Logan – “The Alpha Male”

Learning Objectives

• 1. Discuss the pharmacologic therapies for detoxification for substance use disorders.
• 2. Discuss the pharmacologic therapies for relapse prevention for substance use disorders.

My Belief About Addiction

• A biopsychosocial & spiritual disease model
• A chronic disease, that is, one that is never cured but one that is managed and controlled
• Relapse prevention is a vital concept to understand, explore & embrace
• One does not elect to become addicted
• Every person has some type of addiction
• Addictions is a disease of the BRAIN
The Brain

Addiction and the Brain

Four Primary Areas
- Ventral Tegmental Area (VTA)
- Nucleus Accumbens
- Amygdala
- Prefrontal Cortex
Neurons communicate by sending signals to each other at specialized connections.

What is the connection between two neurons called?

**SYNAPSE!**

The terminals of the sending neuron have vesicles packed with neurotransmitters.

Neurotransmitters are released when the sending neuron fires.

Neurotransmitters send the signal by binding to specific receptors on dendrites of the receiving neuron.
Pathway to Addiction

The Reward Pathway and Addiction

Natural Rewards

Natural Rewards
Food
Water
Sex
Nurturing

Addiction

Addiction
A state in which an organism engages in a compulsive behavior
- behavior is reinforcing (rewarding or pleasurable)
- loss of control in limiting intake
Cycle of Addiction

Intoxication

Preoccupation & Anticipation

Withdrawal & Negative Affect

Morphine is a powerful pain killer used in hospitals

What street drug of abuse is related to morphine?

Heroin (also opium & methadone)

What’s happening outside?
Behavioral effects of heroin use include:
• “rush” = euphoria, reduced anxiety, nausea, drowsiness
• “withdrawal” = intense muscle aches & pain, piloerection, fever, diarrhea, irritability, increased lacrimation (rhinorrhea, tearing of eyes)
• Primarily snorted or used intravenously
• DEATH by respiratory arrest

What’s happening inside?
Activation of opiate receptors = increased transmission = “rush”
Narcotics/Opioids

- Derived from the opium poppy
- Used medically as painkillers with the exception of heroin
- Blocks pain, produces euphoria
- Highly addictive
- Found in snortable, smokable, injectable forms
- ER visits have increased by 50% over the past 2 years

Opioid Addiction

- Morphine
- Heroin
- Codeine
- Oxycodone
- Meperidine
- Fentanyl

Action of Heroin
Opioids

- If dependence develops, drug procurement often dominates the individual’s life and often leads to criminal behavior.
Opioids

- Heroin (diacetylmorphine) is more lipid soluble than Morphine and therefore crosses the blood brain barrier more easily
- Causes more intense euphoria and sedation
- Quickly metabolized
- Excreted in the urine as free or conjugated morphine
- Euphoria, sedation, and analgesia are the desired effects

Heroin

- Overdoses may cause respiratory depression, bradycardia, hypothermia, and death.

Method of Use

- Intravenous
- Nasal Insufflation (snorting)
Complications

- Overdoses may result from variability in the potency of the heroin purchased on the street, rapid loss of tolerance after abstinence, and concurrent use of other central nervous system depressants.
- Other physical complications

Withdrawal

- Symptoms start within 2 to 48 hours of last use
- Abrupt withdrawal of heroin, which has a short half-life, causes prompt and severe withdrawal symptoms

Withdrawal Symptoms

- Restlessness
- Lacrimation
- Rhinorrhea
- Nausea
- Mydriasis
- Muscle Aches
- Diarrhea
Withdrawal Symptoms

- Piloerection
- Tachycardia
- Hypertension

Management

- Clonidine
- Phenobarbital
- Librium
- Suboxone or Subutex
- Symptomatic, for example, Tigan for nausea and vomiting
- Levsin & Robaxin, Flexeril
- Counseling/Psychotherapy/Alternative Therapies

Relapse Prevention

- Naltrexone in dosages previously described
- Note – Can NOT begin Naltrexone Rx. until the patient is opioid naïve for 10 days
- Suboxone
- Subutex
- Methadone
Suboxone

- Buprenorphine, a partial opioid receptor agonist/antagonist
- Drug Addiction Treatment Act of 2000 allows qualified physicians to treat opioid-dependent patients with sublingual Suboxone in their practices
- Suboxone provides a new management option for opioid dependent clients

Suboxone

- Physicians must complete an approved 8 hour course on Suboxone treatment
- Physicians can only have a maximum of 30 (recently changed to 100) clients in their practice at one time
- If more than one physician is in the practice, then an additional clients can be added per physician as long as above requirements are met
- DEA monitors physicians prescribing Suboxone
- Advanced Practice Nurses can not prescribe Suboxone

Suboxone

- Occupies opioid receptor sites
- Blocks effects of opioid agonists
- Not easily displaced by other opioids
- Lower potential for abuse
- Less physical dependence
- Reduced cravings
- Greater safety in accidental overdose
Suboxone

- Initiation of therapy can vary
- Administered sublingually as a tablet
- Now available as melt away strip
- Once daily dosing
- Milder withdrawal profile
- Can be dispensed for take home use
- Maintains clients in outpatient treatment
- Best results are when pharmacology is combined with psychosocial treatment and counseling

Butrans

- Buprenorphine Transdermal System for chronic pain

Methadone

- Most frequently used medication for opioid addiction treatment
- Allows patients to socialize and function normally
- Prevents physical withdrawal symptoms
- Relieves the craving of opioids
Benefits of Methadone

- Administered orally
- Once daily dosing
- Minimal side effect profile
- Safe and effective when dosed correctly

Pharmacology of Methadone

- Long-acting full opioid receptor agonist
- Functions at mu receptor sites
- Mu receptor sites exist on the surfaces of brain cells
- Belief is that the activation of the mu receptors are responsible for the analgesic and euphoric effects of opioids

Methadone Kinetics

- 80% bioabsorption
- Blood levels peak within 2 – 4 hours
- Pain relief within 4 – 6 hours
- Half life is 24 – 36 hours
- Steady state reached within 5 – 7.5 days

*Note: Blood levels are influenced by absorption, metabolism, protein binding, urinary pH, other medications, diet, age, physical activity level, pregnancy & vitamins*
**Methadone Induction**

- Induction is the most risky phase of methadone maintenance treatment.
- START LOW & GO SLOW!!!
- Treatment must be individualized
- Optimal doses for patients will vary
- Understand the cumulative property of methadone
- Communicate with patients

**Initial Dose**

- Use COWS (Clinical Opiate Withdrawal Scale)
  - **Score**  
  - **Maximum Initial Dose**
  - 0 – 5 (no wd) 0 mg.
  - 5 – 12 (mild wd) up to 15 mg.
  - 13 – 24 (Moderate wd) up to 20 mg.
  - 25 – 36 (Mod.Sev.wd) up to 25 mg.
  - > 36 (Severe wd) up to 30 mg.
  - **Note:** *If withdrawal does not follow, methadone treatment cannot be initiated.*

**Goals of Methadone Therapy**

- Ensure individualized and "adequate dose."
- Titrate dose to achieve a steady-state with methadone levels (clinically determined) in the "comfort zone" throughout and beyond the dosing interval.
- Allow time to react to the initial dose
- Allow time to react to a dose increase (3-5 days).
- Avoid overly aggressive (toxicity, overdose) and ultra-slow titration of dosing (continued illicit drug use).
- Continued assessment and monitoring of the patient is essential.
Methadone’s Cumulative Effect

• Dose A is 30 mgs. daily with no increase for 6 days. Cumulative effect by day 6 is equivalent to 59.0625 mgs. of the drug.
• Dose B has an initial dose of 30 mgs. On day 1 and then the dose is increased daily by 10 mgs. for another 5 days, i.e. day 2 the dose is 40 mgs., 50 mgs., 60 mgs., 70 mgs., 80 mgs. Thus by day 6 the cumulative effect of dosing is 139.6875 mgs.

Keys to Methadone Therapy

• ANY SIGN OR SYMPTOM OF OVERMEDIATION DURING THE EARLY INDUCTION PHASE REQUIRES A DOSE REDUCTION!!!
• Beware of the subtle signs/symptoms of overmedication; i.e. feeling good, extra energy, staying awake at work, etc.
• Patients may need more TIME, not more MEDICATION!!!

Adverse Reactions

• Constipation
• Excessive sweating
• Paresthesias in hands and feet
• Weight gain
• < libido/sexual dysfunction
• Rash
Health Conditions That May Affect Dose

- Age
- Hepatitis C
- HIV/AIDS
- Cardiac Risk
- Pain
- Pregnancy
- Lactation

Cardiac Adverse Effects

- FDA Black Box Warning
  - Prolonged QT syndrome in doses greater than 200 mgs. or with IV administration
  - QT prolongation may lead to Torsades de Pointes
  - Need to assess individual risks
  - EKG pre administration???

Torsades de Pointes
Drug Interactions

- Multiple drug interactions exist:
  - Sedatives
  - Antidepressants
  - HIV Medications
  - Antibiotics & Antifungals especially Cipro, Fluconazole and Rifampin
  - Inducers and Inhibitors of the CYP 450 enzyme system

Relapse Prevention

- No relapse prevention medication can be effective without counseling and psychotherapy.
- The issues and triggers in a patient’s life that contribute to dependence and addiction must be explored and addressed

Alcoholism

- 90% of US population uses alcohol
- Amount & frequency of use vary
- Approximately 10% of men meet DSM-IV criteria
- Approximately 3% to 5% meet DSM-IV criteria
- Elderly drink less frequently and lesser amounts of alcohol resulting in their disease being less identifiable according to the criteria established
Medical Complications of Alcoholism

• GI Tract
• Cardiovascular System
• Metabolic Changes
• Central Nervous System Changes
• Nutritional Deficiencies
• Hematopoietic System Changes

Major Diagnostic Tests

• CAGE Questionnaire
• Elevated Liver Enzymes, especially GGT (gamma glutamyl transpeptidase)
• Increased Mean Corpuscular Volume

CAGE

• CAGE
• Have you tried to CUT DOWN on your drinking?
• Are you ANNOYED by people telling you to stop drinking?
  Do you feel GUILTY about your drinking?
  Do you drink on first getting up in the morning (EYE OPENER)?
• Two or more yes responses = (+) test
Detoxification Treatment

- Thiamine 100 mg IM or PO either daily or BID for 3 days, then Thiamine 100 mg po daily for LOS
- Folate 1 mg po daily for LOS
- Tegretol 200 mg po BID for LOS (in select patients)
- Serum Tegretol level after 5 - 7 days
- Patients must be weaned off of Tegretol

Detoxification Treatment

- Librium 50 mg po every 6 hours
- Librium 25 mg po every 6 hours prn for increased s/s of withdrawal
- Decrease dosing daily according to patient response until completely weaned off of medication
- Clonidine 0.1 mg po every 6 hours with holding parameters of systolic BP< 100 or heart rate < 50 - decrease dose on daily basis until weaned off of medication
- Assess patient with CIWA scale prior to administration of Librium

Detoxification Treatment

- Ativan instead of Librium
- Serax effective when liver impairment is present
- Counseling/psychotherapy
- AA
- 12 Step Program
- ALANON
Relapse Prevention

- Campral 666 mgs. TID
- Naltrexone (Revia) 25 mgs. daily at bedtime x 3 nights then increase Naltrexone to 50 mgs. daily at bedtime daily thereafter
- Naltrexone oral challenge
- Vivitrol 380 mgs. once monthly
- Combination of Vivitrol and Campral therapy
- Disulfiram (Antabuse)

Counseling and Psychotherapy

- No relapse prevention medication can be effective without counseling and psychotherapy.
- The issues and triggers in a patient’s life that contribute to dependence and addiction must be explored and addressed.

References

WEB Sites

- [http://www.samhsa.gov/about/csas.aspx](http://www.samhsa.gov/about/csas.aspx) (Centers for Substance Abuse Treatment)
- [http://www.samhsa.gov/](http://www.samhsa.gov/) (Substance Abuse and Mental Health Services Administration)

Questions

- That’s All Folks!!!
Funding for this webinar was made possible (in part) by (1H79T1022022) from SAMHSA. The views expressed in written webinar materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.