®)

• Long-acting so that with a daily dose, a steady state of active opioids can be achieved
• Eliminates or severely reduces opioid craving
• At proper doses, it can create an opioid blockade through antagonist effect
• A ceiling effect makes buprenorphine safer than methadone in preventing respiratory depression
Myth # 2:

• Methadone and Buprenorphine ("replacement medications") just maintain a person’s addiction

Reality:

• Methadone and Buprenorphine stabilize a client and free up their cognitive and intentional resources so that they can begin to engage in treatment
Heroin Addiction

INTOXICATION

WITHDRAWAL
Buprenorphine or Methadone Maintenance
What’s the difference between addiction and physical dependence?
Cycle of Addiction

**DRUG USE**
- Physical relief
- Guilt / shame
- Recall of consequences
- Recall of good intentions
- Feeling of helplessness

**WITHDRAWAL**
- Decreasing well-being
- Increasing stress
- Mental obsession

**CRAVING**
- Loss of cognitive control
- Compromised values
- Compromised intentions
- Amnesia re: consequences
- Rationalization of use

**LOSS OF CONTROL**
- Panicked drug-seeking
- Lying, cheating, stealing
Myth # 3:
• A person is not really in recovery if they’re relying on medications

Reality:
• A person is in recovery when they’re doing what they have to do one day at a time to avoid relapsing to the destructive cycle of addiction
Effect of Stigma on Client Success

Receiving maintenance tx

"I am defective"

Engage with others in treatment

"I'm succeeding"

Continue working the program

Confidence / happiness

"I'm failing"

Depression/Shame

CRAVINGS MAKE THIS FEELING GO AWAY
Methadone Maintenance reduces crime

The Effectiveness of Methadone Maintenance Treatment (p. 182), by J. C. Ball and A. Ross, 1991, New York: Springer-Verlag.
SUBOXONE facilitates client engagement by reducing cravings and preventing withdrawal

Treatment with Buprenorphine

Phase 1: Induction (1 week)
Phase 2: Stabilization (1-2 months)
Phase 3: Maintenance (ongoing)
Phase 4: Medically Supervised Withdrawal optional (3 days to several weeks)
Phase 5: Continued care (ongoing)
Induction Phase
(short-acting opioids)

**Goal**
To find the minimum dose of methadone or buprenorphine at which the patient

1. discontinues or markedly diminishes use of other opioids
2. experiences no withdrawal symptoms, minimal or no side effects, and no uncontrollable cravings for drugs of abuse
Stabilization Phase (1-2 Months)

• **Medical Treatment**
  – Weekly assessments
  – Dosing adjustments as needed

• **Goals**
  – Elimination of objective evidence of opioid use (negative drug screens)
  – Reduced self-reported cravings and illicit opioid use
  – Self-reported increase in opioid blockade such that self-administered illicit opioids induce little or no euphoria
Some issues to address in treatment*

- Psychiatric comorbidity
- Somatic consequences of drug use
- Family and support issues
- Structuring of time in pro-social activities
- Employment and financial issues
- Legal consequences of drug use
- Other drug and alcohol abuse

*Detailed treatment goals and phases available in TIP 43
Criteria for Medically Supervised Withdrawal

• Patient’s desire to commence dose reduction
• Patient’s commitment to becoming medication-free
• Physician’s confidence that tapering would be successful
Factors that should generally precede Medically Supervised Withdrawal

- Extensive period of abstinence from illegal drugs and alcohol (1-2 years)
- Stable housing
- Stable source of income
- No untreated or unstable co-occurring psychiatric disorders
- Engagement in productive activity (e.g. employment, school, volunteering)
- Adequate psychosocial support
- Absence of legal problems

Medically Supervised Withdrawal optional (3 days to several weeks)
Medically Supervised Withdrawal (3 days to several weeks)

Rate of Dose Reduction

• Reduction should be done gradually at a predetermined period or at a rate negotiated by the patient and the physician together

• Rapid dose reduction should be performed only in the presence of a compelling urgency (e.g. impending incarceration, foreign travel, job requirement)
Continued Care (ongoing)

After Medically Supervised Withdrawal

• Patients should be followed with psychosocial services
• Naltrexone/Vivitrol can be used as a key relapse prevention strategy
• Methadone or buprenorphine should be reintroduced if needed for continued progress
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1950’s</td>
<td>Abraham Wikler observes the phenomenon of “conditioned withdrawal”</td>
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<tr>
<td>1960’s</td>
<td>Experiments with antagonist therapy - cyclazocine</td>
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<td>1971</td>
<td>President Nixon creates the Special Action Office for Drug Abuse Prevention</td>
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<tr>
<td>1972</td>
<td>Congress puts aside money to research non-addictive anti-craving medications</td>
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<tr>
<td>1984</td>
<td>FDA approves naltrexone for opioid dependence</td>
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<tr>
<td>2010</td>
<td>FDA approves 28-depot naltrexone (Vivitrol®) for opioid dependence</td>
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Medications of Opioid Addiction

Methadone – agonist
Suboxone – partial agonist
Naltrexone – antagonist

Vivitrol – 28-day injection of naltrexone
Methadone activates the opioid receptors to prevent withdrawal and prevents a person from getting “high” through cross-tolerance.
Suboxone activates the opiate receptors to prevent withdrawal and acts as an antagonist to other opioid agonists, blocking their effect.
With both, the **ADDITION** is curtailed through reduction in craving and compulsion, but **physical dependence** remains.
Naltrexone and Vivitrol® block opiate receptors to prevent an opiate “high” but do not activate the receptors.
Naltrexone and Vivitrol® prevent reinforcement of addictive drugs without causing physical dependence.
VIVITROL reduces client cravings, prevents reactivation of addiction and leads to improved treatment retention

(All participants received twice weekly relapse prevention therapy)

% Opioid free weeks in 6 months

**Graph:**
- **XR-NTX (n=126)**
- **Placebo (n=124)**

**Axes:**
- **Y-axis:** Opioid-free weeks (%)
- **X-axis:** Participants (%)
Limitations of Vivitrol®

- No natural reward
- Compliance is based entirely on internal motivation
- Risk of overdose after medication is discontinued
- Client must be completely opioid free prior to naltrexone induction
Typical Suboxone taper 2-8 weeks

- No self-transportation
- No cash available
- 24-hour companionship

Detox 4 days

1/16
1/8
1/4
1/2
Full tablet (2 days)

Vivitrol injection

Typical Naltrexone taper 3-7 days

8mg (5-14 days)
6mg (5-14 days)
4mg (5-14 days)
2mg (5-14 days)
Which is the best medication?

As with any chronic disease or disorder, the correct medication depends on the characteristics of the patient as well as their stage of treatment.
Ongoing Assessment

Motivation vs. Stability Graph

- **METHADONE**
  - Strongest drug reward
  - Highest level of accountability

- **SUBOXONE**
  - Moderate drug reward
  - Moderate level of accountability

- **VIVITROL**
  - No drug reward
  - Moderate level of accountability
Principles of Individualized MAT

1. Educate regarding options.
3. Provide a clinical opinion
4. Support client in developing a treatment plan with concrete goals.
Myth # 5:

• “Eventually I’ll have to be strong enough to do it without medication!”

Reality:

• Often chronic illnesses such as addiction require chronic medication management to prevent relapse
The world without medication
The world with medication
Myth # 4:

• When individuals are detoxified and abstinent through incarceration, they don’t need medical treatment upon release.

Reality:

• Release from prison can be a death sentence for persons with untreated addiction
STRESS - HPA
REWARD - MLC
Mortality after release from prison


RR=12

RR=4

RR=3.2

RR=Relative Risk
Myth # 6:

• Addiction can best be treated with an intensive treatment episode followed by mutual support participation

Reality:

• The episodic model of addiction treatment does not do justice to the chronic nature of the illness
Lifelong Diabetes Relapse Prevention

- Regular doctor’s visits
- Relapse prevention strategies
- Plan meals carefully
- Exercise / sleep regularly
- Monitor “red flag” symptoms (deterioration of vision, circulation)
- Treat related physical problems
- Take prescribed medication
Lifelong **Addiction** Relapse Prevention

- Regular support groups
- Monitor *emotional* well-being
- Avoid high risk situations
- Exercise / sleep regularly
- Monitor “red flag” symptoms *(cognitive distortions, isolation)*
- Treat related *psychological* problems
- Take prescribed medication
An **individualized chronic care** model for the treatment of addiction, including a full range of available **medications** and **client options** is the key to improving treatment outcomes.

This is the same model of care that is used for every other chronic illness.