

C.O.R.E. Medical Clinic, Inc.

Opioid Presentation


2-28-17

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Pharmacology of opioids*

- ◆ Brain produces natural opioids
- ◆ Brain does not discriminate between natural opioids and opioids that are self-administered, including heroin
- ◆ Natural opioids are involved in a variety of behaviors including:
 - Analgesia
 - Mood
 - Digestion
 - Blood pressure
 - Body temp
 - Respiration
 - Sleep

Pharmacology cont.*

- ◆ Natural opioids play an integral role in the brain's pleasure/reward system
 - ◆ Brain responds to external opioids as if they were biologically essential for survival
 - ◆ When opioid addiction is full blown, the brain chemistry becomes imbalanced and the nervous system is left in an unbalanced state (i.e. withdrawal, pain, craving, etc.)
 - ◆ Creates emotional, mental, and physical distress until more opioids are administered
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Pharmacology cont.*

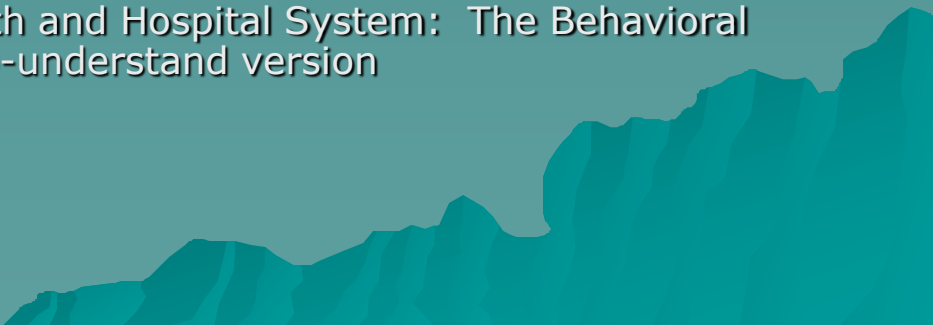
◆ Lock and Key

- If the correct neurotransmitter “key” fits into and “unlocks” the receptor site, then communication between neurons occurs
- Endorphins are chemical “keys” that “unlock” opiate receptor sites
- Endorphins and opioid drugs will bind to opiate receptors and signal a response.
- 3 most studied opiate receptors
 - ◆ Mu
 - ◆ Delta
 - ◆ Kappa

Pharmacology cont.*

- ◆ Some drugs bind with greater strength at the receptor site, therefore producing more “euphoria”
- ◆ EX: Heroin has a greater affinity for binding to the mu, delta, and kappa opiate receptor sites in comparison to morphine, which means heroin will provide a more intense euphoric affect than morphine

*Mark Stanford, PhD, Santa Clara Valley Health and Hospital System: The Behavioral Pharmacology of Methadone: The Easy-to-understand version

A stylized, layered mountain range graphic in shades of teal and blue, located in the bottom right corner of the slide.

Illicit Opioids

- ◆ Heroin
- ◆ Opium
- ◆ Krokodil (crocodile)
 - Desomorphine – shorter acting (high lasts 1 ½ to 2 hours)
 - ◆ Skin turns green and scaly at injection site
 - ◆ Cook codeine with other ingredients (ex: paint thinner, gasoline, hydrochloric acid, red phosphorous and iodine)
- ◆ Home Brewed Heroin – converting yeast into morphine using a complicated 15 step metabolic pathway {Stanford Scientist Christina Smolke discovered final few steps, UC Berkeley and Concordia University (Quebec) filled in the earlier steps}
- ◆ Speed balls (Heroin/morphine and cocaine/amphetamine derivative combined = Depressant and Stimulant)

Prescription Opioids – short acting

- ◆ Short acting (every 2-6 hours)
 - Codeine
 - Fentanyl
 - ◆ Actiq, Duragesic, Fentora
 - Morphine
 - ◆ Avinza, Kadian, MS Contin, Ora-Morph SR
 - Hydrocodone
 - ◆ Lorcet*, Lortab*, Norco*, Vicodin*
 - Hydromorphone
 - ◆ Dilaudid, Exalgo
 - Oxycodone
 - ◆ Oxyfast, Percolone, Roxicodone, Percocet*

* = contains acetaminophen

Prescription Opioids – long acting

- ◆ Long acting (12+ hours)
 - Oxycontin
 - ◆ Extended Release (ER) oxycodone
 - Zohydro
 - ◆ Extended Release (ER) hydrocodone
 - Opana
 - ◆ Extended Release (ER) hydromorphone
 - Fentanyl patch
 - ◆ Time release fentanyl
 - Methadone
 - ◆ Dolophine, Methadose
 - Buprenorphine
 - ◆ Suboxone, Subutex

Treatment for Opioid Addiction

(80% of people with an opioid use disorder are not receiving treatment)

- ◆ Methadone
- ◆ Buprenorphine
- ◆ Naltrexone
 - Compliance issues
 - Doesn't prevent withdrawal syndrome
 - Vivitrol – extended release naltrexone
 - ◆ Monthly injection
- ◆ Cold turkey



Methadone

◆ BENEFITS

- Long half life = 24-36 hours
- Blocking effect
- Prevents withdrawal symptoms
- Gold standard for treating pregnant women addicted to opioids
- Liver safety – breaks down and stores methadone

◆ Formulations

- Liquid
 - ◆ Sugar free (diabetics)
 - ◆ Regular (different agents are mixed to change taste – cherry and orange are the most commonly used)
- Tablets
 - ◆ 5mg
 - ◆ 10mg
 - ◆ 40mg (new law that only allows NTPs to use)

Buprenorphine

- ◆ Two forms
 - Subutex tablet: pure buprenorphine hydrochloride
 - Suboxone film: buprenorphine hydrochloride mixed with naloxone (aka narcan) on a 4:1 ratio
- ◆ Formulations:
 - Formulations: sublingual tablet or film that takes ~5-10 min. to absorb

<u>Subutex (tablet)</u>	<u>Suboxone (film)</u>
◆ 2mg	2mg bup/0.5mg naloxone
◆ 4mg	4mg/1mg
◆ 8mg	8mg/2mg
◆ 12mg	12mg/3mg
- ◆ Benefits
 - Long half life = 37 hours (naloxone = 1.1 hrs)
 - Blocking effect
 - Prevents withdrawal symptoms
 - Ceiling effect – safety mechanism
 - Generic medications are now available, including implants and buckles (attach to cheek)

Zubsolv

- ◆ Sublingual tablet that rapidly dissolves under your tongue (2 minutes or less in most cases)
- ◆ Formulations (contains naloxone)
 - 5.7mg (acts similar to 8mg suboxone/subutex)
 - 1.4mg (acts similar to 2mg suboxone/subutex)
- ◆ Benefits
 - Long half life = 37 hours Blocking effect
 - Prevents withdrawal symptoms
 - Very little gets lost in saliva due to rapid absorption
 - Ceiling effect – safety mechanism
- ◆ Studies:
 - Measured blood levels at different intervals were the same for 5.7 Zubsolv as they were for the buprenorphine formulations

Historical Perspective

- ◆ Drug Addiction Treatment Act (DATA) 2000
 - Allows qualified physicians to treat opioid dependence in a office based setting with schedule III, IV, or V drugs
- ◆ In 2002, buprenorphine was approved for the management of opioid dependence
- ◆ 2009, Roxanne laboratories developed a generic for subutex
 - Several generic products have been introduced to the market over the last 3 years

Pregnancy

- ◆ Methadone is safe to use with pregnant women
 - Used on pregnant women since the 1960s and is considered the “standard of care” by CSAT
- ◆ Buprenorphine is only recommended in treating pregnant patients when the MD believes the potential benefits outweigh the risks.
 - Treatment access issues, already taking bup, stigma of methadone
 - International clinical trial in progress called the MOTHER (Maternatal Opioid Treatment Human Experimental Research) project, which will include 175 participants

2015 Pregnancy Data

- ▶ Deliveries = 8
- ▶ Average Weight = 6 lbs 12 oz
- ▶ Average Height = 18.70 inches
- ▶ Average Dose at Delivery = 73
- ▶ % Babies on Meds = 25%
- ▶ Average Weeks Pregnant = 38
- ▶ Average Days Baby Stayed in Hospital = 4
- ▶ Negative Drug Screens at Delivery = 88%

Dangers of Methadone

◆ Induction

- Start slow
- Patient views: Tolerance and Withdrawal concerns

◆ Heart – QTc interval

- CSAT/SAMHSA trying to develop a standardized protocol
- 2% of population is at risk (1% of those 2% may experience an adverse effect)
- “By entering treatment patients are taking a risk. The greater risk is not getting treatment” Mark Parrino, president of AATOD
- Levo-Alpha Acetyl Methadol (LAAM) was taken off the market due to increased risk of cardiac death

Dangers of Methadone

- ◆ Overdose potential – exacerbated by benzodiazepine abuse
 - Number of methadone deaths increased fivefold between 1999 and 2005. The US Gov. Accountability Office (GAO) attributes this to an increase in prescription methadone which increased eightfold between 1998 and 2006.
 - From 1999 to 2006 the number of fatal poisonings involving opioids more than tripled.

Benzodiazepines

- ◆ Class IV drug
- ◆ Most commonly prescribed medications in the US
 - Most common benzos are klonopin, xanax, ativan, restoril & valium
- ◆ Benzos act by depressing the CNS and prescribed to treat anxiety, sleep disorders, and depression.
- ◆ If taken as prescribed, benzos have a good safety profile
- ◆ Do not take within 2 hours of methadone
- ◆ If abused along with methadone you can achieve a heroin like high
 - Rationalization re: prescriptions

Overdoses

- ◆ Respiratory depressants
- ◆ ~1/2 of deaths involving opioids involve more than one drug with benzos being the most common (Data from the National Vital Statistics System Mortality File)
- ◆ Avoid relationships with “Pams” if at all possible.
- ◆ Anna Nicole Smith – 9 drugs*
 - 3 opioids (morphine, methadone, & hydromorphone)
 - 2 benzos (flurazepam & diazepam)
- ◆ Heath Ledger – 9 drugs*
 - 2 opioids (oxycodone & hydrocodone)
 - 3 benzos (diazepam, alpraxolam, temazepam)
 - 1 OTC sleep aid (doxylamine)

*AT Forum Volume 19, #2, Spring 2009

Recent opioid overdoses

- ◆ 78-91 people die from an OD related to heroin and prescription drugs on average each day
- ◆ Deaths
 - Prince – died from fentanyl OD
 - ◆ Emergency plane landing 6 days earlier due to OD on percocet (narcan saved him)
 - Philip Seymour Hoffman – died from heroin, cocaine, benzodiazepine, and amphetamine OD (found w/ needle still in his arm)

Liberalization of prescribing opioids

- ◆ By 2004, Oxycontin became the most prevalent abused prescription opioid in the United States
- ◆ Part of the problem: Liberalization of use of opioids due to underprescribing
 - Increase in treatment of chronic non-cancer related pain
 - 1997 thru 2002
 - ◆ 73% increase in morphine prescriptions
 - ◆ 226% increase in fentanyl prescriptions
 - ◆ 402% increase in oxycodone prescriptions

Source: Van Zee, A., The Promotion and Marketing of Oxycontin: commercial triumph, public health tragedy. *American Journal of Public Health*. 2009;99:221-226

Rise in Oxycontin Use

- ◆ What is it?
 - Oxycodone with a sustained-release preparation
 - Remove the capsule, you remove the sustained-release component
- ◆ Under advertising addictive properties resulted in a \$634 million law suit
 - Purdue Pharma – sales grew from \$48 million in 1996 to \$1.1 billion in 2000
 - In 2001, Purdue spent ~\$200 million in marketing and promotion of oxycontin
 - ◆ Includes \$40 million in bonuses to pharmaceutical reps (\$15k-\$240K per year per rep)

Source: Van Zee, A., The Promotion and Marketing of Oxycontin: commercial triumph, public health tragedy. *American Journal of Public Health*. 2009;99:221-226

Recent History

- ◆ 1/12/16 State of the Union Address from President Obama
 - One of the first things he mentions is having to come up with a solution for the prescription drug and heroin epidemic
 - CDC has declared this a national epidemic
 - ASAM study determined that health care claims for people with opioid dependence increased 3000% from 2007-2014 (217K to 7 million medical services)


Fentanyl – Sac County

- ◆ DEA reports indicate that the Mexican cartel is obtaining pure fentanyl from China
- ◆ 54 overdoses between 3/25/16-4/10/16, including 13 deaths (11 Sac County, 1 El Dorado County, and 1 Yolo county resident)
- ◆ Age ranges = 18-67 years old
- ◆ Disguised as Norco


Statistics - ASAM

- ◆ 1.9 million Americans live with prescription opioid abuse or dependence
- ◆ 517,00 Americans live with heroin addiction
- ◆ Over 100 Americans die each day from drug overdoses
- ◆ 46 Americans die each day from prescription opioid overdoses
- ◆ 8,200 Americans die annually from heroin ODs
- ◆ 75% of opioid addiction disease patients switch to heroin as a cheaper opioid source
- ◆ In 2012, 259 million opioid pain medication prescriptions were written, enough for every adult American to have a bottle of pills
- ◆ Everyday 2,500 American youth abuse a prescription pain reliever for the first time
- ◆ Every 3 minutes a woman goes to the ER for prescription painkiller misuse or abuse


Other Statistics

- ◆ DEA has ordered a 25% decrease in the manufacturing of many schedule II opioid medications, including a 34% decrease in hydrocodone production
 - ◆ 6 out of 10 ODs were opioid related
 - ◆ 6.5 million Americans over the age 12 used a controlled prescription medication for non-medical purposes in 2015
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Societal Costs

- ◆ Total US societal costs of prescription opioid abuse were estimated at \$55.7 billion in 2007 accounting for healthcare, workplace, and criminal justice costs.
 - ◆ In 2011, there were 420,040 emergency dept. visits involving nonmedical use of opioids.
 - ◆ Prescription opioid-related ODs now outnumber OD deaths involving all illicit drugs combined (including heroin)
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How do we combat this new epidemic?

- Education in home, schools, community, etc.
 - Proper treatment placement: cutting to the chase
 - Monitoring (clinical and medical staff, CURES reports if possible) in medical, outpatient, and inpatient facilities
 - Use of EMR
 - Access to sterile (“clean”) syringes/needles/works
 - Universal Good Samaritan laws
 - Overdose prevention: Naloxone
 - HCV and HIV identification and treatment
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Naloxone

- ◆ Naloxone or Narcan is the medication that reverses OPIOID overdoses. This does not work on other drug overdoses, such as cocaine or methamphetamine overdoses
- ◆ Naloxone kicks the opioids off the receptor site, which revives the individual. The individual will be in opioid withdrawal when they are revived since there are now no opioids on the receptor site.
- ◆ National push to make naloxone more available
- ◆ Training with rescue breathing is recommended, but not required
- ◆ Versions: syringe/vial, nasal spray, automated shot with verbal computerized instructions
- ◆ CORE has a standing order for its patients to received the automated shot naloxone at Physician's Building Pharmacy in Midtown Sacramento
- ◆ HRS does monthly training for our patients, which includes educational materials, overdose kit including two doses of naloxone, two syringes, and alcohol swabs

Future Challenges


- ◆ Stigma – stigma has been reduced as evidenced by residential programs and increases in outside referrals, less resistance from PCPs, etc.
- ◆ STILL EXISTS: Unfortunately it still exists in the AOD and medical communities, which is a real disservice to opioid addicts
 - We are supposed to be able to help, not shame those in seek of appropriate treatment
 - Feeds into self defeating thoughts and feelings of failure
- ◆ How do we reduce stigma? EDUCATION, EDUCATION, EDUCATION
 - Example: 9/17/13 training at county on Opiates and the Brain with patient stories

Future Challenges – cont.

- ◆ New population to treat now
 - Different age groups
 - ◆ Younger generation = oxycontin
 - ◆ 2.8 million older adults abused prescription drugs within the last year
 - Different reasons for entering treatment
 - ◆ Injuries (ex: car accident)
 - Different reasons for beginning drug use
 - ◆ Access – diverted from prescriptions by family/friends or for profit, doctor/dentist shopping, ER visits, etc.
 - ◆ Ex: Younger generation believe prescription medications are safe (In 2005, 2.1 million new drug users identified prescription opioids as the 1st drug they tried, which is higher than marijuana and almost = to the # of new cigarette smokers of 2.3 million)

Sacramento County Opioid Task Force


◆ Four subcommittees

- Engaging the Medical Community/Overdose Prevention
 - Early Intervention/Treatment and Recovery
 - Public Education and Media/Advocating For Change
 - Safe Medication Disposal
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CDPH Opioid Dashboard

- ◆ Sacramento County statistics
 - 2015 = 830.66 opioid prescriptions per 1000 Sacramento residents
 - 2014 = 18.5 opioid OD inpatient hospitalizations per 100,000 residents
 - ◆ 13.4 opioid OD ER visits per 100,000
 - ◆ 3.85 opioid OD deaths per 100,000

C.O.R.E. – services offered

- ◆ Methadone/Buprenorphine treatment
 - Maintenance and Detox (ST & LT)
 - ◆ Individual and group counseling
 - ◆ Psychiatric services (free of charge)
 - ◆ Limited medical services (Hep A & B vaccines, Hep C screening, abscess treatment, TB testing, urinalysis testing, etc.)
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