Pain Management in Optometric Practice in an Era of Opioid Abuse

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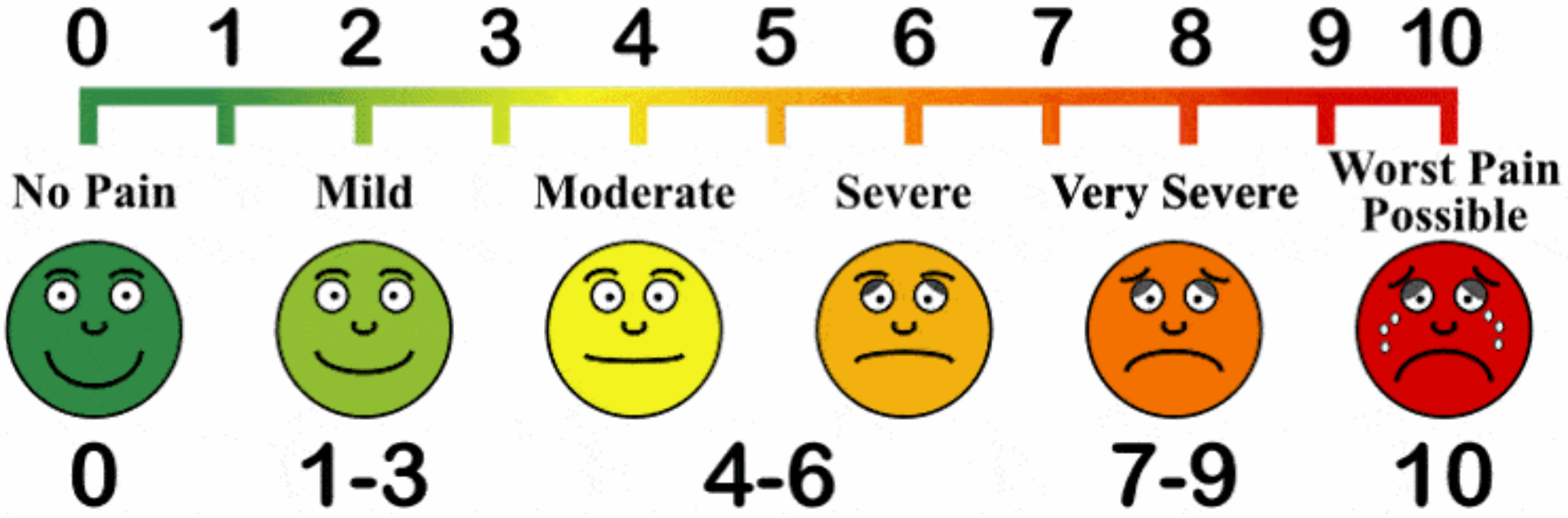
Disclosures:

- Lonsberry: Maculogix, Sun Pharmaceuticals


0 1 2 3 4 5 6 7 8 9 10
No Pain
Mild
Moderate
Severe
Very Severe
Worst Pain Possible
0
1-3
4-6
7-9
10

Addiction

- defined as as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences.
- considered a brain disease because drugs change the brain structure and how it works.
- these brain changes can be long-lasting, and can lead to the harmful behaviors seen in people who abuse drugs.

Why Do People Take Drugs

- To Feel Good:
  - Most abused drugs produce intense feelings of pleasure
- To Feel Better:
  - People who suffer from social anxiety, stress and depression begin the use of drugs to help lessen the feelings of distress
- To Do Better:
  - Some feel pressure to enhance their physical or mental edge
- Curiosity or because others are doing it:
  - Adolescents particular prone to this type of peer pressure

Why Do People Take Drugs

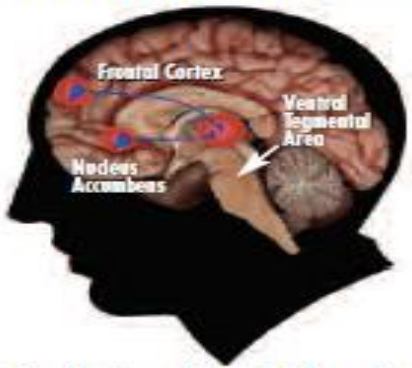
- Initial decision to take a drug is typically voluntary and they may perceive that first time as producing positive effects (and often believe they can control their use).
- With increased use of the drug, other pleasurable experiences lose their appeal and more drug is required to feel “normal” and the person quickly loses the ability for self-control (which is a hallmark of addiction).

Why Do People Take Drugs

- Brain imaging studies have demonstrated that people with addiction have physical changes in areas of the brain that are critical to judgment, decision making, learning and memory, and behavior control
- It is believed that these changes alter the way the brain works and may help explain the compulsive and destructive behaviors of addiction.

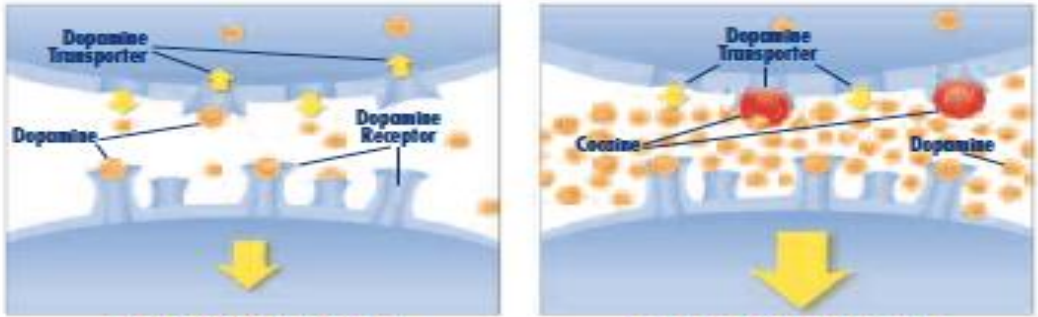
DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

Brain reward (dopamine) pathways



These brain circuits are important for natural rewards such as food, music, and sex.

Drugs of abuse increase dopamine

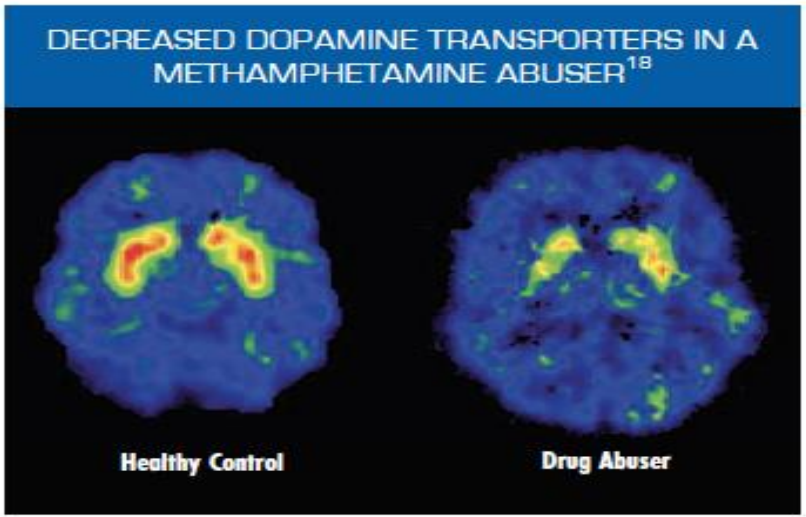


Typically, dopamine increases in response to natural rewards such as food.
When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

National Institue of Drug Abuse: Drugs, Brains and Behaviour. The Science of Drug Addiction

Impaired Brain Function with Long Term Drug Abuse

- Long term drug use decreases the normal dopamine production or receptors making patients feel “flat”
- Patients’ require the drug in order to feel that high and in increased levels to obtain the previous “high”



National Institue of Drug Abuse: Drugs, Brains and Behaviour. The Science of Drug Addiction

Prescription Drug Abuse

- Prescription medications, including opioid pain relievers (such as OxyContin® and Vicodin®), anti-anxiety sedatives (such as Valium® and Xanax®), and ADHD stimulants (such as Adderall® and Ritalin®), are commonly misused to self-treat for medical problems or abused for purposes of getting high or (especially with stimulants) improving performance

Opioid Abuse

- Opioid pain relievers are frequently abused by being crushed and injected or snorted, greatly raising the risk of addiction and overdose.
- there is a common misperception that because medications are prescribed by physicians, they are safe even when used illegally or by another person than they were prescribed for.

Opioid Abuse/Overdose

- Prescription opioid overdose deaths also often involve benzodiazepines.
- Benzodiazepines are central nervous system depressants used to sedate, induce sleep, prevent seizures, and relieve anxiety.
  - Examples include alprazolam (Xanax®), diazepam (Valium®), and lorazepam (Ativan®).
- Avoid taking benzodiazepines while taking prescription opioids whenever possible.

https://www.cdc.gov/drugoverdose/data/overdose.html

Opioid Abuse/Overdose

- The most common drugs involved in prescription opioid overdose deaths include:
  - Methadone (long acting opioid for heroin abuse)
  - Oxycodone (such as OxyContin®)
  - Hydrocodone (such as Vicodin®)
- Overdose rates were highest among people aged 25 to 54 years.
- Overdose rates were higher among non-Hispanic whites and American Indian or Alaskan Natives, compared to non-Hispanic blacks and Hispanics.
- Men were more likely to die from overdose, but the mortality gap between men and women is closing.

https://www.cdc.gov/drugoverdose/data/overdose.html

Opioid Abuse/Overdose

- Prescription opioids can be used to treat moderate-to-severe pain and are often prescribed following surgery or injury, or for health conditions such as cancer.
- there has been a dramatic increase in the acceptance and use of prescription opioids for the treatment of chronic, non-cancer pain, such as back pain or osteoarthritis, despite serious risks and the lack of evidence about their long-term effectiveness.

https://www.cdc.gov/drugoverdose/data/overdose.html

Withdrawal

- The withdrawal syndrome may be very severe (except for codeine) and includes intense dysphoria (state of unease), nausea or vomiting, muscle aches, lacrimation, rhinorrhea, mydriasis, piloerection, sweating, diarrhea, yawning, and fever.
- Beyond the withdrawal syndrome, which usually lasts no longer than a few days, individuals who have received opioids as analgesics only rarely develop addiction. In contrast, when taken for recreational purposes, opioids are highly addictive.
- The relative risk of addiction is 4 out of 5 on a scale of 1 = nonaddictive, 5 = highly addictive.

Opioid Abuse/Overdose

- Research shows that some risk factors make people particularly vulnerable to prescription opioid abuse and overdose, including:
  - Obtaining overlapping prescriptions from multiple providers and pharmacies.
  - Taking high daily dosages of prescription pain relievers.
  - Having mental illness or a history of alcohol or other substance abuse.
  - Living in rural areas and having low income.

https://www.cdc.gov/drugoverdose/data/overdose.html

Opioid Abuse/Overdose

- Anyone who takes prescription opioids can become addicted to them
  - as many as one in four patients receiving long-term opioid therapy in a primary care setting struggles with opioid addiction.
  - In 2014, nearly two million Americans either abused or were dependent on prescription opioid pain relievers.
- Taking too many prescription opioids can stop a person's breathing—leading to death.

https://www.cdc.gov/drugoverdose/data/overdose.html

Preventing Opioid Abuse: PDMP

- A prescription drug monitoring program (PDMP) is an electronic database that tracks controlled substance prescriptions.
- PDMPs can help identify patients who may be misusing prescription opioids or other prescription drugs and who may be at risk for overdose.

https://www.cdc.gov/drugoverdose/data/overdose.html

Preventing Opioid Abuse: PDMP

- PDMPs improve patient safety by allowing clinicians to:
  - Identify patients who are obtaining opioids from multiple providers.
  - Calculate the total amount of opioids prescribed per day (in MME/day-morphine milligram equivalent).
  - Identify patients who are being prescribed other substances that may increase risk of opioids—such as benzodiazepines.

https://www.cdc.gov/drugoverdose/data/overdose.html

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL CONTRIBUTION

Topical Tetracaine Used for 24 Hours Is Safe and Rated Highly Effective by Patients for the Treatment of Pain Caused by Corneal Abrasions: A Double-blind, Randomized Clinical Trial

Neil Waldman, MD, FACEM, Ian K. Densie, and Peter Herbison, DSc

Abstract

Objectives: The objective of this study was to test the hypothesis that topical tetracaine would be safe to use for 24 hours and would not affect corneal healing, that patients would experience more pain relief, and that patients would perceive tetracaine to be more effective than saline eye drops for the treatment of pain caused by corneal abrasions.

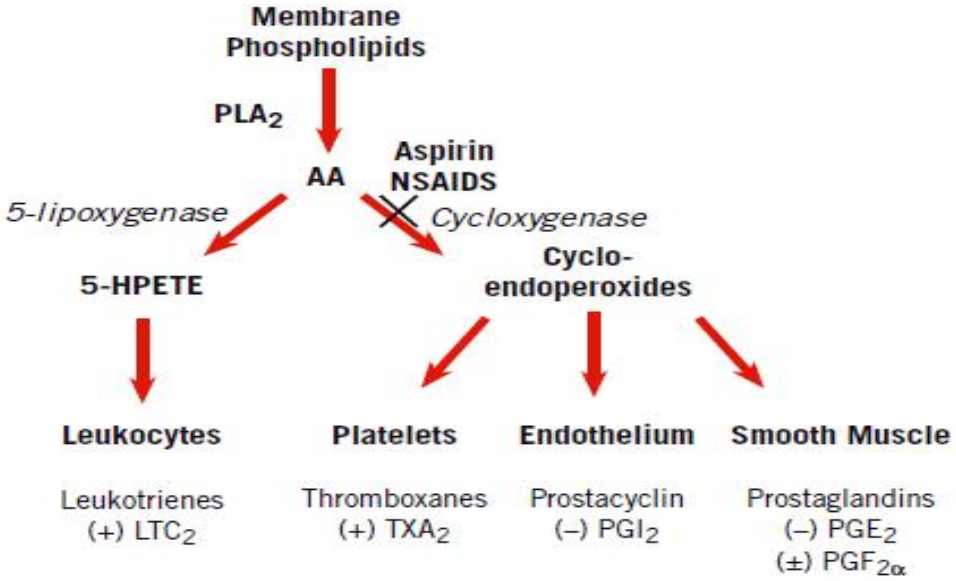
Methods: The study was a 12-month, prospective, double-blind, randomized trial of tetracaine versus saline set in the emergency department (ED) of a regional tertiary care teaching hospital. A total of 116 patients presenting with uncomplicated corneal abrasions were included in this study. The intervention was either undiluted, preservative-free, topical tetracaine hydrochloride 1% or saline, applied up to every 30 minutes while awake for 24 hours. Main safety outcome measures were repeat ED examinations at 48 hours with fluorescein staining and slit-lamp examination, 1-week and 1-month telephone interviews with additional examinations as needed, and monitoring of charts for complications. Secondary outcome measures were 100-mm visual analogue scale (VAS) pain scores recorded every 2 hours while awake for 48 hours and patient-perceived overall effectiveness using a numeric rating scale (NRS) of 0 to 10 obtained during telephone interviews.

Results: At least one follow-up encounter was completed on each of the 116 patients. No complications specifically attributed to topical anesthetic use occurred in the 59 patients in the tetracaine group, and the binomial probability confidence interval (CI) of this occurring is 0 to 6.1. There was no significant difference in corneal healing as measured by the percentage of patients with persistent fluorescein uptake at 48 hours between the two groups (23.9% vs. 21.3%, difference = 2.6%, 95% CI = –14% to 20%, p = 0.761) or persistent symptoms at 48 hours (21.7% vs. 21.3%, difference = 0.4%, 95% CI = –16% to 17%, p = 0.957). There was no clinical difference in VAS pain scores between the groups. Patients in the tetracaine group rated the study drugs' overall effectiveness significantly higher on the NRS (7.7 vs. 3.9) compared to patients in the saline group (difference = 3.9, 95% CI = 2.4 to 5.3, p < 0.0005).

Conclusions: Topical tetracaine used for 24 hours is safe, and while there was no significant difference in patient VAS pain ratings over time, patient surveys on overall effectiveness showed that patients perceived tetracaine to be significantly more effective than saline.

ACADEMIC EMERGENCY MEDICINE 2014;21:374–382

NSAIDs



- Unlike steroids, NSAID's have <u>only</u> <u>one</u> mechanism for decreasing inflammation.
  - Inhibit the enzyme cyclooxygenase which produces prostaglandins, prostacyclins, and thromboxanes from Arachidonic Acid.

Cyclooxygenase Enzymes

COX 1

- Stimulated continuously by normal body physiology
  - Major player involved in secretion of mucous in the stomach and controlling blood flow to the kidneys.

COX 2

- Induced as the result of an immune response to cause higher levels of prostaglandins.

NSAID's also have other properties that make them useful in optometry.

ANALGESIC

NSAID's are primarily used for post-operative care of cataract surgery patients. However, additional uses include following FB removal or corneal abrasions as pain management.

NSAID's also act as antipyretics, but fevers are rarely a big concern in optometry.

Oral Pain Management

Pain Management: Oral Analgesics

- Conditions potentially requiring us of oral analgesics:
  - Corneal ulcers
  - Herpes simplex/zoster
  - Post-surgical
  - Trauma
  - Thermal burns

Oral Analgesics: Guidelines

- Make the proper diagnosis first (ie. Don’t prescribe without knowing what you are prescribing for!)
- Treat the underlying cause for the pain
- Treat the pain at presentation..don’t wait!
- Treat pain continuously over a 24 hour schedule
- Non-prescription drugs should be first choice and tend to be low cost
- Treat patients with the simplest and safest means to alleviate pain

Oral Analgesics: Guidelines

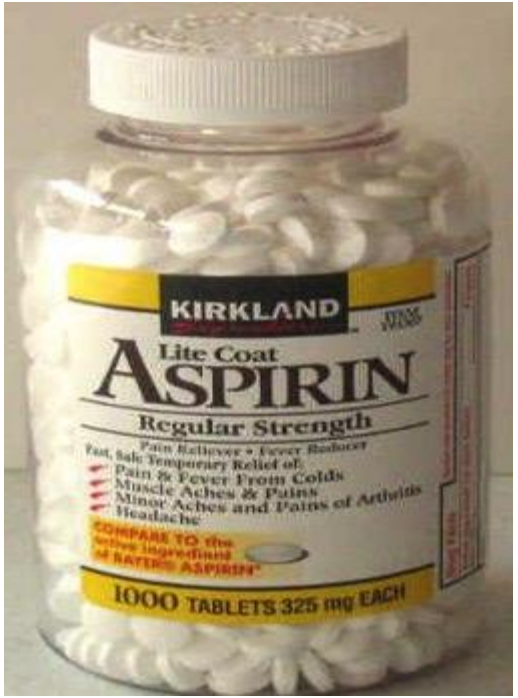
- Mild to moderate pain is often successfully treated with acetaminophen or NSAID
- Moderate to severe pain is best treated with opioid analgesics
- Adjunctive treatments are very valuable in pain management:
  - “RICE”: rest, ice, compression and elevation
  - Mydriatic/cycloplegic useful for ocular pain
  - Bandage CL or pressure patch

Systemic NSAID's

- NSAID's are the drug of choice for treating mild to moderate ocular pain.
  - Very beneficial for treating systemic inflammation as well.
- All NSAID's are rapidly absorbed from the GI tract, highly bound in the plasma, and capable of crossing the blood-brain barrier.
- Exhibit a "ceiling effect" – there is a dosage beyond which no further analgesia occurs.
  - Produce no tolerance or dependence, increasing their safety profile.
- Variability exists in patient responses to NSAID's
  - No definitive recommendation on treatment can be given.
    - If one NSAID does not work – TRY ANOTHER.

Aspirin (ASA)

- Weak organic acid.
- Oldest non-opioid analgesic available today.
  - Reduces pain by inhibiting synthesis of the prostaglandin E_2 by irreversible acetylation and inactivation.
  - Has some CNS effect on pain by acting on the hypothalamus.
- Very good anti-inflammatory and antipyretic properties.



Aspirin

- Commercially available in multiple formulations and dosages.
  - Formulations include controlled-release tablets, enteric coated, etc.
    - Add buffers to help increase GI tolerance.
  - Adult Dosage: 325 – 650 mg every 4 hours
    - Do not exceed 4 g/day.
  - Most Common use of ASA: Inhibit platelet aggregation in patients with history of heart attacks and heart surgery.
    - Most common dosing is 81 mg/day

2019 Aspirin Recommendations

- American College of Cardiology:
  - *Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.*
  - low-dose aspirin should not be routinely given as a preventive measure to adults 70 years and older or to any adult who has an increased risk of bleeding

Acetaminophen

- Mechanism of Action is not well understood.
  - Possibly some CNS component
  - Very weak inhibitor of prostaglandin synthesis

- One of the most commonly used analgesics for mild to moderate pain.
  - Equal analgesic properties to ASA unless associated with inflammation, where it is less effective.

Take home: Good for pain; Good for fever;
No effect on inflammation

Acetaminophen

- Typical Adult Dosage (FDA Based):
  - 650 mg every 4 - 6 hours for Regular Strength (2 X 325)
    - Cannot take more than 10 caplets in 24 hours.
  - 1000 mg every 6 hours for Extra Strength (2 X 500)
    - Cannot take more than 6 caplets in 24 hours.
  - 1300 mg every 8 hours for Extended Release (2 X 650)
    - Cannot take more than 6 capsules in 24 hours.
- Daily dose of Extra Strength Tylenol should not exceed <u>3 grams!</u>
  - This has been recently changed from 4000 mg which can be done with doctor approval.
- Should only be used for short term therapy
- Exhibits a ceiling effect, like NSAIDs and ASA.

Dangers of Acetaminophen

- Acetaminophen overdose is the leading cause of liver failure in the U.S.
  - It sends 56,000 people to the emergency room annually and causes approximately 400 deaths yearly.

- Acetaminophen is used in so many products, people are often unaware that they are taking it, leading to more overdoses.
  - Combined with agents to get wide range of symptom coverage.
    - Antihistamines such as diphenhydramine – Tylenol PM
    - Diuretics such as Pyrilamine maleate – Midol Complete
    - Cough Suppressants such as Dextromethorphan - Nyquil

Combining Meds for More Severe Pain Relief

- Acetaminophen and Aspirin are often combined with each other and various agents to increase their analgesic effect.
  - Frequently seen in combination with narcotic analgesics.
  - Caffeine is also commonly used, especially in the treatment of migraines.
    - Excedrin Migraine
      - Acetaminophen 250 mg
      - Aspirin 250 mg
      - Caffeine 65 mg

Ibuprofen

- Adult analgesic dose: 200-400mg q4hours
  - Maximum Dosage: 2400 mg/day for pain (approved for 3200 mg/day in arthritis treatment)
- OTC: 200 mg tabs (US) 400 and 600 mg (Canada)
- Rx: 300, 400, 600, 800mg tabs
- Peak levels 1-2 hours
- Most renal toxic of all the NSAID's
- Brand Names: Motrin, Advil, and Nuprin

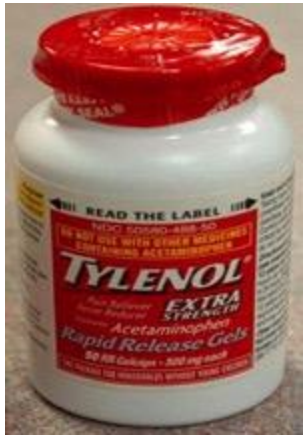
Consider Combining APAP with NSAID's for Mild to Moderate Pain Relief

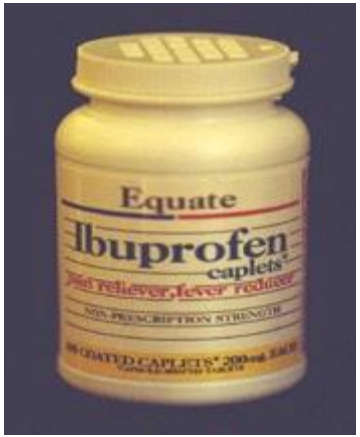
1:00 pm: Two 325mg Tylenol

3:00 pm: Two 200mg Ibuprofen

5:00 pm: Two 325mg Tylenol

7:00 pm: Two 200mg Ibuprofen





Alternated every 2 hours while awake

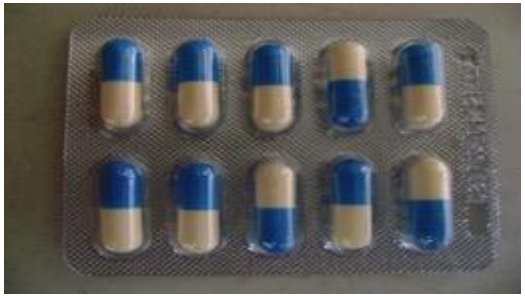
- Each medication is q 4 hours.

Naproxen Sodium

- Type of Medication Determines Dosage (This is for Naproxen Sodium):
  - OTC: 220mg tablets (Aleve)
  - Rx: 275 and 550 mg tablets (Anaprox and Anaprox DS)

- Adult Dose:
  - OTC: 220 or 440 initial dose followed by 220 mg q 8 – 12 hours.
  - Rx: 550 initial dose, followed by 275mg q6-8h or 550mg q12hours.
    - Maximum Dose: 1375mg/day.

Indole Acetic Acids: Indomethacin



- Rx Only
- Available as 25, 50, 75 ER, and IV
- Adult Dosage: 25 - 50 mg TID
- Mainly used as a short term anti-inflammatory especially for conditions that do not respond to less toxic NSAIDS.
  - Indomethacin has a very high level of intolerance compared to other NSAID's.

NSAIDS Black Box Warning

- BLACK BOX WARNING:
  - May increase the risk of serious thrombotic events, MI, and stroke.
  - Increase risk of serious GI adverse effects such as bleeding, ulcer, and perforation.

Contraindications to NSAIDs

- Avoid in:
  - Pregnancy (especially the late trimesters)
  - Active Peptic Ulcer Disease
  - Cross Sensitivity to ASA
  - Previous Hypersensitivity to NSAIDs
  - Chronic Renal Insufficiency

- At Risk Patients Include:
  - Dehydration
  - HTN or CHF
  - Use of ACE Inhibitors
  - Advanced Age

Cox-2 Inhibitors

- Selective agents for only COX-2 designed to protect the GI system from the side effects seen with NSAID's.

- Major agent available on the market is Celecoxib (Celebrex).
  - Other agents Valdecoxib (Bextra) and Rofecoxib (Vioxx) were removed from the market due to increased risk of heart attacks and strokes.

- It is approved for the treatment of osteoarthritis and rheumatoid arthritis.
  - Dosage: 100 mg BID or 200 mg daily

COX-2 Selective Agents

- Must avoid use in patients with cardiovascular risk factors.
  - Studies have shown that the greater the Cox-2 selectivity the greater the risk for hypertension from NSAID's.

- Celebrex has still been shown to cause GI bleeding in patients at risk and should not be consider "safe".

NSAID-related ulcers

- COX-2 inhibitors such as celecoxib (Celebrex) are less likely to cause ulcers than aspirin
- Proton pump inhibitors (e.g. Losec^{R} Prevacid® or Prilosec ®) help to offset the risk of NSAID-related stomach ulcers
  - patients should be treated with concomitant proton pump inhibitors once daily, which results in ulcer healing rates of approximately 80% at 8 weeks in patients continuing to take NSAIDs

Oral Analgesics: Guidelines

- Never exceed maximum recommended dosages:
  - ASA: 8 grams/day
  - Acetaminophen: 4 grams/day?? (3000 likely safer limit)
  - Naproxen sodium: 1375 mg/day
  - Ibuprofen: 1200 mg/day OTC and 2400 mg/day prescription
  - Codeine: 360 mg/day

Opioids Information

- Drug of first choice for the treatment of **severe** acute pain.
  - Block the body's natural protective mechanism for protecting areas in pain – thus never prescribe unless you know the direct cause of the pain.

- Often administered in combination with acetaminophen or aspirin to enhance the analgesic effect.
  - FDA recommended in 2011 that all prescription narcotics containing acetaminophen standardize and limit the dosage to 325 mg.
    - This is to be slowly phased in over three years (just required in January 2014).

Tolerance to Opioids

- Patients experience shorter durations of analgesia from similar dosages, followed by increased levels of pain. Requires dosages to continually be adjusted to provide desired effects.

- Withdrawal can occur if long term use is discontinued abruptly resulting in increased heart rates and blood pressure, nausea, vomiting, dilated pupils, photophobia, shivering, etc. These symptoms peak approximately 2 to 3 days after the last dose and will subside over weeks.

Patient Education

- Avoid all depressants – especially using along with alcohol.
- Must educate all patients of risks of these symptoms and caution them for driving or operating dangerous machines.
- Stomach upset can be helped by consuming the medication with food.
- Watch for signs of breathing difficulty or changes in blood pressure.

Opioids Contraindications

- Avoid in patients with history of hypersensitivity to narcotics.
  - True allergic reactions are rare and often involve skin rashes or contact dermatitis.
- Avoid in patients with acute bronchial asthma or COPD.
- Avoid in patients with a history of depression or suicidal tendencies.
- Avoid in patients with history of addiction.
- Avoid in pregnancy (Most opioids are pregnancy category C).
  - Drug Effects seem to be insignificant in nursing infants, but should recommend waiting at least 4 – 6 hours to nurse.
- Use caution in kidney or liver dysfunction due to increased accumulation of the medication.
- Must be very cautious of drug interactions and always review medications with your patient prior to prescribing.

Scheduled Medications – Most Opioids

Schedule	Description	Optometric Medications
I	Not commercially available; no approved indication	
II	Very addictive medications that are accepted for medicinal use	Oxycodone = OxyContin, OxyFast Oxycodone + APAP = Percocet or Tylox Oxycodone + ASA = Percodan Oxycodone + NSAID = Combunox Hydromorphone (Dilaudid) Codeine Sulfate = Codeine Generic Meperidine (Demerol) **Hydrocodone + APAP = Lortab or Vicodin** **Hydrocodone + Ibuprofen = Vicoprofen**
III	Significant abuse risk, but less potent than I or II. May still contain narcotics.	Codeine + APAP = Tylenol 3 and Tylenol 4
IV	Relatively low abuse potential and limited risk	Propoxyphene (Darvon) Propoxyphene with APAP = Darvocet (Removed from Market in November 2010). Pentazocine + APAP (Talacen) Tramadol
V	Very limited abuse potential. May be OTC in some states.	Acetaminophen

Schedule III Opioids: Codeine

- Prodrug that relies on the cytochrome P-450 system to be metabolized to active drug morphine.
  - Schedule II medication if prescribed alone (Codeine Sulfate 15, 30, 60 mg generic.)

- Analgesic effect occurs within 20 minutes of ingestion and reaches a maximum at 1 – 2 hours.
  - Ceiling effect occurs.

Schedule III Opioids: Codeine

- Usually administered in combination with .
  - Tylenol 3 = Codeine 30 mg and Acetamenophin 300 mg
    - Dosage: 1-2 tablets every 4 hours.
  - Tylenol 4 = Codeine 60 mg and Acetamenophin 300 mg
    - Dosage: 1 tablet every 4 – 6 hours
  - Also available as generic with 15, 30, or 60 mg of Codeine with 300 mg of Acet. or elixer of 12 mg codeine + 120 mg Acet. per 5 mL.
    - Elixer can be used in children for pain management if >3 years.

The FDA has mandated that all prescription medications have no more than 325 mg of Acetaminophen in each capsule/tablet by January 2014.

Schedule II Opioids: Hydrocodone

- Approximately 6X more potent than codeine.
- Milder Side Effects than Codeine: Less constipation and sedation.
- Clinically believed to cause more euphoria than codeine, but this is not backed by clinical studies.

Schedule II Opioids: Hydrocodone

- Used in combination with APAP and Ibuprofen.
  - Lortab: Hydrocodone 5, 7.5, and 10 mg with APAP 325 mg
    - Dosage: 1-2 tablet every 4-6 hours
  - Lortab Elixer: Hydrocodone 10 mg with APAP 300 / 15 mL
    - Dosage: 3 tsp every 4-6 hours
  - Vicodin: Hydrocodone 5 mg with Acetaminophen 300 mg
  - Vicodin HP: Hydrocodone 10 mg with Acetaminophen 300 mg
    - Dosage: 1 tablet every 4-6 hours
  - Vicodin ES: Hydrocodone 7.5 mg with Acetaminophen 300 mg
    - Dosage: 1 tablet every 4 – 6 hours
  - Vicoprofen: Hydrocodone 7.5 mg with Ibuprofen 200 mg
    - Dosage: 1 tablet every 4-6 hours
  - Norco: Hydrocodone 5, 7.5, and 10 with 325 mg APAP

Schedule II Opioids: Oxycodone

- Approximately 10-12X more potent than codeine
  - As potent as parenteral morphine when given orally.

- Lower level of side effects in comparison to morphine, but high level of euphoria produced, thus higher level of abuse risk.

Schedule II Opioids: Oxycodone

- Available in combination with APAP, ASA, or Ibuprofen.
  - Percocet Tablets
    - 2.5, 5, 7.5 or 10 mg Oxycodone with 325 mg Acetaminophen
    - Dosage: 1 tablet every 6 hours
  - Tylox Capsules
    - 5 mg Oxycodone with 300 mg Acetaminophen
    - Dosage: 1 tablet every 6 hours
  - Percodan Tablets
    - 4.5 mg Oxycodone HCl
    - 0.38 mg Oxycodone terephthalate
    - 325 mg Aspirin
    - Dosage: 1 tablet every 6 hours
  - Combunox
    - 5 mg Oxycodone with 400 mg Ibuprofen
    - Dosage: 1 tablet daily to QID

Schedule IV: Tramadol (Ultram)

- Central acting narcotic
  - Synethetic analogue of codeine.
  - Binds to mu receptors and inhibits norepinephrine and serotonin reuptake.
  - Potential for abuse is very low, but has occurred.

- Available as 50 mg tablets.

- Dosage: 50 – 100 mg q4 – 6 hours.
  - Analgesia occurs after 1 hour.
  - Maximum dose: 400 mg/day

Tramadol Extended Release (Ultram ER)

- Available dosages of 100, 200, and 300 mg extended.
  - Begin taking 100 mg daily X 5 days
  - Increase by 100 mg if relief not met to 200 mg X 5 days.
  - 300 mg maximum daily.
- Does not work on all patients – some need heavy doses every 4-6 hours.

- More for chronic pain control.

Tramadol + APAP (Ultracet)

- Combination of:
  - 325 mg of APAP
  - 37.5 mg of Tramadol
- Dosage: 2 tablets every 4 – 6 hours
- Max: 8 tablets daily

Tramadol

- Must use with extreme caution in patients taking MAO inhibitors.
- Despite low risk for addiction should still use caution in patients with history of problems.
- Similar side effects to all opioids such as dizziness, nausea, dry mouth, and sedation.
- Avoid in patients with liver or renal impairment.
- Inferior pain relief with risk of side effects has limited Tramadol’s use clinically.