RN Essentials

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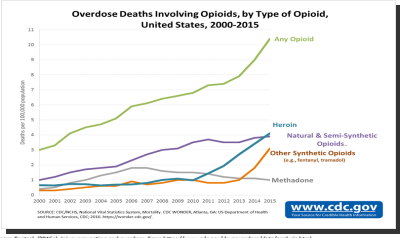
Objectives

- Describe various evidence-based pharmacotherapeutic options to address the opioid epidemic
- Explain the differences between methadone, buprenorphine, and naltrexone
- Identify the nurse's role in assessment in induction, maintenance, and detoxification using opioid replacement therapies

Background

- Nurses working across settings have essential roles:
  - Assessment/screening
  - Inductions and maintenance
    - Inpatient and outpatient
  - Education and counseling

"…Not a Moral Failing" -Surgeon General, 2016



Reference: Centers for Disease Control. (2016a). Injury prevention and overdose. From https://www.cdc.gov/drugoverdose/data/analysis.html

Opioid Replacement Treatment Background

- Methadone-FDA approved treatment with DATA 2000 Waiver
  - May not be prescribed for treatment of opioid addiction from office setting
- Suboxone-FDA approved
  - Nurse practitioners can now prescribe and dispense with a DATA waiver
  - CARA legislation

Why Opioid Replacement Therapy?

- Route of administration
  - Faster route has a greater abuse potential
    - Injecting IV >Injecting SQ>Oral
- Drug Half life
  - Briefer half-life has a greater abuse potential
    - Heroin >Methadone
- Lipophilicity (faster across blood brain barrier)
  - Higher lipohilicity has a greater abuse potential
    - Heroin >Morphine >Methadone

Policy Updates and Evidence for Buprenorphine and Methadone

www.compa-ny.org

- "News" section

Opiate Receptors and Effect of Agonist

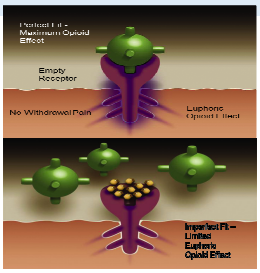
Mu_1 (μ_1)	analgesia, euphoria
Mu_2 (μ_2)	constipation, respiratory depression
Kappa	spinal analgesia, dysphoria
Delta	unknown

References: Grissinger, 2011; Ducharme, Fraser, & Gill, 2012; Ferrari, Coccia, Bertolini, & Sternieri, 2004.

Opioid Replacement Therapy

Methadone

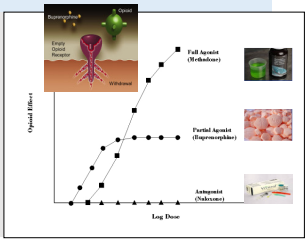
Buprenorphine
(Suboxone=Buprenorphine/ Naloxone)



Reference: National Alliance of Advocates for Buprenorphine Treatment, 2015.

Full Versus Partial Opioid Agonist

- Work differently depending on:
  - Affinity, Intrinsic activity, Dissociation
- Methadone and Buprenorphine
  - Ameliorate opioid withdrawal
  - Reduce opioid cravings
  - Treat pain (to varying degrees)
- Partial Agonist vs. full agonist
  - Attenuated euphoria
  - Reduced side effects
  - "Ceiling effect" on respiratory depression
  - Potentially lower abuse/diversion potential
  - Less severe withdrawal



Reference: National Alliance of Advocates for Buprenorphine Treatment, 2015.

Antagonist Therapy-Naltrexone (Vivitrol)

- Opioid antagonist
- Completely blocks opioids for 4-6 weeks
- Who would potentially benefit from:
  - Pill
  - Injection

Choosing an Opioid Replacement Pharmacotherapeutic

Nursing Assessment-Choice, Induction, and Maintenance

Interview Questions, Subjective	Physical, Objective
• **What is the patient's goal?** • Type: Drug and route • Duration & quantity • Side effects, effect on mood • Withdrawal (Dependence) • Aberrant behaviors, **overdoses**. • Prior treatments (compliance, etc.) • Other substances • Benzodiazepines, withdrawal seizures • Psychiatric history • Pain-"Opioid-Induced Hyperalgesia" • Medical history-HIV (meds), sleep apnea, falls, osteopenia, hypogonadism, etc.	• COWS: Withdrawal • Skin assessment: Track marks • Urine toxicology: All synthetics and non-synthetics • Labs (hepatic, renal): Methadone has more interactions • Electrocardiogram: >500; Greater risk with methadone • Testosterone levels: Greater risk with methadone • Osteopenia: Greater risk with methadone • History of prescriptions: Objective evidence of tolerance and/or aberrant behaviors

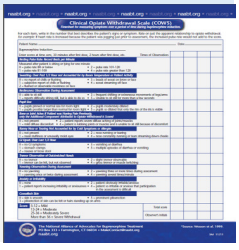
Interpreting Urine Drug Testing[2,3-5]

Drug or Class	Expected Results	Considerations
Opioids-Semisynthetic (derived from opium)		
Hydrocodone (Lorcet, Lortab, Norco, Vicodin)	**Opiates Immunoassay**–positive **Confirmatory**–hydrocodone, possibly hydromorphone	• "Opiates" immunoassay may detect semisynthetic opioids + hydrocodone > hydromorphone > oxycodone • Negative result does not exclude use and confirmatory testing (GC/MS) is required • Hydrocodone is metabolized in small amounts to hydromorphone, both may be found in urine • Oxycodone is metabolized to oxymorphone, both may be found in urine • Hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively
Hydromorphone (Dilaudid, Exalgo)	**Opiates Immunoassay**–may be positive **Confirmatory**–hydromorphone	
Oxycodone (Roxicet, OxyCotonin)	**Opiates Immunoassay**–may be positive **Oxycodone Immunoassay**–positive **Confirmatory**–oxycodone possibly oxymorphone	
Oxymorphone (Opana)	**Oxycodone Immunoassay**–positive **Confirmatory**–oxymorphone	
Opioids-Synthetic (man-made)		
Fentanyl	**GC/MS**–fentanyl and norfentanyl	• Current "opiates" immunoassays do not detect synthetic opioids • Confirmatory testing (GC/MS) is needed
Meperidine (Demerol)	**GC/MS**–normeperidine, possibly meperidine	
Methadone (Methadose)	**Methadone Immunoassay**–positive **GC/MS**–methadone, EDDP	
Propoxyphene (Darvon, Darvocet)	**Propoxyphene Immunoassay**–positive **GC/MS**–propoxyphene & norpropoxyphene	

Confirmatory testing. Chromatography (gas chromatography-mass spectrometry (GC/MS) or liquid chromatography-mass spectrometry (LC/MS)) Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

COWS-Clinical Opiate Withdrawal Scale

- Any setting
- Initiation of medication
  - Implications vary depending on last use and type of ORT
- Detoxification from any opioid
- Taper from methadone or suboxone



References: Bart, 2012; National Alliance of Advocates for Buprenorphine Treatment, 2015

Heroin versus Methadone versus Buprenorphine

	Heroin	Methadone	Buprenorphine
Route	IV	PO	Sublingual; 5-20 mins to dissolve
Onset	Immediate	30 minutes	30-60 minutes
Duration	3-6 hours	Half-life: Opioid-tolerant=24-36 hours Opioid-naïve=Can be 55 hours	24-60 hours & Can bind on receptors >24 hours
Euphoria	First 1-2 hours	None with correct dosage	None with correct dosage
Withdrawal	After 3-4 hours	Usually fter 24-36 hours	Usually after 24-36 hours

References: Grissinger, 2011; Ducharme, Fraser, & Gill, 2012; Ferrari, Coccia, Bertolini, & Sternieri, 2004.

Side Effects and Drug Interactions

Methadone

- Prolonged QTC
- Hypogonadism
- Sedation, CNS depression
- Lengthy List of Medication Interactions
  - HIV medications-Population-specific care

Buprenorphine

- Drug-to-drug interactions rare
- Headache, nausea, anxiety, insomnia, pain, constipation
- Urinary retention, allergic reactions rare
- Vomiting-rare
  - May consider Subutex without the naloxone component
- CNS depression
  - Benzos, Alcohol, Other Sedatives
    - Case reports of deaths with concurrent use of other sedative but NOT absolute contraindication
      - Risk for overdose lower than methadone
- Liver toxicity-Less common vs. methadone
  - Case reports of elevated transaminase, in those infected with HCV
    - Some recovered after stopped injected
    - Some sublingual users did not recover

References: Grissinger, 2011; Ducharme, Fraser, & Gill, 2012; Ferrari, Coccia, Bertolini, & Sternieri, 2004.

Methadone

Induction-Tolerance Level

Opioid-tolerant	Unknown tolerance or high risk for overdose

• Assessment findings
  • UDS + opiates, withdrawal symptoms present, track marks
• Day 1: start 30 mg PO x 1 and may give additional 10 mg 1 hr later if no oversedation
• Day 2: 50 mg daily and increase to 90 mg daily in 10 mg increments every 3 days as tolerated.
  • Hold for sedation and side effects
	• Methadone 10 mg daily x 3 days
	• Increase to 60 mg by 5 mg every 3-5 days as tolerated

Dosing

Adjustments-During Induction	Maintenance

• Adjust dose 5-10 mg at a time
• 5 days for full effect of dose change
  • Has long half-life
• May make adjustments faster if going down on dose or titrating toward previous dose.
• Helpful to remind patients "you don't need a higher dose you need more time for current dose to build up"
	• Typically 80-120 but research varies
	  • 35 inter-individual difference in methadone pharmacokinetics
	• Rapid Metabolizer test
	  • EKG>150 mg, check ECG for prolonged QTc
	  • Consider checking peak/trough to see if rapid metabolizer of methadone
	  • Pregnant Females
	  • Consider split dosing

Methadone Maintenance

- Clinic setting
  - Labs, pregnancy, peak/trough as necessary, BAC
- Often patients want to stop methadone
  - Prior overdoses? Risks?
  - Options?
- Tapering may take more than one year
  - Last 30 mg is associated with worst cravings and withdrawal
  - High risk for relapse

Buprenorphine

Precipitating Withdrawal

- Suboxone (buprenorphine with naloxone)
  - Developed to decrease abuse potential
  - Formulated with naloxone
  - Naloxone blocks opiate effect if injected
  - Naloxone has minimal bioavailability
- Precipitated Withdrawal
  - Due to Buprenorphine Activity if taken orally
  - Primarily due to Naloxone Activity if injected
- Treatment:
  - May give a benzodiazepine
  - May give another dose of buprenorphine
  - Cardiac complications if extreme-ICU

Induction-With Physical Dependence

Long-Acting

- Abstain about 48+ hours
- Assess for withdrawal
  - Cows
- Methadone:
  - Lipophilicity a factor
  - Decrease the daily dose until ≤30 mg of methadone
  - Begin induction at least 48-96 hours after last dose of methadone
  - No more methadone given
- Fentanyl
  - Specific UDS, remember to remove patches!

Short-Acting

- 8 to 12 hours
  - Oxycodone (Percocet®, crushed Oxycontin), Hydrocodone (Vicodin), Heroin, Morphine
- Abstain 8-12 hours (mild withdrawal)
- If patient is not in documented withdrawal review history:
  - Assess, support and wait
  - Questions on use, specific time, amount, etc.
  - Importance placed on the drug of choice (half-life, etc.)

Induction

Physical Dependence

- COWS scale shows opiate withdrawal
  - >8-12
- Start with 2-4 mg
- Reassess approx. 1 hour after administration
  - Recall onset of action
- Continue to titrate until symptoms resolve
- Reassess patient 40minutes to 1 hour after first dose
- Dose with 2mg sl
  - Reassess over the next few hours
- Stabilize day one around 8mg or per your protocol

Without or Unknown Physical Dependence

- E.g., Prison Population or Recently Detoxed
- COWS
  - Still perform
- Start with 1-2 mg first day

Symptomatic Medication

- Ibuprofen: muscle aches
- Tylenol: pain, headache
- Maalox: GI distress
- Immodium: Diarrhea
- Compazine: Nausea, Vomiting
- Bentyl: abdominal cramps
- Benedryl, Trazadone, Tylenol PM: Sleep
- Clonidine: Severe anxiety

Typical Target Dose

- First day: Up to 8mg
- Second day: Up to 16 mg
- Final dose usually 8-16 mg
  - Receptor 95% occupied at 16mg-24 mg
- Very few patients need up to 32mg (max)
  - Target dose 8-16mg
- Usually stabilized by third day

Buprenorphine Maintenance

Clinical Staff

- Not all dosages and formulations are equal
- Monitoring of labs
- Not necessary to stop buprenorphine when having surgery
- Pregnancy

Patient Education

- Patients know how to adjust their dose!
  - Idea is to hold cravings
- Proper storage and handling
  - Out of sight, Labeled, Sharing pills is diversion-criminal offense
- Sales
- Risk of Overdose
  - Other sedatives
  - Narcan kit dispensed
- Precipitated Withdrawal
  - If on Methadone and UseSuboxone
- Harm Reduction
  - Clean needles, risk of HCV, HIV

Special Populations

- Pregnant Females
  - Consider Subutex, split dosing
- Pain
  - Understanding of Opioid-Induced Hyperalgesia
  - Split-dosing
- Hepatic dysfunction
  - Monitor for elevated liver enzymes
- Recent Detox
  - High risk for overdose if return to full agonist use

Pregnancy

- Methadone "preferred" treatment
  - Inconsistency across States
  - My breastfeed if not HIV +
  - May breastfeed if Hep C+ but must speak to clinician first
  - Neonatal Abstinence Syndrome (NAS)
- Buprenorphine category C-Risk cannot be ruled-out
  - NAS
    - Within 12 to 48 hours, peaks 72 to 96, lasts 120-168 hours (some seen 6 to 10 weeks)
    - Found to be less intense than methadone

Reference: Substance Abuse Services and Mental Health Administration, 2014.

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