Psychopharmacology

Part 3

Presented by Demetra Antimisiaris, PharmD, CGP, FASCP
Associate Professor
Department of Family Medicine and Geriatrics
Associate, U of L Department of Neurology
PART 3

- Pain Medications
- Polypharmacy
- Cannabis
- Hallucinogens
- Steroids
Two pathways originating in lower brain stem modulate transmission of pain.
  – Physical component
  – Descending NE and 5HT which activate endorphin neurons. (antidepressants can effect too)

Affective component and emotional response to pain.
  – Chronic pain treatment focuses on behavioral modification, CBT, biofeedback

Judicious opioid use is important
Controlled Substances Guidelines

The following should be documented in every chart when chronic controlled substances are being prescribed.

Guidelines per Kentucky Medical Board of Licensure

1. Complete History and Physical to Include:
   (date completed)
   - Nature and intensity of the pain/condition
   - Current and past treatments for pain/condition
   - Underlying or coexisting disease or condition
   - Effect of the pain/condition on physical and psychological function
   - History of any substance abuse
   - Family History, esp. any 1st degree relative with chemical dependence problems

2. Document 1 or more recognized medical indication(s) for the use of the controlled substance
   (date completed)

3. Document through patient records or clinical trial that non-addictive medication regimens have been inadequate or unacceptable for solid clinical reasons
   (date completed)

4. Kasper report initially and as needed to aid in documenting the patient’s history of drug utilization (needs to be kept separate from chart)
   (date completed)

5. Signed Controlled Substances Contract on chart.
   (date completed) Controlled Substance Contract not applicable because:

6. Documented Treatment Plan
   (date completed)

7. Documented discussion of risk, benefits, and limitation of treatments
   (date completed)

8. Documentation of Medication: Date, Type, Dosage, Quantity, and Refills
   (date completed)

   (date completed)

10. Document diagnostic, therapeutic, laboratory results, and consultations or evaluations
    (date completed)
Table 3. Factors Associated with the Risk of Opioid Overdose or Addiction.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication-related</td>
<td></td>
</tr>
<tr>
<td>Daily dose &gt;100 MME*</td>
<td>Overdose, addiction</td>
</tr>
<tr>
<td>Long-acting or extended-release formulation (e.g., methadone, fentanyl patch)</td>
<td>Overdose</td>
</tr>
<tr>
<td>Combination of opioids with benzodiazepines</td>
<td>Overdose</td>
</tr>
<tr>
<td>Long-term opioid use (&gt;3 mo)†</td>
<td>Overdose, addiction</td>
</tr>
<tr>
<td>Period shortly after initiation of long-acting or extended-release formulation (&lt;2 wk)</td>
<td>Overdose</td>
</tr>
<tr>
<td>Patient-related</td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 yr</td>
<td>Overdose</td>
</tr>
<tr>
<td>Sleep-disordered breathing‡</td>
<td>Overdose</td>
</tr>
<tr>
<td>Renal or hepatic impairment‡</td>
<td>Overdose</td>
</tr>
<tr>
<td>Depression</td>
<td>Overdose, addiction</td>
</tr>
<tr>
<td>Substance-use disorder (including alcohol)</td>
<td>Overdose, addiction</td>
</tr>
<tr>
<td>History of overdose</td>
<td>Overdose</td>
</tr>
<tr>
<td>Adolescence</td>
<td>Addiction</td>
</tr>
</tbody>
</table>

‡ The risk of opioid overdose increases in a dose–response manner at opioid doses of more than 20 morphine milligram equivalents (MME).
† Although addiction is associated with long-term but not short-term opioid use, the prescription of a higher quantity of opioids than is needed for acute pain contributes substantially to the availability of opioids for diversion and abuse.
‡ Sleep-disordered breathing refers to conditions that manifest as abnormal breathing patterns during sleep and includes obstructive sleep apnea and central sleep apnea.
§ Patients with these disorders are at increased risk because the disposition of various opioid drugs is affected by hepatic and renal impairments, which reduce drug clearance and increase bioavailability.
Table 4. Mitigation Strategies against Opioid Diversion and Misuse.

Several mitigation strategies for risk assessment of opioid misuse have been proposed.\textsuperscript{74} These include the following:

**Screening tools to identify patients with a substance-use disorder.** Such tools include the Opioid Risk Tool; the Screener and Opioid Assessment for Patients with Pain (SOAPP), version 1.0; SOAPP-Revised; and the Brief Risk Interview; or the use of a simple question such as “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?” since patients who score above a certain threshold (e.g., ≥1 to the sample question) may be at increased risk for opioid abuse.\textsuperscript{75}

**Use of data from the Prescription Drug Monitoring Program.** Such data can be used to identify doctor shopping, which is frequently an indication of drug misuse or diversion.

**Use of urine drug screening.** Such screening, which can be performed before prescription of opioids and periodically as part of regular follow-up, can provide information on drug use not reported by patients and may help in identifying patients who are not taking their prescribed opioids and might be diverting them.

**Doctor–patient agreement on adherence.** Such personal contracts can help doctors in monitoring a patient’s adherence to prescribed opioid medications.

However, a recent review of the evidence showed that only limited data are available regarding the efficacy of any of these strategies.\textsuperscript{76}
OPIOID RECEPTORS

• Opioid Receptors
  – Mu Receptors
  – Kappa Receptors
  – Delta Receptors

• Classification
  – Pure agonists
  – Pure antagonists
  – Mixed antagonists – antagonists
  – Partial agonists
• **Effects**
  – Analgesia
  – Bradycardia
  – Respiratory depression
  – Physical dependence
  – Euphoria
  – Can release histamine
  – Stimulates chemoreceptor trigger zone (nausea)
  – Suppress cough

• **Tolerance and Dependence**
  – Molecular basis is thought to involve glutaminergic mechanism
  – Activation of NMDA receptors correlates to resistance
  – Glutaminergic receptors (NMDA) may regulate mRNA of mu receptors
  – Ketamine found to prevent late onset and long lasting enhancement in pain sensitivity after initial analgesic effect dissipated.
# Opioid Effects

## Table 9.1: Acute Effects of Opioids and Rebound Withdrawal Symptoms

<table>
<thead>
<tr>
<th>Acute Action</th>
<th>Withdrawal Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia</td>
<td>Pain and irritability</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Hyperventilation</td>
</tr>
<tr>
<td>Euphoria</td>
<td>Dysphoria and depression</td>
</tr>
<tr>
<td>Relaxation and sleep</td>
<td>Restlessness and insomnia</td>
</tr>
<tr>
<td>Tranquilization</td>
<td>Fearfulness and hostility</td>
</tr>
<tr>
<td>Decreased blood pressure</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Constipation</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Pupillary constriction</td>
<td>Pupillary dilation</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Hyperthermia</td>
</tr>
<tr>
<td>Drying of secretions</td>
<td>Lacrimation, runny nose</td>
</tr>
<tr>
<td>Reduced sex drive</td>
<td>Spontaneous ejaculation</td>
</tr>
<tr>
<td>Peripheral vasodilation</td>
<td>Chilliness and “gooseflesh”</td>
</tr>
</tbody>
</table>
Treatment of dependence:

Old theory: medically managed withdrawal to opioid free state.

Newer theory: lifelong opioid maintenance

Area of great debate.
Medical literature shows increased rate of mortality with use of opioids.
<table>
<thead>
<tr>
<th>DRUG (GENERIC)</th>
<th>DOSAGE</th>
<th>MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxecta</strong> (oxycodone HCl)</td>
<td>5, 7.5 mg (tablets)</td>
<td>AVERSION technology impedes opioid extraction via dissolution of tablets using water or alcohol, which causes the tablet to form into a viscous gel, trapping the active ingredient</td>
</tr>
<tr>
<td><strong>Exalgo</strong> (hydromorphone HCl)</td>
<td>8, 12, 16, 32 mg (tablets)</td>
<td>Osmotic Extended-Release Oral Delivery System (OROS) technology uses an osmotically active bilayer core enclosed in a semipermeable tablet shell membrane that allows both a consistent 24-h delivery rate and provides a barrier to abuse</td>
</tr>
<tr>
<td><strong>Opana ER</strong> (oxymorphone HCl)</td>
<td>5, 7.5, 10, 15, 20, 30, 40 mg (tablets)</td>
<td>INTAC is a tamper-resistant technology designed to prevent modification of the drug into a fine powder and provide resistance to dissolution via liquids, as the remnants of a broken tablet will form a viscous gel to trap the active ingredients</td>
</tr>
<tr>
<td><strong>OxyContin</strong> (oxycodone HCl)</td>
<td>10, 15, 20, 30, 40, 60, 80, 160 mg (film-coated tablets)</td>
<td>Reformulated to form viscous hydrogel when mixed with aqueous liquid for dissolution</td>
</tr>
<tr>
<td><strong>Suboxone</strong> (buprenorphine/naloxone)</td>
<td>2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg (sublingual film)</td>
<td>Combines buprenorphine, a partial opioid agonist-antagonist, and naloxone, an opioid antagonist. Buprenorphine provides analgesia while its combination with naloxone prevents IV abuse</td>
</tr>
</tbody>
</table>
Table 2. Formulations for Deterrence of Abuse.

When opioids are diverted because of their rewarding effects, they are typically taken at higher doses than were originally prescribed. In other cases, the pills are crushed so that the drug can be snorted, smoked, or injected. These routes of administration result in faster drug delivery into the brain, which in turn is associated with a rapid and more intense drug effect. Thus, strategies for abuse-deterrent formulations have been developed to minimize the likelihood that the opioids will be injected or snorted or taken at higher doses than prescribed.27,28 These strategies include the following:

**Combining the opioid agonist with an antagonist.** Mixing the opioid with naloxone or naltrexone will interfere with the opioid effects if the drug is injected but not if it is taken orally or sublingually. Examples include Embeda (morphine sulfate plus naltrexone hydrochloride) and Targiniq ER (oxycodone plus naloxone).

**Delivering the opioid in a form that cannot be crushed and extracted.** Examples of such drug-delivery technologies include opioids approved by Food and Drug Administration (FDA) in abuse-deterrent formulations such as Hysingla (hydrocodone) and the new formulation of OxyContin (oxycodone), as well as opioids not approved as abuse-deterrent formulations, including Exalgo (hydromorphone), Nucynta ER (tapentadol), Opana ER (oxymorphone), Oxecta (oxycodone), and Xartemis (oxycodone and acetaminophen).

**Combining the opioid with a substance that triggers an adverse response.** If the drug is tampered with or used at a higher dose than indicated, such formulations are designed to produce adverse results. Examples include Lomotil (diphenoxylate hydrochloride plus atropine) and Acurox (oxycodone plus niacin).

**Developing prodrugs that require enzymatic activation.** Such formulations could provide a chemical barrier to in vitro conversion into the active opioid. There are currently no abuse-deterrent formulations approved by the FDA that use this strategy. Examples being developed include prodrugs for hydrocodone, oxycodone, and hydromorphone that require molecular cleavage by trypsin in the digestive system to release the parent opioid.
• 4:1
• Sublingually, naloxone exerts no clinically significant effect leaving buprenorphine to predominate.
• IV, physically dependent patients will experience withdrawal effects of naloxone.
• Buprenorphine has ceiling effects which limits addiction risk.
Hepatic (liver) toxicity
• Reversibly blocks effects of opioids.
• Low dose naltrexone:
  – Inhibiting opioid receptors cause body to increase production of endorphins or encephalins to compensate for blocked receptors.
  – Persist after naltrexone has been eliminated from body.
  – Use in pain, fibromyalgia, fatigue thought to be due to effect on microglia which can modulate body’s response to inflammation. (anti-inflammatory)
• Combination with opioids (oxycodone) w ultra low dose naltrexone to block paradoxical hyperalgesia of long-term use opioid withdrawal.

Methylnatrexone (Relistor®): μ-opioid antagonist (peripherally acting) which effects constipation, itching, without effecting analgesia or precipitating withdrawals.
METHADONE

Synthetic opioid used for maintenance therapy, blocks euphoric effects seen with opiates.

- Popularity increasing among physicians for chronic pain treatment.
- Has NMDA receptor activity and helps neuropathic pain better than many opiates. Decreased anti-nociceptive (reduced sensitivity to painful stimuli) effect of opioids.  
  - (+ μ opioid receptor activity)
- Tolerance may be lesser than other opioids.
- Inexpensive.
- Q-T prolongation and sudden cardiac death risk requires EKG monitoring.
### Table 5. Alternative Treatments for Chronic Pain.*

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonpharmacologic</strong></td>
<td>Cognitive-behavioral therapy(^{109})</td>
</tr>
<tr>
<td></td>
<td>Exercise therapy(^{110-113})</td>
</tr>
<tr>
<td></td>
<td>Complementary medicine(^{114}) (e.g., yoga, meditation, acupuncture)</td>
</tr>
<tr>
<td><strong>Nonopioid analgesics</strong></td>
<td>Acetaminophen</td>
</tr>
<tr>
<td></td>
<td>Nonselective nonsteroidal antiinflammatory drugs; recommended as first-line pharmacotherapy for osteoarthritis(^{115}) and low back pain(^{118}) in multiple guidelines</td>
</tr>
<tr>
<td></td>
<td>Cyclooxygenase-2 inhibitors</td>
</tr>
<tr>
<td></td>
<td>Anticonvulsants (gabapentin or pregabalin)†</td>
</tr>
<tr>
<td></td>
<td>Antidepressants (tricyclics and serotonin and norepinephrine reuptake inhibitors)†</td>
</tr>
<tr>
<td><strong>Interventional and neural-stimulation therapies</strong></td>
<td>Epidural injection; may provide short-term improvement for certain pain-associated conditions (e.g., lumbar radiculopathy)(^{1})</td>
</tr>
<tr>
<td></td>
<td>Brain, spinal cord, and nerve stimulation, including transcranial magnetic stimulation, transcranial direct current stimulation, electrical deep-brain stimulation, and stimulation devices for peripheral nerves or tissues(^{117-120})</td>
</tr>
<tr>
<td><strong>Biofeedback</strong></td>
<td>Electromyography to help patients learn to control muscle tension and electroencephalography to help patients learn to influence brain electrical signals in order to modulate pain; may be beneficial in treatment of headaches, some forms of chronic back pain, and other pain disorders(^{121})</td>
</tr>
<tr>
<td></td>
<td>Neurofeedback with the use of functional magnetic resonance imaging as a supplemental approach for chronic pain management(^{122})</td>
</tr>
</tbody>
</table>

* Evidence of efficacy varies for these strategies, and research is ongoing to assess their value in the management of chronic pain.
† Multiple guidelines recommend the use of antidepressant and anticonvulsant medications as either first-line or second-line treatment for neuropathic pain.\(^{123}\)
Cannabis

- Cannabinoid Receptor/therapeutic uses:
  - Weight loss drug (antagonist, pulled by EU after a few years)
  - Analgesia by modulating sensory input from tissue injury and reducing release of nociceptive neurotransmitters like substance P and glutamic acid.
  - Chronic pain syndrome use

- Effects:
  - Memory impairment
  - Increased appetite
  - Impairment to focus attention and filter out irrelevant information

- Side Effects:
  - Increased HR, BP, dry mouth, dizziness, slight nausea.

- Tolerance and Dependence:
  - Tolerance does develop
PSYCHEDELIC DRUGS/HALLUCINOGENS

• Anticholinergic psychedelics:
  – Scopolamine
  – Delirium
  – Drowsiness
  – Euphoria
  – Tachycardia, blurred vision, HTN, increased body temp.

• Catecholamine Like psychedelics:
  – Mescaline
  – Synthetic Amphetamine Derivatives
PSYCHEDELIC DRUGS/HALLUCINOGENS

• Serotonin like psychedelic drugs:
  – LSD
  – DMT
  – Psilocybin and Psilocin (mushrooms)
  – Ololiuqui
  – Phencyclidine (PCP- Ketamine related)

• Toxicity
  – Psychotic states
  – Recurrent major affective disorder (or persistent)
  – “burnout” disruption of personality or chronic brain syndrome.
Steroids

- Anabolic-androgenic steroids
  - Chemicals related to male hormone testosterone

- Mechanism of action
  - DHEA and androstenedione (precursor to testosterone)
  - Negative feedback on hypothalamus inhibits further stimulation of testosterone release

- Effects
  - Muscle building effects, masculinizing
  - Enhanced physical strength
  - Endurance
### TABLE 14.1 Anabolic-androgenic steroids

<table>
<thead>
<tr>
<th>Name</th>
<th>Route</th>
<th>Brand name</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>APPROVED IN UNITED STATES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone cypionate</td>
<td>im</td>
<td>Depo-Testosterone, Virilon</td>
</tr>
<tr>
<td>Nandrolone phenpropionate</td>
<td>im</td>
<td>Durabolin</td>
</tr>
<tr>
<td>Nandrolone decanoate</td>
<td>im</td>
<td>Deca-Duraboli</td>
</tr>
<tr>
<td>Danazol</td>
<td>po</td>
<td>Danocrine</td>
</tr>
<tr>
<td>Fluoxymesterone</td>
<td>po</td>
<td>Halotestin</td>
</tr>
<tr>
<td>Methyltestosterone</td>
<td>po</td>
<td>Android, Metandren, Testred, Virilon</td>
</tr>
<tr>
<td>Oxymetholone</td>
<td>po</td>
<td>Anadrol-50</td>
</tr>
<tr>
<td>Slanozolol</td>
<td>po</td>
<td>Winstrol</td>
</tr>
<tr>
<td><strong>APPROVED OUTSIDE UNITED STATES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone enanthate</td>
<td>im</td>
<td>Delatestryl</td>
</tr>
<tr>
<td>Testosterone propionate</td>
<td>im</td>
<td>Testex, Oreton propionate</td>
</tr>
<tr>
<td>Methenolone enanthate</td>
<td>im</td>
<td>Primobolan Depot</td>
</tr>
<tr>
<td>Ethylestrenol</td>
<td>po</td>
<td>Maxibolan</td>
</tr>
<tr>
<td>Mesterolone</td>
<td>po</td>
<td></td>
</tr>
<tr>
<td>Methandrostenolone</td>
<td>po</td>
<td>Dianabol</td>
</tr>
<tr>
<td>Methenolone</td>
<td>po</td>
<td>Primobolan</td>
</tr>
<tr>
<td>Norethandrolone</td>
<td>po</td>
<td></td>
</tr>
<tr>
<td>Oxandrolone</td>
<td>po</td>
<td>Anavar</td>
</tr>
<tr>
<td>Oxymesterone</td>
<td>po</td>
<td>Oranabol</td>
</tr>
<tr>
<td><strong>APPROVED FOR VETERINARY USE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bolasterone</td>
<td>im</td>
<td>Finject 30</td>
</tr>
<tr>
<td>Boldenone undecylenate</td>
<td>im</td>
<td>Equipoise</td>
</tr>
<tr>
<td>Stanozolol</td>
<td>im</td>
<td>Winstrol</td>
</tr>
<tr>
<td>Mibolerone</td>
<td>po</td>
<td></td>
</tr>
</tbody>
</table>
• Toxicity
  – Endocrine
  – Cardiovascular
  – Liver
  – Psychological
  – Aggressive behavior

• Dependence
  – Withdrawal symptoms when removed
  – Psychological depression, fatigue, restlessness, insomnia, loss of appetite, decreased libido.
### TABLE 14.2 Effects of anabolic-androgenic steroids

**POSITIVE EFFECTS**
- Transient increase in muscular size and strength
- Treatment of catabolic states
- Trauma
- Surgery

**ADVERSE EFFECTS**

**Cardiovascular**
- Increase in cardiac risk factors
- Hypertension
- Altered lipoprotein fractions
- Increase in LDL/HDL ratio
- Reported strokes/myocardial infarctions

**Hepatic effects associated with oral compounds**
- Elevated liver enzymes
- Peliosis hepatis (greater than 6 months' use)
- Liver tumors
- Benign
- Malignant (greater than 24 months' use)

**Reproductive system effects**
- In males
  - Decreased testosterone production
  - Abnormal spermatogenesis
  - Transient infertility
  - Testicular atrophy
- In females
  - Altered menstruation

**Endocrine effects**
- Decreased thyroid function

**Immunologic effects**
- Decreased immunoglobulins IgM/IgA/IgG

**Musculoskeletal effects**
- Premature closure of bony growth centers
- Tendon degeneration
- Increased risk of tendon tears

**Cosmetic**
- In males
  - Gynecomastia
  - Testicular atrophy
  - Acne
  - Acceleration of male pattern baldness
- In females
  - Clitoral enlargement
  - Acne
  - Increased facial/body hair
  - Coarsening of the skin
  - Male pattern baldness

**Psychologic**
- Risk of habituation
- Severe mood swings
- Aggressive tendencies
- Psychotic episodes
- Depression
- Reports of suicide

**Legislation**
- Classified as Schedule III controlled substance
POLYPHARMACY
What is Polypharmacy?

- 5 or more medications taken simultaneously
- More medications used than are clinically warranted.
- A Random Uncontrolled Experiment

Types of Polypharmacy
- Too many drugs
- Inappropriate choices
- Inappropriate combinations
- Administration errors
- Way off label use
- Inappropriate dosing
- Inappropriate prescriber
Silent Epidemic

A side effect of modern medical care

– 15 minute office visit/Hospital visit
– New drugs added annually
– Multiple specialists
– Over the counter products and supplements
A Pill for Every Ill
Total drug burden is important

Average of 2.8 drugs discontinued per patient

1 year mortality rate
- 45% in control
- 21% in study group

Annual referral rate to acute care
- 30% in control group
- 11.8% in study group

The U.S. consumes 80 percent of the world's opioids and 99 percent of its hydrocodone.

PBS News Hour June 2011
"If you remember, I did mention possible side-effects."
Signs of Medication Related Problems: ???

- mental status changes
  - Agitation
  - Manic behavior
  - Any change in affect
  - confusion
- Not eating
- Not sleeping
- Somnolence
- Falls

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Akathesia and Agitation
Is it the drug or the disease?

Signs and Symptoms (multiple & nonspecific)

Diagnosis or Drug Side Effect?

New Treatment Added

How often are symptoms attributed to medication side effects?
Seems Innocent Enough

Strongly anticholinergic
Lots of Tylenol

Look different; but are alike

OTC

Can alter other drug kinetics!

Sometimes anticholinergic, changes stomach pH
Gabapentin, a newly controlled substance in KY.

• More commonly used for "bridging"...to ease withdrawal symptoms until the next "fix" of an opioid, benzodiazepine, or cocaine.

• Gabapentin isn't scheduled in most of the country, like pregabalin (Lyrica)...so it doesn't usually raise concerns about abuse or diversion.

• Both gabapentin and pregabalin have calming effects...and higher doses can sometimes cause mild euphoria.

• Some people take high doses of gabapentin recreationally.
Heath Ledger
1979-2008

OTC stuff
• Doxylamine
  – NyQuil
  – Unisom
  – And who knows what else!

Prescription stuff
• Oxycodone
• Hydrocodone
• Diazepam
• Temazepam
• Alprazolam

Chief Complaints:
insomnia, anxiety, depression, pain and common cold per friends and family from the investigation

Two physicians (one in LA, one in Houston) were exonerated because “they had prescribed other medications, not the pills that killed him”
What if?

You took hands full of random non controlled Rx and OTC pills at a pharm party?

*Gabapentin
+Fluoxetine
-Digoxin
*Furosemide
-Nifedipine
*Celecoxib

How many? Of which? Your physiology
What’s in this bag?

Methadone X 5
Viagra X 3
Oxycodone X 2

Respiratory depression
Sedation
confusion

Respiratory depression
Drops bp, raises ht rate

Neurotoxic
Cardiac sudden death, inability to respond to Viagra induced bp drop, and oxycodone induced respiratory depression

Sedation
confusion
To Crush or not To Crush?
END OF PART 3

https://www.drugabuse.gov/drugs-abuse/commonly-abused-drugs-charts

• Questions?

• Comments?

• Share Ideas?