Rx and OTC Drug Challenges and Solutions for Persons in Recovery

CAPTASA 31 JANUARY 2015

Brian Fingerson, BS Pharm, R.Ph., FAPhA

KYPRN – Kentucky Professionals Recovery Network since 1986

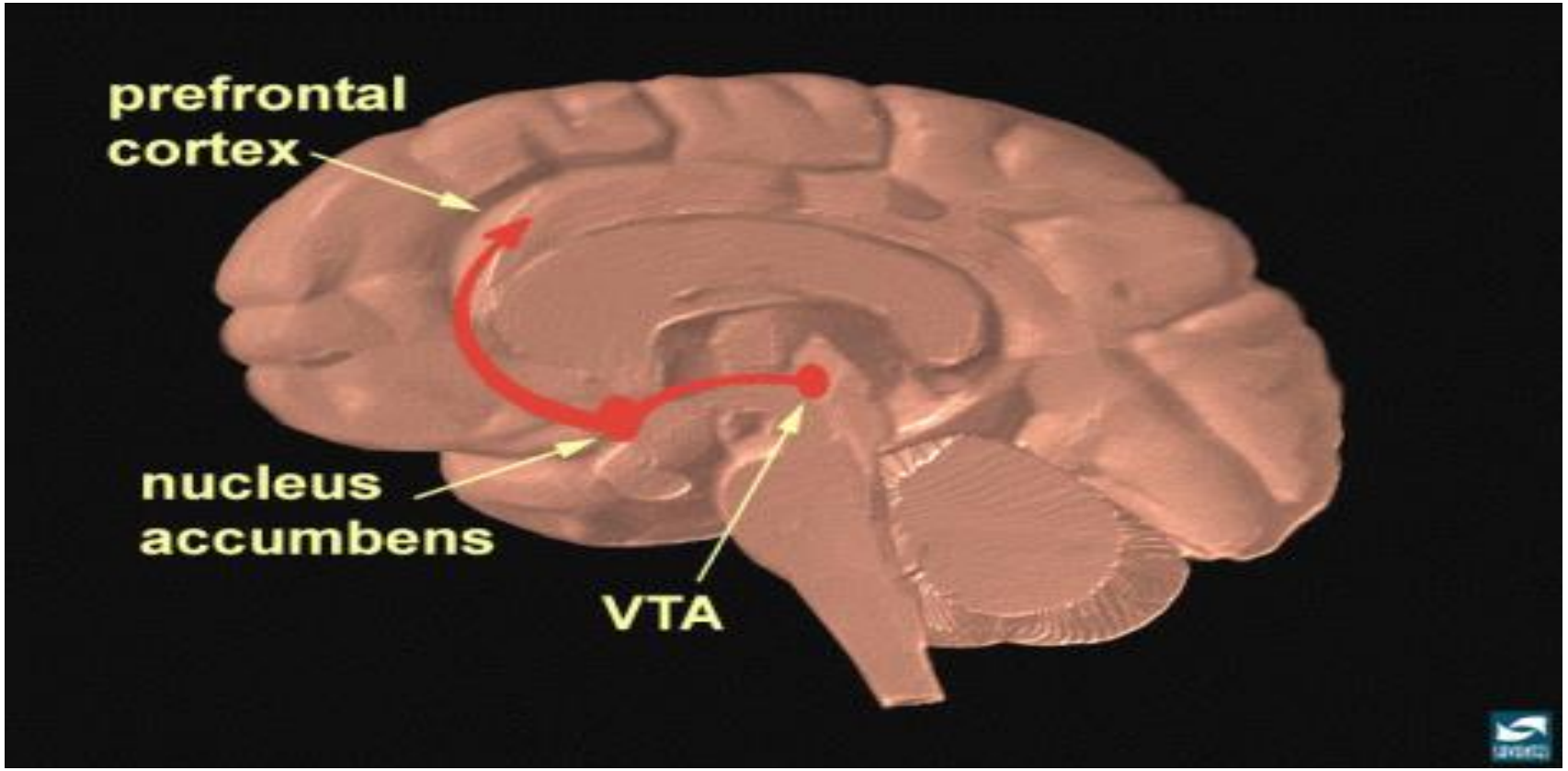
Clients/professions include: Accountants, Pharmacy, Dentistry, Physical Therapy, Veterinary Medicine, Respiratory Care, Optometry, Chiropractic, Social Work

Work with these professionals through their licensing Boards as well as with private pay clients for Disease State Management and Medication Therapy Management in substance use disorder clients

Disclosure Statement

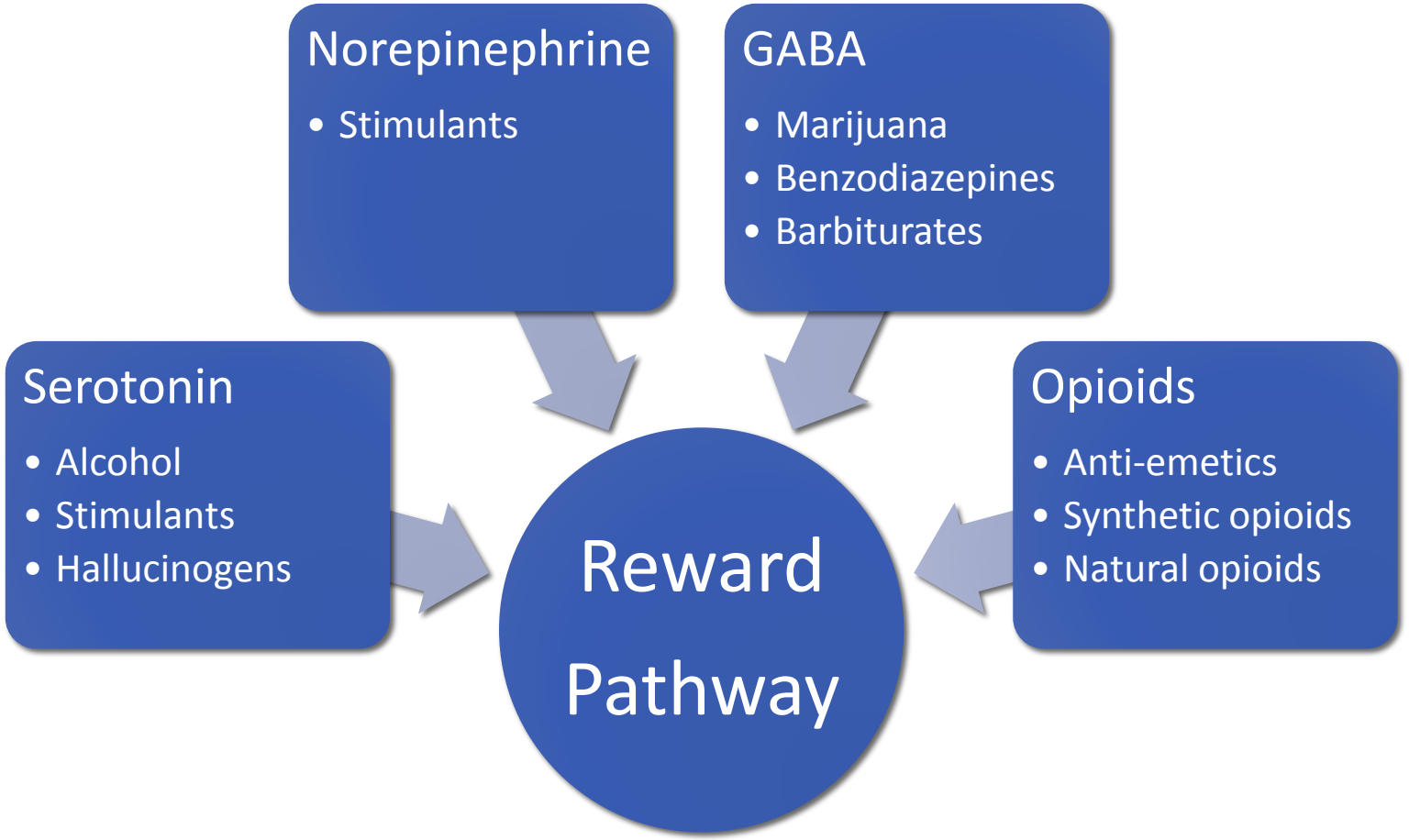
Brian Fingerson, R.Ph., declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

Reward Pathway



http://www.drugabuse.gov/publications/teaching-packets/neurobiology-drug-addiction/section-ii-reward-pathway-addiction/3-reward-pathway

It’s not only about dopamine



It’s not only about dopamine

Glutamate is the major excitatory transmitter in the brain

Glutamate is considered to be the major mediator of excitatory signals in the mammalian central nervous system and is involved in most aspects of normal brain function including cognition, **memory** and learning.

Sleep Aids

Treatments

- Treat underlying cause of insomnia
- Transient or short-term insomnia
  - Short-acting hypnotics for 7-10 days
- Chronic insomnia
  - Recommended duration of drug therapy is not established

OTC Sleep Aids

Antihistamines

Diphenhydramine and doxylamine

- Rapid tolerance to sleep-inducing effect
- Anticholinergic side effects e.g. *"can't see, can't spit, can't pee, can't poop, tachycardia"*
- Hangover effect, cognitive impairment, and delirium

Antidepressants

- Low doses of sedating antidepressants (amitriptyline, trazodone, doxepin, mirtazapine)
- Decrease sleep-onset latency and wakefulness
- Trazodone is the most widely utilized - controversial
  - Can cause orthostatic hypotension, dry mouth, constipation, and priapism

Antipsychotic **Seroquel** (quetiapine) at low doses has sedating effects

- Has street value!

Benzodiazepines

- **How they work:**
  - Bind to GABA receptors; reduce sleep-onset latency & wakefulness and increase sleep efficiency
- **The Problem:**
  - More than short-term treatment can lead to tolerance and dependence
  - Hangover effect
    - Most common with Dalmane (flurazepam) and Doral (Quazepam)
  - Anterograde amnesia
  - Cognitive deficits
  - Rebound insomnia
  - Withdrawal
  - Controlled substances!

Benzodiazepine Receptor Agonists ("Z"-Drugs)

- **How they work**
  - Act on the benzodiazepine component of the GABA-A receptor complex - selectively bind to the alpha-1 receptor
- **The problem**
  - All are major CNS depressants
    - Cause sedation, cognitive impairment, perceptual disturbances, dizziness
  - All are controlled substances
    - Highly abuse
  - Examples: zolpidem; zaleplon; eszopiclone

Alternatives

Non-pharmacologic Treatments –

- Address the hyper-arousal, cognitive, and conditioning factors that perpetuate insomnia
- Produce reliable, long-term improvement

Cognitive Behavioral Therapies –

- Sleep-hygiene strategies
- Stimulus control
- Relaxation therapy

Sleep Hygiene

- Go to bed at same time each night
- Get up at same time each day
- Exercise daily (6 hrs before bedtime)
- Use bedroom only for sleep and sex
- Do not smoke
- Avoid caffeine before bed
- Sleep in a quiet, darkened room
- Do not go to bed hungry, but don’t eat a big meal near bedtime either

Stimulus Control

- Go to sleep only when sleepy
- Use the bed or bedroom only for sleep
- If not asleep in 20 min, get up, go into another room and engage in a relaxing activity. Go back to bed when sleepy.
- Repeat step above if still unable to sleep
- Set alarm for same time each morning

Melatonin and Melatonin-Receptor Agonist

Melatonin

- Effective for treating circadian rhythm sleeping disorders (jet lag)
- Does not appear to be effective for primary, chronic insomnia

Ramelteon (Rozerem®)

- Selective for MT_1 and MT_2 receptors
- Involved in circadian rhythm mediation
- Mainly for sleep onset insomnia

✓No rebound insomnia or withdrawal effects

✓No abuse potential or behavioral impairment

✓Not a controlled substance

Summary – Sleep Aids

Lower risk	Gray Area	Higher risk
Abilify Buspar (buspirone) Elavil Geodon Melatonin Paxil Risperdal Rozerem Sinequan (doxepin) Thorazine Trilafon	Vistaril/Atarax (hydroxyzine pamoate) Desyrel (trazodone)	**Any controlled substance. This includes, but not limited to:** Ambien (zolpidem) Chloral hydrate Dalmane (flurazepam) Lunesta (eszopiclone) Equanil (meprobamate) Placidyl (ethchlorvynol) Restoril (temazepam) Soma (carisoprodol) Sonata (zaleplon) **Any OTC sleep aid, including, but not limited to:** **Any med ending in "PM"** Benadryl Nytol Sleep-Eze Sominex

Psychiatric Medications

DIAGNOSIS ISSUES

Antipsychotics

1st generation antipsychotics: Haldol (haloperidol), Loxitane (loxapine), Prolixin (fluphenazine)

2nd generation antipsychotics: Abilify (aripiprazole), Invega (paliperidone), Risperdal (risperidone), Seroquel (quetiapine), Geodon (ziprasidone), Zyprexa (olanzapine)

How they work

- Block dopamine receptors → leads to decreased dopamine levels, which helps decrease symptoms of schizophrenia and bipolar disorder. Some can also be used in depression not well managed by other medications.

Generally safe, but some of the drugs have a street market

- ***May be problematic:***
  - Seroquel

Antidepressants

Monoamine oxidase Inhibitors (MAO-I's): Eldepryl (selegiline), Parnate (tranylcypromine)

- Increase dopamine levels

Tetracyclic antidepressants (TCA's): Elavil (amitriptyline), Pamelor (nortriptyline), Tofranil (imipramine)

- Increase levels of norepinephrine and serotonin

Selective serotonin reuptake inhibitors (SSRI's): Zoloft (sertraline), Paxil (paroxetine), Prozac (fluoxetine), Celexa (citalopram), Lexapro (escitalopram)

- Increase levels of serotonin

Serotonin norepinephrine reuptake inhibitors (SNRI's): Effexor, Pristiq

- Increase levels of norepinephrine and serotonin

Miscellaneous: Wellbutrin (bupropion)

- Increases levels of norepinephrine and dopamine

Antidepressants

All considered “lower risk”, but….

The problem:

- All affect levels of neurotransmitter in the brain which regulate mood
  - Serotonin, norepinephrine, dopamine
  - The brain in a recovering addict or alcoholic has imbalanced levels of these neurotransmitters esp. early in recovery, and regardless of the use of medications, the brain will likely still be imbalanced. It needs to time to rebalance itself
- Some antidepressants can be sedating and therefore abused
  - TCA’s are most sedating, however side-effect level is higher
- Some antidepressants have a street market

Anti-anxiety agents

Benzodiazepines: Xanax (alprazolam), Ativan (lorazepam), Valium (diazepam)

- How they work: Bind to GABA and enhance its inhibitory effects
- Very high risk in recovering persons – high relapse potential
- Problems:
  - Street market exists
  - Potential for dependence
  - Cause CNS depression
    - Sedation, dizziness, confusion, slowed movement

Other options:

- Buspar (buspirone)
- Inderal (propranolol)
  - situational anxiety
- Low-dose antidepressants

Anti-anxiety Agents

Lower risk	Gray Area	Higher risk
• Buspar (buspirone) • Inderal (propranolol)	• Seroquel • Vistaril/Atarax (hydroxyzine)	All benzodiazepines, including: • Ativan (lorazepam) • Halcion (triazolam) • Klonopin (clonazepam) • Librium (chlordiazepoxide) • Valium (diazepam) • Xanax (alprazolam)

Stimulants

ADHD medications: Adderall (amphetamine salts), Ritalin (methylphenidate)

- How they work:
  - stimulate activity in the brain, increase concentration
- The Problem:
  - Street market
  - Highly abused
  - Effects similar to methamphetamine

ADHD Medications

Lower risk	Gray Area	Higher risk
• Catapres (clonidine) • Intuniv (guanfacine) • Strattera (atomoxetine) • Tenex (guanfacine) • Wellbutrin (bupropion)	• Provigil (modafinil)	All products containing amphetamine salts or methylphenidate, including: • Adderall • Concerta • Dexedrine • Ritalin

Cough/Cold/Allergy

ESPECIALLY THIS TIME OF YEAR!

Cough/Cold

Think twice:

Any product containing pseudoephedrine

- Non-prescription decongestion - has stimulating properties (Sympathomimetic)
- Ingredient in some formulas to make methamphetamine
- consider use of phenylephrine containing product instead

Acceptable when used with caution:

Acetaminophen

Ibuprofen

Mucinex tablets

Duratuss G

Mucofen

Robitussin plain

Tessalon Perles

Cough/Cold

Lower risk	Gray Area	Higher risk
• Mucinex (guaifenesin) • Liquid formulations of guaifenesin • Tessalon Perles (benzonatate)	• Dextromethorphan- found in many cough syrups, usually ones ending in “dm.” This is safe if used as directed, but is abused by many if taken in large quantities. Use with caution. • Duratuss	• Anything containing codeine or hydrocodone as an ingredient • Any OTC or prescription med containing alcohol, such as Nyquil or Comtrex

How do Antitussives/Expectorants work?

Any cough medications containing narcotics such as codeine or hydrocodone should not be used.

- These medications bind to opiate receptors in the central nervous system, altering the perception of and response to pain and produce generalized central nervous system depression and may alter mood or cause sedation.

Any preparation containing dextromethorphan should be used with caution because dextromethorphan acts on opioid receptors in the brain.

- Respiratory depression and perceptual distortions can also be seen in those people taking large doses.

Allergy Preparations

Safe	Gray Area	Dangerous
• Allegra (fexofenadine) • Clarinex (desloratadine) • Claritin (loratadine) Zyrtec (cetirizine) • Ocean Saline		• Actifed (triprolidine) • Allegra D • Benadryl (diphenhydramine) — only to be used for an extreme allergic reaction • Chlor-trimeton (chlorpheniramine • Claritin D • Dimetapp, Dimetane (brompheniramine) Tavist (clemastine fumerate) • Zyrtec D

Caution:

-Sedating antihistamines have the potential to alter judgment and cause fatigue or sedation.

-Decongestants are stimulating and can trigger relapse.

Herbal Products

Be extremely cautious in using herbal products. They are not well-regulated and may contain ingredients that could interfere with other meds you are taking or could affect your sobriety. Two products to avoid are Valerian and St. John's Wort.

What to look for

Avoid OTC medications that contain alcohol. Read the label.

- These medications are typically liquid medicines
- Syrups available that are alcohol-free, such as Tussin DM. Typically noted in larger print on labels

When absolutely necessary, choose non-drowsy type meds. Take the medication as directed for the minimum time needed.

GI Medications

TUMMY AND GUT

Constipation: What to avoid

Drugs

- Dulcolax (bisacodyl)
- Ex-Lax (Senna)
- Senokot (Senna)

Mechanism

- High rate of abuse
- Physiological dependence for bowel movements

Constipation: What is lower risk

Drugs

- Metamucil (psyllium)
- Citrucel (methylcellulose)

Mechanism

- Low potential for abuse
- Safe for daily use
- No physiological dependence

Nausea & Vomiting: Cautions i.e. think twice

Drugs

- Compazine (prochlorperazine)
- Phenergan (promethazine)
- Tigan (trimethobenzomide)
- Zofran (ondansetron)
- Inapsine (droperidol)

Mechanism

- Have effects on dopamine and/or serotonin
- Sedative effects

Nausea & Vomiting: What has lower risk

Drugs

- Emetrol (phosphorylated carbohydrates)
- Reglan (metoclopramide)

Mechanism

- Decreased risk of dependence

Diarrhea: Caution i.e. think twice

Drugs

- Lomotil (atropine/diphenoxylate)
- Motofen (atropine/difenoxin)
- Immodium A-D liquid (loperamide) – some of the generics can contain ethyl alcohol – read label carefully

Mechanism

- Diphenoxylate and difenoxin activate opioid receptors and cross into the CNS
- Liquid preparations may contain alcohol, check labeling

Diarrhea: What is lower risk

Drugs

- Imodium (loperamide) solid dosage forms – short-term use with caution

Mechanism

- Opioid agonist with poor penetration of CNS
- Low risk for activation of reward system

Summary of Gastrointestinal Agents

Lower risk	Gray Area	Higher risk
Laxatives	Laxatives	Laxatives
Metamucil	Dulcolax (bisacodyl)	N/A
Miralax	Ex-Lax (Senna)	
Colace (docusate)	Senokot (Senna)	Anti-emetics
		Compazine (prochlorperazine)
Anti-emetics	Anti-emetics	Phenergan (promethazine)
Emetrol	Dramamine (dimehydrinate)	Tigan (trimethobenzomide)
Pepto-bismol	Transderm-Scop (scopolamine)	Zofran (ondansetron)
Reglan		Inapsine (droperidol)
	Anti-diarrheals	
Anti-diarrheals	N/A	Anti-diarrheals
Immodium (loperamide)		Lomotil (atropine/diphenoxylate)
		Motofen (atropine/difenoxin)
		Immodium A-D liquid (loperamide)

Pain Relief

Pain relief is one of the most frequent reasons why people seek medical attention.

Prescription pain relievers are one of the most abused substances in the United States.

Signs and symptoms of narcotic abuse:

- Analgesia
- Sedation
- Euphoria
- Respiratory depression
- Miosis
- Nausea/vomiting
- Itching/flushed skin
- Constipation
- Slurred speech
- Confusion/poor judgment

Prescription Pain Relievers with Abuse Potential

Opiates: morphine and codeine are both natural products isolated from opium, which comes from the poppy plant.

Opioids: semi-synthetic and synthetic manipulations of morphine.

- Buprenex (buprenorphine)
- Combunex (oxycodone/APAP)
- Demerol (meperidine)
- Dilaudid (hydromorphone)
- Duragesic (fentanyl)
- Kadian (morphine)
- Lortab (hydrocodone/APAP)
- Methadone
- MS Contin (morphine sulfate)
- Norco (hydrocodone/APAP)
- OxyContin (oxycodone)
- Percocet (oxydodone/APAP)
- Percodan (oxycodone/aspirin)
- Roxanol (morphine sulfate)
- Roxicodone (oxycodone)
- Tylenol #2, #3, and #4 (codeine/APAP)
- Ultram (tramadol)
- Vicodin (hydrocodone/APAP)

How They Work

Opioids relief pain by binding opioid receptors in the central nervous system which causes inhibition of ascending pathways of pain. Three types of opioid receptors have been discovered, of which the mu receptor plays the biggest role of pain relief.

Opioids act throughout many areas of the brain; however, the three areas of most importance are as follows:

- The spinal cord: the entry pathway for the perception of pain into the brain were opioids block pain.
- The brain stem: the area of the brain that controls automatic motor functions where opioids cause cough suppression, respiratory depression, and analgesia.
- The limbic system: the area of the brain that controls feelings of emotions through which opioids induce euphoria, alleviation, and well being.

Why They're a Problem

When opioids bind mu receptors in the limbic system, also known as the brain's reward system, they cause a release of dopamine from the ventral tegmental area (VTA) into another part of the brain called the nucleus accumbens (NA).

Not only does this spike in dopamine produce the pleasurable effects described previously, but it also engraves a lasting memory in the other areas of the brain called "conditioned associations" that associate these feelings of euphoria, alleviation, and well being with the stimulus that produced them.

Over time, these "conditioned associations" can lead to cravings for the opioid that have the potential to bring about abuse and later addiction as users require more and more opiate to receive the same feeling of pleasure.

Lower risk alternatives

These medicines are lower risk alternatives when prescribing or recommending analgesics to patients of addiction as they provide pain relief without stimulating the reward pathway of the brain's limbic system:

- Tylenol (acetaminophen)
- NSAIDs:
  - Advil (ibuprofen)
  - Aleve (naproxen)
  - Anaprox (naproxen)
  - Cataflam (diclofenac)
  - Celebrex (celecoxib)
  - Daypro (oxaprozin)
  - Indocin (indomethacin)
  - Mobic (meloxicam)
  - Motrin (ibuprofen)
  - Naprosyn (naproxen)
  - Orudis (ketoprofen)
  - Relafen (nabumentone)
  - Toradol (ketorolac)
  - Voltaren (diclofenac)

NSAIDs and APAP

Moore PA, Hersh EV. Combining ibuprofen and acetaminophen for acute pain management after third molar extractions. *JADA.* 2013;144(8):898-908.

- Looked at the number needed to treat (NNT), defined as “the number of patients needed to be treated to obtain one additional patient achieving at least 50 percent maximum pain relief over 4 to 6 hours compared with placebo” of 59 systemic, quantitative, evidence based reviews published by the Cochrane Collaboration.
- The lowest NNT was found to be 1.6 (95% CI, 1.4 – 1.8) for the combination of 200 mg ibuprofen with 500 mg APAP compared to a 2.2 NNT (95% CI, 1.8-2.9) for 60 mg codeine and 1000 mg APAP combination and 2.3 NNT (95% CI, 2.0-6.4) for 10 mg oxycodone and 650 mg acetaminophen combination.

Summary

Opioids and opiates are problem drugs when used in patients of addiction due to their manipulation of the brain's "reward system".

- Dopamine release in the brain's limbic system creates pleasure and euphoria in the opiate user.
- "Conditioned associations" associate these feelings with the drug that induced them, leading to cravings and potential addiction.

Non-narcotic analgesics are less risky alternatives for pain relief without the risks of addiction.

- NSAIDs and acetaminophen

Lower risk	Gray Area	Higher risk
• NSAIDs • Acetaminophen		• Opiates and opioids

Muscle Relaxants

A diverse class of drugs that do not share a common chemical structure or mechanism of action.

- **Grouped together solely on the basis of the indication approved by the FDA.**

Indications:

- Muscle spasticity (upper motor neuron syndrome): A chronic condition caused by damage to the brain of spinal cord that results in painful and debilitating involuntary muscle spasms.
  - Muscles display hypertonia and hyperreflexia
  - Ex.) Multiple sclerosis, cerebral palsy, stroke
- Muscle Spasms: An acute condition involving local factors of specific muscle groups rather than nerve damage in the central nervous system.
  - Muscles do not display hypertonia or hyperreflexia
  - Ex.) Tension headaches, neck and back pain, fibromyalgia

Why they are risky for recovering folks

Centrally acting skeletal muscle relaxers are typically not abused alone, but are often taken along with other central nervous system depressants such as alcohol, benzodiazepines, and narcotics.

- Central nervous system depression creates anxiolytic and sedative properties
- The relaxant works synergistically to prolong or even increase the effects of the other abused substance

Additionally, when used for a prolonged duration of time, withdrawal symptoms such as anxiety, tremors, insomnia and in some cases hallucinations and seizures may result.

Muscle relaxants with and abusive dependency potential:

- Flexeril (cyclobenzaprine)
- Dantrium (dantrolene)
- Lioresal (baclofen)
- Norflex (orphenadrine)
- Parafon Forte (chlorzoxazone)
- Robaxin (methocarbamol)
- Skelaxin (metaxalone)
- Soma (carisoprodol)
- Zanaflex (tizanidine)

Lower risk alternatives

Analgesia:

- Acetaminophen and NSAIDs are currently recommended as first line therapy for acute muscle spasms and may also help to relieve pain associated with the involuntary muscle spasms associated with muscle spasticity.

Non-pharmacological Treatment

- Physical therapy
- Exercise therapy
- Manipulation or mobilization
- Progressive relaxation
- Massage
- Yoga
- Acupuncture
- Heating pads

Summary

Centrally acting skeletal muscle relaxants that induce central nervous system depression rather than directly inducing skeletal muscle relaxation in the periphery have addiction potential due to their anxiolytic and sedative properties.

Muscle relaxants are rarely abused on their own but are more often used to prolong or enhance the effects of other abused substances such as alcohol and narcotics.

NSAIDs and acetaminophen along with non-pharmacological therapies are safe alternatives to muscle relaxants to avoid the risk of abuse and dependency.

Lower risk	Gray Area		Higher risk
• NSAIDs • Acetaminophen	• Flexeril (cyclobenzaprine) • Dantrium (dantrolene) • Lioresal (baclofen) • Norflex (orphenadrine) • Parafon Forte (chlorzoxazone)	• Robaxin (methocarbamol) • Skelaxin (metaxalone) • Soma (carisoprodol) • Zanaflex (tizanidine)	

Things to consider

People in recovery must be especially careful when taking any kind of over-the-counter (OTC) or prescription medications.

- Many OTC meds contain alcohol or other ingredients that could endanger their sobriety by triggering a relapse.
- People in recovery must be vigilant in protecting their sobriety. They must read ingredients, ask questions, and use much caution in using any kind of medication.
- Golden Rule: If in doubt about a specific medication, contact your pharmacist/addictionologist or another knowledgeable person for guidance.
- Having an expert in the field of addiction manage medication regimens on patients who are in recovery is vital IMHO. MTM (medication therapy management)

Research done by:

Katie Gordon, Pharm.D. Candidate
University of Missouri- Kansas City School of Pharmacy at MU

Jessica Luebbering, Pharm.D. Candidate
University of Missouri- Kansas City School of Pharmacy at MU

Brent Curry, Pharm.D. Candidate
University of Kentucky College of Pharmacy

Eva Atala, Pharm.D. Candidate
Sullivan University College of Pharmacy

Travis Huber, Pharm.D. Candidate
Purdue University College of Pharmacy

References

1. Ramakrishnan K, Scheid DC. Treatment options for insomnia. Am Fam Physician. 2007 Aug; 76(4):517-26
2. Psychiatr Clin N Am 2006;29:871-919
3. *Guide for safe recovery*. (2008). Atlanta: Talbott Recovery Campus. https://www.talbottcampus.com/pdf/MedGuide.pdf (accessed 10/19/2014
4. "Postoperative Pain Relief and Non-opioid Analgesics." *The Lancet* 337.8740 (1991): 524-26. *Safe Drug Use for the Recovering Addict or Alcoholic*. Ridge View Institute, 01 Sept. 2012. (accessed 10/19/2014)
3. Clatts M, Giang L, Goldsamt L, Colon-Lopez V. Nonmedical use of promethazine hydrochloride among heroin injectors in Vietnam: Unrecognized risks and unintended consequences. Substance Use & Misuse. 2010; 45:515-527.
4. Drugfacts: Cough and Cold Medicine Abuse. Bethesda: National Institute on Drug Abuse; 2014 [cited 2014 October 27]. Available from http://www.drugabuse.gov/drugs-abuse/emerging-trends
5. Drugs, Brains, and Behavior: The Science of Addiction. Bethesda: National Institute on Drug Abuse; 2014 [cited 2014 October 27]. http://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain
6. Promethazine. In: Lexi-drugs online [database on the Internet]. Hudson (OH): Lexicomp, Inc.; 2013 [cited 2014 October 27]. Available from: http://online.lexi.com.
7. Shapiro B, Lynch K, Toochinda T, Lutnick M, Cheng H, Kral A. Promethazine misuse among methadone maintenance patients and community-based injection drug users. J Addict Med. 2013; 7(2):96-101
8. Substance Abuse and Addiction Help Center. WedMD. Available at: http://www.webmd.com/mental-health/addiction/painkillers-and-addiction-narcotic-abuse. Accessed October 12, 2014.
9. The Science Behind Drug Abuse. National Institute on Drug Abuse. Available at: http://teens.drugabuse.gov/drug-facts/prescription-pain-medications-opioids. Accessed October 12, 2014.
10. Kosten TR, George TP. The Neurobiology of Opioid Dependence: Implications for Treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20.
Evaluating Prescription Drugs Used to Treat Muscle Spasms and Spasticity. Consumer Health Reports. Available at:
11. http://consumerhealthchoices.org/wp-content/uploads/2012/08/BBD-MuscleRelaxants-Full.pdf. Accessed October 12, 2014.

Questions?

Brian Fingerson, RPh

202 Bellemeade Road

Louisville, KY 40222-4502

502-749-8385

Email = kyprn@att.net