

Opioid Issues for the Patient and Practitioner

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2 hours

**Course Category:** Pharmacology (PH)

**Course Description:**

This is an oral pharmacology course that describes the appropriate use of opioid medications, with an emphasis on pain management within the scope of optometry and general pain management. Case anecdotes will include management of ocular pain, with specific emphasis on oral/systemic medications. Opioid medications will be evaluated in terms of risk versus benefit, with an emphasis on appropriate use of pain medications, evaluation of potential addiction, and a description on how to protect both patient and practitioner.

**Course Objectives:**

1. Describe the differences between nociceptive and neuropathic pain
2. List and describe how to interpret pain scales
3. Describe the commonly prescribed pain medication classes in terms of mechanisms, side effects, drug interactions, and applicability for pain management:
  - a. Opioids
    - i. Codeine-based
    - ii. Morphine-based
    - iii. Novel agents
  - b. Combination therapy
4. When given a patient case, choose an appropriate pain treatment plan for the management of ocular pain, in terms of drug(s), dosing issues, duration of treatment, and a monitoring plan for efficacy and toxicity
5. Identify and describe some of the potential signs, symptoms, and behaviors associated with opioid or substance abuse, and describe ways to respond to this issue
6. List systems available to evaluate a patient for potential opioid/substance abuse
7. Describe the treatment issues and options associated with the treatment of ocular pain in a patient with a drug abuse history

**Course Outline:**

- 1) Disclosures
  - a) Greg Caldwell, OD, FAAO
  - b) Disclosures: Tracy Offerdahl
- 2) NIH: National Institute on Drug Abuse- As of March 2018
  - a) Every day, more than 115 people in the United States die after overdosing on opioids
  - b) The misuse of and addiction to opioids
    - i) Prescription pain relievers, heroin, and synthetic opioids such as fentanyl
  - c) Serious national crisis that affects public health as well as social and economic welfare

- d) The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse alone in the United States is \$78.5 billion a year
  - i) Including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement
- 3) What do we know about the opioid crisis?
  - a) NIH: National Institute on Drug Abuse (March 2018)
  - b) Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them
  - c) Between 8 and 12 percent develop an opioid use disorder
  - d) An estimated 4 to 6 percent who misuse prescription opioids transition to heroin.
  - e) About 80 percent of people who use heroin first misused prescription opioids
  - f) Opioid overdoses increased 30 percent from July 2016 through September 2017 in 52 areas in 45 states
  - g) The Midwestern region saw opioid overdoses increase 70 percent from July 2016 through September 2017
  - h) Opioid overdoses in large cities increase by 54 percent in 16 states
- 4) What are HHS and NIH doing about it?
  - a) In the summer of 2017, NIH met with pharmaceutical companies and academic research centers to discuss:
    - i) Safe, effective, non-addictive strategies to manage chronic pain
    - ii) New, innovative medications and technologies to treat opioid use disorders
    - iii) Improved overdose prevention and reversal interventions to save lives and support recovery
- 5) Two major types of pain:
  - a) **Nociceptive Pain** – normal processing of stimuli that damages normal tissues; how pain becomes conscious;
    - i) responsive to non-opioids and opioids
  - b) **Neuropathic**: abnormal processing of sensory input by the peripheral or central nervous system;
    - i) treatment includes adjuvant analgesics
    - ii) sometimes much harder to treat
- 6) Drug Treatment Options...
  - a) Neuropathic Pain
    - i) Not the focus of today's discussion...
  - b) Adjuvants – multipurpose & specific to type of pain
    - i) Anti-seizure medications that address nerve damage/inflammation
      - (1) Gabapentin (Neurontin)
      - (2) Pregabalin (Lyrica)
      - (3) Topiramate (Topamax)
  - c) Sleep, depression, anxiety, muscle aches/spasms
- 7) Goals of Pain DO Differ...
  - a) The goal for managing **acute pain** is to keep the patient as comfortable as possible while minimizing the **adverse drug reactions (ADRs)** from the pain meds.
  - b) The goals for managing **chronic pain** are to keep the patient as comfortable as possible (this may not mean the patient is pain free), and integrating the patient back into a "normal life" and activities of daily living, while minimizing the ADRs from the pain meds.
- 8) Pain Assessments and Scales
  - a) Adds objective data to a patient's feeling of pain.
    - i) It is a subjective problem to assess!
    - ii) Remember...no patient should needlessly suffer!
  - b) "Eyeball" the patient!
    - i) Does the injury or wound or diagnosis fit the patient's presentation?
      - (1) BP
      - (2) HR
    - ii) Additional autonomic nervous system tidbits
      - (1) Sweating
      - (2) Nausea/vomiting

- (3) Pupil size
- (4) ACUTE vs CHRONIC
- 9) Combination Pain Scale...
- 10) Drug Treatment Options...Nociceptive Pain
- 11) 3 Groups of analgesics
  - a) Non-opioids – acetaminophen & NSAIDs
  - b) Opioids –  $\mu$  agonists & mixed agonist-antagonists
  - c) Adjuvants – multipurpose & specific to type of pain
    - i) Sleep, depression, anxiety, muscle aches/spasms
- 12) Opioids (“narcotics”)
  - a) Mainstay of therapy for the treatment of pain
  - b) NO maximum daily dose limitation
  - c) Useful for acute and chronic pain
  - d) They mimic the actions of endogenous opioid compounds:
    - i) enkephalins, dynorphins, endorphins
- 13) Controlled Substance Schedules:
  - a) Schedule I – not considered to be medically necessary, research only
    - i) Heroin; “Medical” Marijuana
  - b) Schedule II - More likely to be abused
    - i) “Narcotic”: Morphine, fentanyl, meperidine, hydromorphone, oxycodone, methadone, hydrocodone
    - ii) ADD/ADHD meds: Methylphenidate, dexamphetamine, amphetamine salts
  - c) Schedule III - Safer, less likely to be abused
    - i) Combination products with APAP or ASA (codeine)
  - d) Schedule IV – Safer, less likely to be abused
    - i) Tramadol (Ultram)
    - ii) Benzodiazepines (lorazepam, diazepam, oxazepam)
    - iii) Sleep agents (zolpidem, etc.)
  - e) Schedule V – safest, least likely to be abused
    - i) Expectorants with codeine
- 14) State-By-State Restrictions...
- 15) Marijuana
  - a) Still considered to be “C1” or “Schedule I”
  - b) Federal government “ignores” it
- 16) Hydrocodone products
  - a) C3 to C2 as of 2014
  - b) “hydrocodone exception”
    - i) NJ, etc.
- 17) Mechanisms of Action:
  - a) relieve pain and induce euphoria by binding to the opioid receptors ( $\mu$ ,  $\kappa$ ,  $\delta$ ) in the brain and spinal cord:
    - i) Mu, kappa, delta receptors in other places = ADRs
      - (1) Mu: analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction
      - (2) Kappa: analgesia, diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation
      - (3) Delta: analgesia
- 18) Formulations...
  - a) **Immediate release:**
    - i) AKA short-acting; breakthrough
    - ii) Uses: acute pain; breakthrough pain
      - (1) Ex: Percocet, Tylenol w/ codeine, tramadol, Vicodin, etc.
  - b) **Controlled release:**
    - i) AKA long-acting; sustained release; extended release
    - ii) Uses: basal control of chronic pain; typically NOT for acute pain nor in opioid naïve patients!

(1) Ex: OxyContin, MS Contin, Duragesic patch, etc.

19) Morphine Products

- a) Morphine
  - i) Standard for comparison of other agents
  - ii) Used for severe pain
  - iii) Multiple BRAND/TRADE names for long-acting morphine products, with very diverse delivery and release systems
- b) MSIR (IR caps) (q 3-4 hours prn)
- c) MS Contin (CR tabs) (q 8-12 hours)
- d) Kadian (CR caps) (q 12 – 24 hours)
- e) Avinza (CR caps) (q 24 hours)

20) Hydromorphone Products

- a) Hydromorphone (Dilaudid) tablets (“take 1 – 2 tablets every 4 to 6 hours as needed for pain”)
- b) Hydromorphone ER (Exalgo) tablets (take once per day)
- c) Used for severe pain
- d) Very potent
  - i) Example: Compare to morphine  
(1) 30mg PO morphine = 8mg PO hydromorphone

21) Codeine-Based

- a) Codeine – C3; Schedule III
- b) Hydrocodone – C2; Schedule II
- c) Oxycodone – C2; Schedule II
- d) Codeine tablets
  - i) WEAK analgesic: 30mg PO morphine = 200mg PO codeine
- e) Add acetaminophen/ aspirin – Schedule III
  - i) Tylenol #2 = 300 mg acetaminophen & 15 mg codeine
  - ii) **Tylenol #3** = 300 mg acetaminophen & 30 mg codeine
  - iii) Tylenol #4 = 300 mg acetaminophen & 60 mg codeine
  - iv) 1 – 2 tablets every 4 – 6 hours as needed for pain (not to exceed **3 grams** of APAP per day)
- f) Add expectorant – Schedule V

22) OxyCONTin (Controlled release tablets (q 12 hours...once in a while q 8 hours); new formulation is out to help control abuse

- a) Oxycodone Products
  - i) Immediate Release; short-acting tablets
    - (1) OxyIR (IR cap) 5 mg
    - (2) Roxicodone solution 5 mg/5 mL
    - (3) with APAP:
      - (a) *Percocet* and *Endocet* (oxycodone/APAP dose) – 2.5/325, 5/325, 7.5/325, 7.5/500, 10/325, 10/500, 10/650 tablets
      - (b) “Take 1 – 2 tablets by mouth every 4 to 6 hours as needed for pain”; not to exceed 3 grams of APAP per day
  - ii) Roxicet solution– oxycodone 5 mg + 325 mg APAP/ 5 mL
  - iii) Percodan (oxy + asa) – no one uses this product
- b) Beware of combination with acetaminophen (*Percocet*), various strengths
  - i) 30mg PO morphine = 20mg PO oxycodone

23) Hydrocodone Products

- i) Hysingla ER, Zohydro ER – long-acting, single ingredient hydrocodone
- b) Immediate-Release Products:
  - i) Hydrocodone + APAP (*Norco*, *Vicodin*, *Lortab*); Hydrocodone (7.5 mg)+ IBU 200 mg (*Vicoprofen*)
  - ii) “*Vicodin*” = 5/500, *Vicodin ES* = 7.5/750, *Vicodin HP* = 10/660
    - (1) GENERIC/Brand new doses= 5/300; 7.5/300; 10/300
  - iii) *Lortab* = 2.5/300, 5/300, 7.5/300, 10/300
  - iv) *Norco* = 5/325, 7.5/325, 10/325

- (1) "Take 1 – 2 tabs/caps every 4 – 6 hours as needed for pain (not to exceed 3 grams of APAP per day)
  - (2) CIII - for moderate/severe pain – works well
  - (3) AS OF AUGUST 2014, hydrocodone products are ALL CII!!
  - v) 30mg PO morphine = 20-30mg PO hydrocodone
- 24) Miscellaneous
- a) Fentanyl Patch (Duragesic)
    - i) MOST potent opioid
    - ii) Black Box Warning against use in acute pain and in opioid naive patients
  - b) Meperidine (Demerol)
    - i) ACTIVE metabolites = undesirable
  - c) Methadone
  - d) Typically reserved for morphine/codeine allergic patients
- 25) Methadone tidbits...
- a) Chronic pain or opioid abuse deterrent
  - b) 2-phase elimination
    - i) Alpha phase = 8 hrs
      - (1) Offers pain control
    - ii) Beta phase = 16+ hrs
      - (1) Mitigates withdrawal symptoms
  - c) Patient 1: On a short-acting pain med = likely being used to treat chronic pain
    - i) Twice per day dosing
  - d) Patient 2: On methadone ONLY; lower doses
    - i) Once daily dosing
- 26) Tramadol – an Optometrist’s best friend
- a) Tramadol (Ultram) tabs
  - b) Tramadol with 325 mg APAP (Ultracet), Tramadol ER tabs
  - c) tramadol (50 – 100 mg q 4 – 6 hours; do not exceed 400 mg/day)
    - i) Dual action: mu receptors & inhibits neuronal uptake of serotonin & norepinephrine
    - ii) Lowers seizure threshold; increases serotonin levels
      - (1) watch drug interactions with other meds that ↑ serotonin
        - (a) Selective serotonin reuptake inhibitors (SSRIs): fluoxetine/Prozac
        - (b) Migraine meds (“triptans”): sumatriptan/Imitrex
    - iii) Not controlled
      - (1) AS OF AUGUST 2014, NOW A C4 (Schedule IV)
      - (2) “tramies” = abuse potential; helps decrease withdrawal symptoms
- 27) Specific Medications Using Numeric Pain Scale
- a) Mild pain = 1 – 3
    - i) Acetaminophen, Ibuprofen, Tramadol
  - b) Moderate pain = 4 – 6
    - i) Tramadol
    - ii) Tylenol with codeine
    - iii) Acetaminophen with oxycodone (Percocet)
    - iv) Acetaminophen with hydrocodone (Vicodin, etc.)
  - c) Severe pain = 7 – 10
    - i) Tylenol with hydrocodone (Vicodin, etc.)
    - ii) Tylenol with oxycodone (Percocet, etc.)
    - iii) Morphine, Hydromorphone, Fentanyl Patch
- 28) Opioid Effects/ADRs:
- a) CONSTIPATION-anticipate it!
    - i) All patients should receive a stool softener + stimulant combo: docusate + senna/Senna+S
  - b) Pruritis – allergy versus normal release of histamine
  - c) Nausea/vomiting

- d) Triggers CTZ
  - e) Codeine “allergy”
  - f) Sedation
  - g) Inhibition of cough reflex
  - h) Confusion
  - i) Euphoria – mu receptors
  - j) Dysphoria/Hallucinations – kappa receptors
  - k) Miosis
  - l) Respiratory depression – this is what kills a patient
- 29) Opioid Allergies
- a) If a patient is allergic to morphine and/or codeine, then they may only be able to safely take:
    - i) Methadone
    - ii) Meperidine
    - iii) Fentanyl
    - iv) Tramadol
  - b) ASK appropriate questions...
    - i) “what happens when you take \_\_\_\_\_?”
- 30) Opioid Antagonists
- a) Naloxone (Narcan) & Naltrexone (ReVia)
    - i) Used to treat opioid overdose
  - b) Rapidly reverse effects of morphine & other opioid agonists
  - c) States are offering these to patients, friends, and family members for patients ON opioids for pain management OR for addicts!
  - d) Causes “antagonist-precipitated withdrawal”
    - i) within 3 minutes after injection the s/sx of withdrawal appear; peak in about 10-20 minutes and subside in about 1 hour
  - e) Adverse effects: insomnia, headache, nervousness, low energy, agitation, diarrhea, vomiting
- 31) Mixed Opioid Agonist-Antagonist
- a) Exhibit partial agonist or antagonist activity at the opioid receptors
  - b) Morphine/Naltrexone (Embeda), Oxycodone/Naltrexone (Troxyca ER) – TREATMENT of chronic pain; C2
  - c) Buprenorphine (Buprenex), Buprenorphine/Naloxone (Suboxone) – TREATMENT of opioid abuse; C3
  - d) Adverse effects
    - i) Less respiratory depression & less abuse potential?
  - e) Precipitate withdrawal in an opioid-dependent patient
- 32) Alternatives for Pain Control
- a) Acetaminophen (APAP)
    - i) Mild to low-Moderate pain
    - ii) ADRs: liver, kidney?
  - b) Traditional NSAIDs and COX-2 Inhibitors
    - i) Ibuprofen, naproxen sodium (Aleve), celecoxib (Celebrex), meloxicam (Mobic)
    - ii) Mild to low, mid-moderate pain
    - iii) ADRs: GI, CV, acute kidney failure, ↑BP
  - c) Corticosteroids
    - i) Inflammatory pain
    - ii) ADRs: cataracts, ↑BP, fluid retention, GI
- 33) Painful Ocular Problems – things to consider...
- a) Acute or chronic?
    - i) YOU are in charge!
    - ii) Legal and ethical issues – do not allow yourself to be bullied by the patient!
  - b) Work with other practitioners!
  - c) Only a pain specialist should write RXs for CII medications for chronic pain issues
- 34) Painful Ocular Problems – things to consider...
- a) Use the tools that are available!

- i) State databases
    - (1) **PDMP** = **P**rescription **D**rug **M**onitoring **P**rogram
  - ii) Pharmacists
- 35) Tolerance
  - a) Escalation of dose to maintain effect (analgesia or euphoria)
  - b) Happens to everyone
  - c) Regarding euphoria = may be life threatening because respiratory depression does not show much tolerance
- 36) Pseudo-Addiction
  - a) The end result of the under treatment of pain.
  - b) Patients will know exactly how many pills they have left
  - c) They may try to get appointments earlier than needed
    - i) They may seem anxious...
  - d) Typically “cured” by changing/improving pain meds.
  - e) “True Addiction” (formerly “psychological dependence”)
  - f) Compulsive use despite harm
  - g) Many times triggered by cravings in response to specific cues
    - i) Lifestyle is geared to the acquisition of the drugs
    - ii) Borrowing from others, injecting oral formulations, prescription “loss”, requesting specific drugs (not always a sign...as some drugs just work better)
  - h) Quality of life is not improved by the medication and eventually it becomes compulsive (“wanting without liking”)
  - i) Relapse is very common even after “successful” withdrawal...it is a relapsing disease that is incredibly hard to treat
- 37) Addiction
  - a) Remember, this is compulsive use despite harm!
    - i) Fast talkers
    - ii) New patients
    - iii) Unequal diagnosis and pain response
    - iv) Vitals
    - v) Specific requests to agents
    - vi) Strange “allergies”
    - vii) Excuses
      - (1) “I got robbed”; “I lost it”; “The pharmacy didn’t give me enough”...
- 38) Ways to respond
  - a) Avoid getting “bullied”
  - b) Avoid acting like you are judging the patient
  - c) State data bases
    - i) Call your local pharmacy/pharmacist
  - d) Legal/ethical issues
    - i) If you didn’t write it down, then it didn’t happen!
    - ii) If you accidentally give an addict a script for a pain medication, you won’t get into “trouble”...
- 39) Withdrawal from opioids...
  - a) Time of onset, intensity, and duration of abstinence syndrome depends on the drug previously used (related to the half-life/“t ½” )
  - b) Rhinorrhea, lacrimation, yawning, chills, gooseflesh, hyperventilation, hyperthermia, mydriasis, muscular aches, vomiting, diarrhea, anxiety, hostility
    - i) Number and intensity of signs and symptoms are largely dependent on the degree of physical dependence that has developed
  - c) Administration of an opioid at the time of s/sx of withdrawal = suppression of abstinence signs and symptoms almost immediately
- 40) Pain Management in Eye Care
  - a) Conditions Which May Require Pain Management

- i) Large cornea abrasions
    - (1) Cornea burn
    - (2) PRK/PTK
  - ii) Orbital trauma
  - iii) Orbital blowout fractures
  - iv) Scleritis
- 41) Pain Reliever Help
  - a) Know your maximum daily allowances
  - b) APAP 3000 mg (4000 mg\*)
  - c) ASA 6000 mg
  - d) Ibuprofen 3200 mg
  - e) Naproxen Sodium 1650 mg (Aleve/Anaprox)
  - f) Naproxen 1500 mg (Naprosyn)
  - g) Propoxyphene HCl 600 mg
  - h) Codeine 240 mg
  - i) Hydrocodone 60 mg
- 42) Two and Two and Four and Two
  - a) Two and Two
    - i) Analgesic
      - (1) Ibuprofen
        - (a)  $200 \text{ mg} \times 2 = 400 \text{ mg}$
        - (b)  $400 \text{ mg TID/QID} = 1200 \text{ mg}$
      - (2) Acetaminophen
        - (a)  $500 \text{ mg} \times 2 = 1000 \text{ mg}$
        - (b)  $1000 \text{ mg TID/QID} = 3000 \text{ mg}$
  - b) Four and Two
    - i) Analgesic and Anti-inflammatory
    - ii) Ibuprofen
      - (1)  $200 \text{ mg} \times 4 = 800 \text{ mg}$
      - (2)  $800 \text{ mg TID/QID} = 3200 \text{ mg}$
    - iii) Acetaminophen
      - (1)  $500 \text{ mg} \times 2 = 1000 \text{ mg}$
      - (2)  $1000 \text{ mg TID/QID} = 3000 \text{ mg}$
- 43) Crystalline Retinopathies
  - a) Talc – intravenous drug use
  - b) Tamoxifen - used in treating breast cancer
    - i) Daily 10-20 grams
    - ii) > 1 year of therapy with a total of > 100 grams
  - c) Canthaxanthin- used as an oral tanning agent
  - d) Treatment
    - i) Stop the drug
    - ii) No additional systemic testing is necessary if a history of medication or drug use is clear
- 44) Question and Thank you
  - a) Greg Caldwell, OD, FAAO
  - b) Tracy Offerdahl, Bpharm, PharmD