Pain management, Identification of Addiction, Practices of Prescribing, and Dispensing of Opioids

> Tracy Offerdahl, PharmD Greg Caldwell, OD, FAAO 2 hour course

Biography – Tracy Offerdahl

 Dr. Offerdahl attended Temple University School of Pharmacy in Philadelphia, PA, for both her undergraduate and graduate degrees. Upon completion of her Doctor of Pharmacy degree, she completed a Residency at Temple University Hospital, where much of her time was spent in internal medicine and infectious diseases. She is currently on faculty at Salus University, Pennsylvania of Optometry, and the Philadelphia College of Osteopathic Medicine, and she has a practice site in Villanova, PA. Dr. Offerdahl is currently earning another degree in holistic medicine, a certificate in veterinary pharmacy, and she lectures extensively to the optometry community regarding systemic drugs.

Biography – Greg Caldwell

- Greg Caldwell, O.D., is a 1995 graduate of the Pennsylvania College of Optometry. He completed a one-year residency in primary care and ocular disease at The Eye Institute in Philadelphia Pennsylvania. He is a fellow of the American Academy of Optometry (AAO) and a Diplomate of the American Board of Optometry (ABO). He currently works in Duncansville, Pennsylvania as an ocular disease consultant. Dr. Caldwell's primary focus is the diagnosis and management of anterior and posterior segment ocular disease and he has been a participant in multiple FDA investigations. Dr. Caldwell has lectured extensively throughout the county and over twelve countries internationally. In 2010 he served as President of the Pennsylvania
- Optometric Association (POA) and served on the AOA Board of Trustees 2013-2016. He is President of the Blair/Clearfield Association for the Blind.

Disclosures- Greg Caldwell, OD, FAAO

- Will mention many products, instruments and companies during our discussion
 - I don't have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association President 2010
 - POA Board of Directors 2006-2011
- American Optometric Association, Trustee 2013-2016
 - Thank you to the members and those who join
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Shire, BioTissue, Optovue, Alcon, Allergan, Aerie
- Advisory Board: Allergan, Sun, Arerie
- Envolve: PA Medical Director, Credential Committee
- Optometric Education Consultants- Scottsdale, Nashville, and Quebec City, Owner



Disclosures- Tracy Offerdahl, PharmD

Boiron: honorarium, webinar/speaker

 Has not received any assistance from any commercial interest in the development of this course

Course Objectives

- Describe the differences between nociceptive pain and neuropathic pain
- List and describe how to interpret pain scales
- Describe the commonly prescribed pain medication classes in terms of mechanisms, side effects, drug interactions, and applicability for pain management:
 - Opioids
 - Codeine-based
 - Morphine-based
 - Novel agents
 - Combinations therapy
- 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
- 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
- List systems available to evaluate a patient for potential opioid/substance abuse
- Describe the treatment issues and options associated with the treatment of ocular pain in a patient with a drug abuse history

NIH: National Institute on Drug Abuse As of March 2018

- Every day, more than 115 people in the United States die after overdosing on opioids
- The misuse of and addiction to opioids
 - Prescription pain relievers, heroin, and synthetic opioids such as fentanyl
- Serious national crisis that affects public health as well as social and economic welfare
- 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
 - Including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement

What do we know about the opioid crisis? NIH: National Institute on Drug Abuse (March 2018)

- Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them
- Between 8 and 12 percent develop an opioid use disorder
- An estimated 4 to 6 percent who misuse prescription opioids transition to heroin.
- About 80 percent of people who use heroin first misused prescription opioids
- Opioid overdoses increased 30 percent from July 2016 through September 2017 in 52 areas in 45 states
- The Midwestern region saw opioid overdoses increase 70 percent from July 2016 through September 2017
- Opioid overdoses in large cities increase by 54 percent in 16 states

What are HHS and NIH doing about it?

- In the summer of 2017, NIH met with pharmaceutical companies and academic research centers to discuss:
 - Safe, effective, non-addictive strategies to manage chronic pain
 - New, innovative medications and technologies to treat opioid use disorders
 - Improved overdose prevention and reversal interventions to save lives and support recovery

Two major types of pain:

- Nociceptive Pain normal processing of stimuli that damages normal tissues; how pain becomes conscious;
 * Responsive to non-opioids and opioids
- <u>Neuropathic</u>: abnormal processing of sensory input by the peripheral or central nervous system;
 - * Treatment includes adjuvant analgesics
 - * Sometimes much harder to treat

Drug Treatment Options... Neuropathic Pain

- Not the focus of today's discussion...
- Adjuvants multipurpose & specific to type of pain
 - Anti-seizure medications that address nerve damage/inflammation
 - Gabapentin (Neurontin)
 - Pregabalin (Lyrica)
 - Topiramate (Topamax)
 - Sleep, depression, anxiety, muscle aches/spasms

Goals of Pain DO Differ...

- The goal for managing <u>acute pain</u> is to keep the patient as comfortable as possible while minimizing the *adverse drug reactions (ADRs)* from the pain meds
- The goals for managing <u>chronic pain</u> 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

Pain Assessments and Scales

• Adds objective data to a patient's feeling of pain

- It is a subjective problem to assess!
- Remember...no patient should needlessly suffer!
- "Eyeball" the patient!
 - Does the injury or wound or diagnosis fit the patient's presentation?
 - BP
 - HR
 - Additional autonomic nervous system tidbits
 - Sweating
 - Nausea/vomiting
 - Pupil size
 - ACUTE vs CHRONIC

Combination Pain Scale...

PAIN MEASUREMENT SCALE



Combination Pain Scale...



Drug Treatment Options... Nociceptive Pain

- 3 Groups of analgesics
 - Non-opioids acetaminophen & NSAIDs
 - Opioids μ agonists & mixed agonist-antagonists
 - Adjuvants multipurpose & specific to type of pain
 - Sleep, depression, anxiety, muscle aches/spasms

Opioids ("narcotics")

- Mainstay of therapy for the treatment of pain
- NO maximum daily dose limitation
- Useful for acute and chronic pain
- They mimic the actions of endogenous opioid compounds:
 - enkephalins, dynorphins, endorphins

Controlled Substance Schedules

- Schedule I not considered to be medically necessary, research only
 - Heroin; "Medical" Marijuana
- Schedule II More likely to be abused
 - "Narcotics": Morphine, fentanyl, meperidine, hydromorphone, oxycodone, methadone, hydrocodone
 - ADD/ADHD meds: Methylphenidate, dexmethamphetamine, amphetamine salts
- Schedule III Safer, less likely to be abused
 - Combination products with APAP or ASA (codeine)
- Schedule IV Safer, less likely to be abused
 - Tramadol (Ultram)
 - Benzodiazepines (lorazepam, diazepam, oxazepam)
 - Sleep agents (zolpidem, etc.)
- Schedule V safest, least likely to be abused
 - Expectorants with codeine

State-By-State Restrictions...

Marijuana

- Still considered to be "C1" or "Schedule I"
- Federal government "ignores" it

Hydrocodone products

- C3 to C2 as of 2014
- "hydrocodone exception"
 - NJ, ect

Mechanisms of Action:

- Relieve pain and induce euphoria by binding to the opioid receptors (mu, kappa, delta) in the brain and spinal cord
 - Gamma is not an opioid receptor subtype
- Mu, kappa, delta receptors in other places = ADRs
 - Mu: analgesia, euphoria, miosis, sedation, constipation, respiratory depression, addiction
 - Kappa: analgesia, diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation
 - Delta: analgesia

Formulations...

• Immediate release:

- AKA short-acting; breakthrough pain
 - "breakthrough pain" = acute pain that occurs after a chronic pain patient has taken their long-acting product
 - Ex: Cancer patient takes OxyContin at 7am. Their next dose is due at 7pm, however they have an acute pain problem at 12 noon...they would take a dose of their short-acting ("breakthrough pain") opioid to treat the acute pain.
- Uses: acute pain; breakthrough pain
 - Ex: Percocet, Tylenol w/ codeine, tramadol, Vicodin, etc.

• Controlled release:

- AKA long-acting; sustained release; extended release
- Uses: basal control of chronic pain; typically NOT for acute pain nor in opioid naïve patients!
 - "basal control" = basic or low-level pain control that lasts for 24 hours
 - Ex: OxyContin, MS Contin, Duragesic patch, etc.

Morphine Products

- Morphine
 - Standard for comparison of other agents
- Used for severe pain
- Multiple BRAND/TRADE names for long-acting morphine products, with very diverse delivery and release systems

Morphine Products

- MSIR (IR caps) (q 3-4 hours prn)
- MS Contin (CR tabs) (q 8–12 hours) Kadian (CR caps) (q 12 24 hours) Avinza (CR caps) (q 24 hours)

Clinical pearls \bullet

- ANY long-acting products (MS Contin, OxyContin, etc.) should NEVER be chewed, crushed, or cut in half, as this results in the ENTIRE dose being released at once and this may result in death due to overdose!
 - Death is typically due to respiratory depression
 - Morphine sulfate (Avinza) would be the most dangerous medication in the class if crushed or chewed

Hydromorphone Products

• Hydromorphone (Dilaudid) tablets

- Take 1 2 tablets every 4 to 6 hours as needed for pain
- Hydromorphone ER (Exalgo) tablets
 Take once per day
- Used for severe pain
- Very potent
 - Equianalgesic
 - 30 mg PO morphine = 8 mg PO hydromorphone

Codeine-Based

Codeine – C3; Schedule III

- Hydrocodone C2; Schedule II
- Oxycodone C2; Schedule II

Codeine tablets

- The WEAKEST opioid analgesic (codeine)
 - Equianalgesic
 - 30mg PO morphine = 200 mg PO codeine
- Add acetaminophen/aspirin Schedule III
 - Tylenol #2 = 300 mg acetaminophen & 15 mg codeine
 - Tylenol #3 = 300 mg acetaminophen & 30 mg codeine
 - Tylenol #4 = 300 mg acetaminophen & 60 mg codeine
 - 1 2 tablets every 4 6 hours as needed for pain
 - Not to exceed <u>3 grams</u> of APAP per day
- Add expectorant Schedule V

Oxycodone Products...

Oxycodone (OxyCONtin)

- Controlled release tablets
 - q 12 hours...once in a while q 8 hours
- Generally not appropriate for acute pain due to the fact that it is long acting

OxyCONtin -Controlled release tablets q 12 hours...once in a while q 8 hours New formulation is out to help control abuse

Manual Crushing Followed by Dissolution



Crushed New Formulation

Crushed Original Formulation

Tampering for IV Abuse

New formulation results in gelatinous material which cannot be drawn into a syringe for injection (the syringe is empty)

New formulation







Oxycodone Products

- Immediate Release; short-acting tablets
- OxyIR (IR cap) 5 mg
- Roxicodone solution 5 mg/5 mL
- With APAP:
 - Percocet and Endocet (oxycodone/APAP dose)
 - 2.5/325, 5/325, 7.5/325, 7.5/500, 10/325, 10/500, 10/650 tablets
- Take 1 2 tablets by mouth every 4 to 6 hours as needed for pain
 - Not to exceed 3 grams of APAP per day

Oxycodone Products

- Roxicet solution— oxycodone 5 mg + 325 mg APAP/ 5 mL
- Percodan (oxy + asa) no one uses this product
- Beware of combination with acetaminophen (Percocet), various strengths
- Equianalgesic
 - 30 mg PO morphine = 20 mg PO oxycodone

Hydrocodone Products

• Hysingla ER, Zohydro ER – long-acting, single ingredient hydrocodone

- Immediate-Release Products:
 - Hydrocodone + APAP (Norco, Vicodin, Lortab)
 - Hydrocodone (7.5 mg)+ IBU 200 mg (Vicoprofen)
- **"Vicodin" = 5/500**, Vicodin ES = 7.5/750, Vicodin HP = 10/660
 - <u>GENERIC/Brand new doses</u>= 5/300; 7.5/300; 10/300
- Lortab = 2.5/300, 5/300, 7.5/300, 10/300
- Norco = 5/325, 7.5/325, 10/325

Hydrocodone Products

"Take 1 – 2 tabs/caps every 4 – 6 hours as needed for pain
Not to exceed 3 grams of APAP per day

CIII - for moderate/severe pain – works well

- As of August 2014, hydrocodone products (with and without acetaminophen) are ALL CII
- Equianalgesic dosing:
 - 30 mg PO morphine = 20 mg PO hydrocodone

Miscellaneous

• Fentanyl Patch (Duragesic)

- MOST potent opioid (Fentanyl)
- Black Box Warning against use in acute pain and in opioid naïve patients
- Meperidine (Demerol)
 - ACTIVE metabolites = undesirable effects that include drugseeking, hallucinations, anxiety, CNS toxicity

Methadone

 Typically reserved for morphine/codeine allergic patients

Methadone tidbits...

- Chronic pain or opioid abuse deterrent
- 2-phase elimination
 - Alpha phase = 8 hrs
 - Offers pain control
 - Beta phase = 16+ hrs
 - Mitigates withdrawal symptoms
- Patient 1: On a short-acting pain med = likely being used to treat chronic pain
 - Twice per day dosing
- Patient 2: On methadone ONLY; lower doses
 - Once daily dosing

Methadone tidbits...

- Don't think only used for heroin addicts
 - Helps prevent the symptoms of withdrawal
 - May be used to treat chronic pain
 - May be used to treat opioid addiction

Acute Ocular Pain

- Based on the classes of drugs covered to this point, hydrocodone and acetaminophen would be the best choice to manage ocular pain
- Better than morphine, oxycodone, and fentanyl

Tramadol – an Optometrist's best friend

- Tramadol (Ultram) tabs
- Tramadol with 325 mg APAP (Ultracet), Tramadol ER tabs

• Tramadol 50 – 100 mg q 4 – 6 hours

- Do not exceed 400 mg/day
- Dual action: mu receptors & inhibits neuronal uptake of serotonin & norepinephrine
- Lowers seizure threshold; increases serotonin levels
 - Clinical pearl: Watch drug interactions with other meds that ↑ serotonin
 - As this may cause dangerous levels of serotonin!
 - Examples of serotonergic agents:
 - Selective serotonin reuptake inhibitors (SSRIs): fluoxetine/Prozac
 - Migraine meds ("triptans"): sumatriptan/Imitrex
- Not controlled (was once non-controlled)
 - As of AUGUST 2014, now a CIV (Schedule IV)
 - Addicts call tramadol "tramies" = abuse potential; addicts use it because it helps decrease withdrawal symptoms

Specific Medications Using Numeric Pain Scale

- Mild pain = 1 3
 - Acetaminophen, Ibuprofen, Tramadol
- Moderate pain = 4 6
 - Tramadol
 - Tylenol with codeine
 - Acetaminophen with oxycodone (Percocet)
 - Acetaminophen with hydrocodone (Vicodin, etc.)
- Severe pain = 7 10
 - Oxycodone (Oxycontin)
 - Tylenol with hydrocodone (Vicodin, etc.)
 - Tylenol with oxycodone (Percocet, etc.)
 - Morphine, Hydromorphone, Fentanyl Patch

Opioid Effects/ADRs:

- <u>CONSTIPATION</u> anticipate it! (note it's in capital letters)
 - All patients should be treated for this problem and should receive a stool softener + stimulant combo
 - docusate + senna/Senna+S
 - Clinical pearl: Side effect of opioids, treat immediately, it occurs in all patients taking opioids
- <u>Pruritus</u> normal histamine release PARTICULARLY problematic with parenteral (IV) formulations more than with oral formulations
 - Clinical pearl: IV delivery causes more pruritus than oral
- Nausea/vomiting
 - All opioids trigger CTZ (chemoreceptor trigger zone) = central "vomiting center"
 - Codeine has the highest affinity for the CTZ! Which is why many patients state that they are "allergic to codeine"
 - Codeine "allergy" MANY with "codeine allergy" state that their "allergy" is actually nausea/vomiting...not TRUE allergy
- <u>Sedation</u> patients will become tolerant to this after a few weeks of consistent opioid use

Opioid Effects/ADRs:

- Inhibition of cough reflex
- Confusion
- Euphoria due to mu receptor agonist portion of the mechanism
- Dysphoria/Hallucinations due to kappa receptor agonist portion of the mechanism
- Miosis
- Respiratory depression this is what kills a patient

Opioid Allergies

If a patient is allergic to morphine and/or codeine, then they may only be able to safely take:

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- Methadone
- Meperidine
- Fentanyl
- Tramadol
- ASK appropriate questions...
 - "what happens when you take

Opioid Antagonists

Naloxone (Narcan) & Naltrexone (ReVia)

* Used to treat opioid overdose





Naloxone (Narcan) & Naltrexone (ReVia)

Rapidly reverse effects of morphine & other opioid agonists

- States are offering these to patients, friends, and family members for patients ON opioids for pain management OR for addicts!
- Causes "antagonist-precipitated withdrawal"
 - Within 3 minutes after injection the s/sx of withdrawal appear; peak in about 10-20 minutes and subside in about 1 hour
- Adverse effects: insomnia, headache, nervousness, low energy, agitation, diarrhea, vomiting

Mixed Opioid Agonist-Antagonist

- Exhibit partial agonist or antagonist activity at the opioid receptors
- Morphine/Naltrexone (Embeda), Oxycodone/Naltrexone (Troxyca ER) – TREATMENT of chronic pain; C2
- Buprenorphine (Buprenex), Buprenorphine/Naloxone (Suboxone) – TREATMENT of opioid abuse; C3
- Adverse effects
 - Less respiratory depression & less abuse potential?
- Precipitate withdrawal in an opioid-dependent patient

Alternatives for Pain Control

Acetaminophen (APAP)

- Mild to low-Moderate pain
- ADRs: liver, kidney?

Traditional NSAIDs and COX-2 Inhibitors

- Ibuprofen, naproxen sodium (Aleve), celecoxib (Celebrex), meloxicam (Mobic)
- Mild to low, mid-moderate pain
- ADRs: GI, CV, acute kidney failure, 🛛 BP

Corticosteroids

- Inflammatory pain
- ADRs: cataracts, 2 BP, fluid retention, GI

Painful Ocular Problems – things to consider...

- Acute or chronic?
 - YOU are in charge!
 - Legal and ethical issues do not allow yourself to be bullied by the patient!
- Work with other practitioners!
- Only a pain specialist should write RXs for CII medications for chronic pain issues

Painful Ocular Problems – Things to consider...

- Use the tools that are available!
 - State databases
 - PDMP = <u>Prescription</u> <u>Drug</u> <u>Monitoring</u> <u>Program</u>
 - Pharmacists

Tolerance

- Escalation of dose to maintain effect
 - Analgesia or euphoria
 - Happens to everyone
- Regarding euphoria = may be life threatening because respiratory depression does not show much tolerance

Pseudo-Addiction

- The end result of the undertreatment of pain
- Patients will know exactly how many pills they have left
- They may try to get appointments earlier than needed
 - They may seem anxious...
- Typically "cured" by changing/improving pain meds

"True Addiction" (formerly "psychological dependence")

- Compulsive use despite harm
- Many times triggered by cravings in response to specific cues
 - Lifestyle is geared to the acquisition of the drugs
 - Borrowing from others, injecting oral formulations, prescription "loss", requesting specific drugs (not always a sign...as some drugs just work better)
- Quality of life is not improved by the medication and eventually it becomes compulsive ("wanting without liking")
- Relapse is very common even after "successful" withdrawal...it is a relapsing disease that is incredibly hard to treat

Addiction

Remember, this is compulsive use despite harm!

- Fast talkers
- New patients
- Unequal diagnosis and pain response
- Vitals
- Specific requests to agents
- Strange "allergies"
- Excuses
 - "I got robbed"; "I lost it"; "The pharmacy didn't give me enough"...

Ways to respond

- Avoid getting "bullied"
- Avoid acting like you are judging the patient
- State databases
 - Call your local pharmacy/pharmacist
- Legal/ethical issues
 - If you didn't write it down, then it didn't happen!
 - If you accidentally give an addict a script for a pain medication, you won't get into "trouble"...

Withdrawal from opioids...

- Time of onset, intensity, and duration of abstinence syndrome depends on the drug previously used (related to the half-life/"t ½")
- Rhinorrhea, lacrimation, yawning, chills, gooseflesh, hyperventilation, hyperthermia, mydriasis, muscular aches, vomiting, diarrhea, anxiety, hostility
 - Number and intensity of signs and symptoms are largely dependent on the degree of physical dependence that has developed
- Administration of an opioid at the time of s/sx of withdrawal = suppression of abstinence signs and symptoms almost immediately

Pain Management in Eye Care

Conditions Which May Require Pain Management

- Large corneal abrasions
 - Cornea burn
 - PRK/PTK
- Orbital trauma
- Orbital blowout fractures
- Scleritis



Corneal burn with Curling iron

Pain Reliever Help

- Know your maximum daily allowances
- APAP 3000 mg (4000 mg*)
- ASA 6000 mg
- Ibuprofen 3200 mg
- Naproxen Sodium 1650 mg (Aleve/Anaprox)
- Naproxen 1500 mg (Naprosyn)
- Propoxyphene HCl 600 mg
- Codeine 240 mg
- Hydrocodone 60 mg



Maximum Tylenol Dose Lowered To Prevent Overdoses



Read more > Healthy Living Health News, Max Tylenol Dose Lowered, Maximum Tylenol Dose Lowered, Tylenol, Tylenol Dose, Tylenol Dose Lowered, Tylenol Max Dose, Tylenol Maximum Dose, Tylenol Overdose, Tylenol Overdoses, Healthy Living News



TRENTON, N.J. — Johnson & Johnson said Thursday that it's reducing the maximum daily dose of its Extra Strength Tylenol pain reliever to lower risk of accidental overdose from acetaminophen, its active ingredient and the top cause of liver failure.

The company's McNeil Consumer Healthcare Division said the change affects Extra Strength Tylenol sold in the U.S. – one of many products in short supply in stores due to a string of recalls

Starting sometime thi stall, labels on Extra Strength Tylenol packages with now list the maximum daily dose as six pills, or a total of 3,000 milligrams, down from eight pills a day, or 4,000 milligrams. Beginning next year, McNer will also reduce the maximum dail

dose for its Regular Strength Tylenol and other adult pain relievers containing acetaminophen, the most widely used pain killer in the country.

Besides Tylenol, acetaminophen is the active ingredient in the prescription painkillers Percocet and Vicodin and in some nonprescription pain relievers, including NyQuil and some Sudafed products. It's found in thousands of medicines taken for headaches, fever, sore throats and chronic pain.

But people taking multiple medicines at once don't always realize how much acetaminophen they are ingesting, partly because prescription drug labels often list it under the abbreviation "APAP."

Two years ago, a panel of advisers to the Food and Drug Administration called for sweeping restrictions to prevent accidental fatal overdoses of acetaminophen.

Then in January the FDA said it would can the amount of acetaminophen in Vicodin. Percocet and



Two and Two Four and Two

Two and Two Analgesic

- Ibuprofen
 - 200 mg x 2= 400 mg
 - 400 mg TID/QID= 1200 mg
- Acetaminophen
 - 500 mg x 2= 1000 mg
 - 1000 mg TID/QID= 3000 mg

Four and Two Analgesic and Anti-inflammatory

- Ibuprofen
 - 200 mg x 4= 800 mg
 - 800 mg TID/QID= 3200 mg
- Acetaminophen
 - 500 mg x 2= 1000 mg
 - 1000 mg TID/QID= 3000 mg



Can replace ibuprofen with Aleve if desired

Crystalline Retinopathies

- Talc intravenous drug use
- Tamoxifen used in treating breast cancer
 - Daily 10-20 grams
 - > 1 year of therapy with a total of > 100 grams
- Canthaxanthin- used as an oral tanning agent
- Treatment
 - Stop the drug
 - No additional systemic testing is necessary if a history of medication or drug use is clear







Thank you! Tracy and Greg