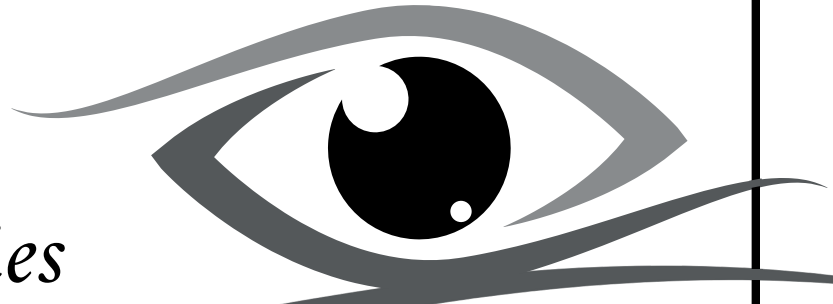




College of Optometry
UNIVERSITY OF HOUSTON

Monthly FOCUS

LIVE Webinar Series



PowerPoint
Lecture Handouts



Monthly FOCUS Live Webinar Series Agenda

Wednesday, April 3, 2024

6:45 pm to 7:00 pm Virtual Conference Entry Period

7:00 pm to 7:05 pm Announcements & CE Credit Overview

7:05 pm to 7:55 pm **Pain Management in Eye Care**
Presented by Danica Marrelli, OD, FAAO

1 D/T Hour

COPE ID #
90960-PH

7:55 pm to 8:00 pm Questions & Answer Session/Conclusion

Pain Management in Eye Care

Danica J. Marrelli, OD, FAAO
University of Houston College of Optometry

Dmarrelli@uh.edu

1

FINANCIAL DISCLOSURE

- I have received speaking fees and/or advisory board fees from:
 - Allergan
 - Bausch & Lomb
 - Carl Zeiss Meditec
 - Glaukos
 - M&S Technologies
 - Santen
 - Thea
- All relevant financial relationships have been mitigated

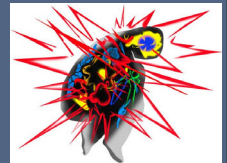
2

Agenda

- General Concepts of Pain
- Optometric Indications for Pain Management
- Topical Agents
- Ancillary measures
- Oral Agents – Non-controlled substances
- Controlled Substances

3

PAIN



- Pain is not a disease
 - Symptom of a disorder that must be diagnosed
 - Must treat the disorder AND manage the pain
- Pain = unpleasant sensory and emotional experience *associated with actual or potential tissue damage*
- Pain is the most common reason for seeking medical care
- At least 75 million Americans suffer from chronic pain
- *Analgesia: No pain is felt despite the presence of a normally painful stimuli*

4

PAIN MANAGEMENT

- Acute: injury, inflammation (most ocular pain)
- Chronic
- Neuropathic: from diseases of the nerves or injury to nerves

5

ACUTE PAIN

- Acute pain has a specific and obvious cause (inflammation, trauma, surgery, infection)
 - Before prescribing pain medication, you MUST find the cause of the pain
- Limited duration
- Resolves when the source of pain is detected and treated (a few exceptions; e.g. post-herpetic neuralgia)
- May be treated with topical/local treatment
 - Fewer side effects/complications
- Most ocular pain is acute in nature

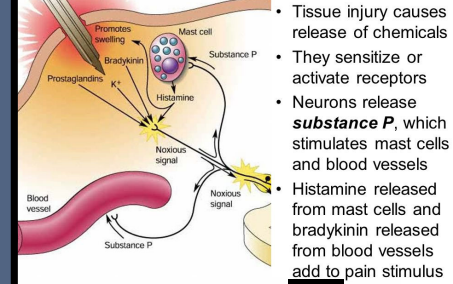
6

EFFECTS OF PAIN

- Physiologic Effects:
 - Tachycardia
 - Systemic hypertension
 - Tachypnea
 - Exacerbation of pre-existing cardiovascular disease
- Psychologic Effects:
 - Uncooperativeness
 - Poor sleep patterns
 - Anxiety/depression

7

Pain Mediators



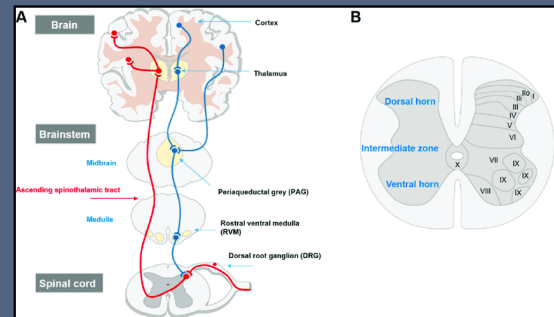
- Tissue injury causes release of chemicals
- They sensitize or activate receptors
- Neurons release **substance P**, which stimulates mast cells and blood vessels
- Histamine released from mast cells and bradykinin released from blood vessels add to pain stimulus

8

Physiology of Pain

- Sensations of pain are modulated by both ascending and descending pathways in CNS
- **ASCENDING PATH:**
 - Nociceptors (pain receptors) are found on primary afferent nerve endings; send action potential to dorsal horn of SC
 - Alpha-delta fibers: sharp localized pain (somatic pain); activated by chemical, thermal, or mechanical stimuli (cramping, gnawing)
 - C-fibers: dull, diffuse, aching pain (visceral pain); stimulated by bradykinin and prostaglandins (more vague, deep pain)
 - Alpha-delta and C-fibers release substances in dorsal horn of SC that activate secondary neurons (form ascending spinothalamic pathway) which projects to thalamus, then third order neuron to somatosensory cortex
- **DESCENDING PATH:** starts in midbrain/medulla, project downward to dorsal horn
 - Release norepinephrine, 5-HT, and other neurotransmitters; inhibit ascending pathway activity

9



10

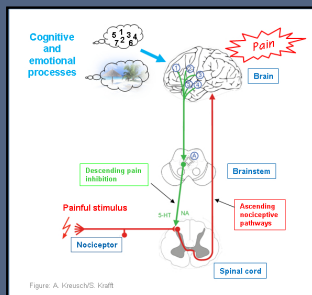


Figure: A. Knaus/US: Knaus

11

CAUSES OF OCULAR PAIN

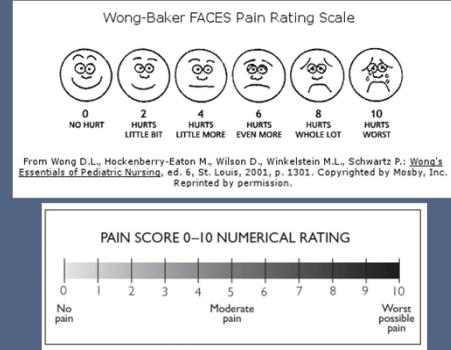
- Adnexal issues:
 - Hordeolum
 - Dacryocystitis
 - Skin injury or lesion
 - Orbital fracture
- Cornea/Conjunctiva
 - Lacerations
 - Abrasions
 - Thermal and Chemical burn/injury
 - Inflammatory keratitis
 - Infectious corneal ulcers
 - Foreign body
- Uveitis
- Hyphema
- Rapid elevation in IOP (Acute Angle Closure, Post-op spike, etc)
- Post-Surgical Pain

12

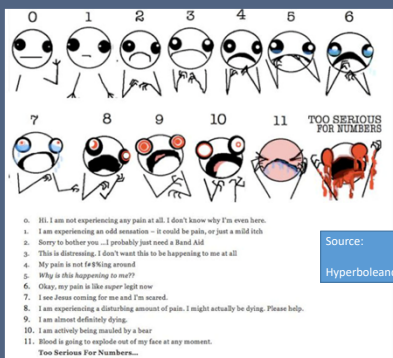
Before Your Write...

- Assess pain (scale)
- Determine etiology of pain – MUST BE A VISIBLE CAUSE
- Medical history:
 - Contraindications to therapy: liver, kidney, pregnancy, psychiatric meds
 - Drug history: what is patient taking (OTC)
 - Allergy history – Aspirin???

13



14



15

PAIN MANAGEMENT

- PERIPHERAL AGENTS: NSAIDs
 - Act on peripheral pain receptors and prevent sensitization/discharge of nociceptors
 - Do not produce tolerance or dependence
 - Good for mild-moderate pain
 - Oral and topical ophthalmics
- ACETAMINOPHEN (?)
- CENTRAL AGENTS: OPIOIDS
 - Interact with specific receptors in the CNS – interrupt pain message and its emotional response
- OTHER AGENTS

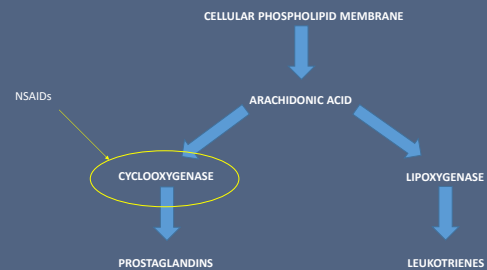
16

PERIPHERALLY ACTING AGENTS

- Prevent sensitization and discharge of nociceptors
- NSAIDs (including aspirin)
 - Block the formation of inflammatory and pain mediation (e.g. prostaglandins) at the cyclooxygenase pathway
 - Have analgesic, anti-inflammatory, and anti-pyretic properties

17

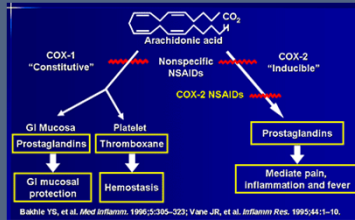
INFLAMMATORY CASCADE



18

CYCLOOXYGENASE

- COX-1: Constitutive enzyme; involved in normal tissue function
- COX-2: Inducible enzyme; responsible for production of prostanoid mediators of inflammation



19

NSAIDs: THE CYCLOOXYGENASE BLOCKERS

- **ASPIRIN** = Acetylsalicylic acid (ASA)
 - Block cyclooxygenase (non-specific)
 - Analgesic vs Anti-inflammatory dose
 - Acetylated vs non-acetylated
 - Irreversibly block platelets
 - Best for use as an anti-coagulant
 - None are safe in potential "bleeders"
 - Adult dose is 325-650mg every 4 hours (not more than 4g/day)
 - Take with food, full glass of water



20

Aspirin

- Contraindications:
 - Upper GI disease
 - Bleeding disorders
 - CHILDREN <18 y with viral illness, pox disease (Reye syndrome)
 - Allergy
 - Pregnancy

21

NON-SELECTIVE NSAIDs other than ASA

- Less bleeding potential
- Less GI upset
- Greater efficacy compared to ASA
- All have same efficacy in comparable dosages
- All have same side effects

22

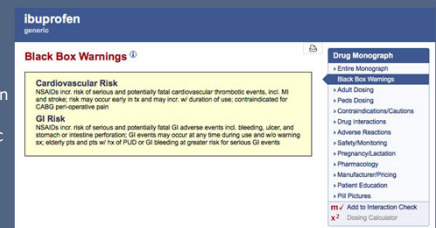
Non-ASA NSAIDs

- Non-selective:
 - Diclofenac 50mg qid (200mg/day)- Rx only
 - **Ibuprofen 800mg qid (MAX 2400-3200mg/day) – OTC and Rx**
 - Ketoprofen 300mg/day (200mg/day sustained release) – Rx only
 - Naproxen sodium 220mg q 8-12 h- OTC and Rx
- Cox-2 inhibitors:
 - Celecoxib (Celebrex) 400mg loading dose, then addition 200mg on day one; after day 1: 200mg bid – Rx only

23

NSAID SIDE EFFECTS, ADVERSE EFFECTS

- Inhibit platelets (only ASA is irreversible)
- GI upset
- GI ulcer/bleeding/perforation
- Increased risk of serious cardiovascular thrombotic events (heart attack/stroke) – FDA increased warnings in 2015



24

NSAIDs - PRECAUTIONS

- Avoid in asthmatics and those with nasal polyps
- **ALLERGIC TO ONE = ALLERGIC TO ALL**
- Diabetics: risk of increased protein binding in Type 2 DM
- All diabetics at risk of renal insufficiency
- Children with fever: NO ASA
- Avoid in pregnant/nursing mother
- Avoid in patients with GI problems
- Avoid in patients with bleeding disorders, vitamin K deficiency, anticoagulant therapy

25



26

TOPICAL OPHTHALMIC NSAIDS

- ketorolac tromethamine
 - 0.5% (Acular [®], **generic**, Acular PF)
 - Seasonal allergic conjunctivitis: 1 drop qid
 - Post-op pain and inflammation: begin 24 hours post-op, continue x 2 weeks
 - 0.45% Acuvail – less stinging
- nepafenac (Post-op inflammation and pain)
 - 0.1% (Nevanac) – tid
 - 0.3% (Ibuprofen) – once daily (qd)
- diclofenac 0.1% (Voltaren [®], **generic**) – pain and inflammation after surgery
 - Cataract and refractive surgery – qid dosing
 - Corneal melt with generic version previously reported
- bromfenac – pain and inflammation after cataract surgery
 - 0.07% (Prolensa [®])
 - 0.09% (Bromday, **generic**)
- flurbiprofen 0.03% (**generic**)
 - Used by surgeon DURING surgery (provides miosis)

27

MANAGING CORNEAL PAIN

- Lubricants
- Bandage CL
- Pressure patch
- Cycloplegia
- Topical NSAIDs (OFF-LABEL)

28

CYCLOPLEGIA

- Don't forget the cycloplegia to decrease pain associated with ciliary body spasm
 - Corneal abrasion
 - Corneal FB
 - Infectious keratitis
 - Anterior uveitis

29

ANALGESIC PHARMACOLOGY what else besides NSAIDs???

- Acetaminophen (n-Acetyl-P-aminophenol) = APAP
- Unknown central mechanism
- Antipyretic – works on hypothalamus
- NO ANTI-INFLAMMATORY EFFECT
- NO INHIBITION OF PLATELETS

30

ACETAMINOPHEN – WHEN TO USE

- Drug of FIRST CHOICE in:
 - Children
 - Viral-induced fever
 - Pregnancy
 - Nursing mothers
 - Patients with GI disorders
 - Patients with bleeding/clotting disorders

31

ACETAMINOPHEN – WHEN TO RECONSIDER

- Acetaminophen is associated with liver failure in alcoholics (>3 drinks/day)
- Liver failure = decreased drug metabolism = overdose
- **MAXIMUM ADULT DOSE:** 4 g/day (now lower recommendation ~3200mg/day)
 - Regular strength: 325mg/tablet or capsule
 - Dose: 1-2 pills every 4-6 hours
 - DO NOT EXCEED 10 tablets in 24 hours
 - Extra strength: 500mg/tablet or capsule
 - Dose: 1-2 pills every 4-6 hours
 - DO NOT EXCEED 6 pills in 24 hours

32

PEDIATRIC AVAILABILITY

- Oral suspension 160mg/5ml
- Chewable tablet 160mg/tablet
- Dissolvable powder 160mg/powder pac

33

ACETAMINOPHEN Liver metabolism

- Major pathway: Majority of drug is metabolized to produce non-toxic metabolite
- Minor pathway: Small amount of drug produces highly reactive intermediate (acetylimidoquinone) that conjugates with glutathione and is inactivated
- At TOXIC levels, the minor pathway cannot keep up (liver's supply of glutathione is limited), causing an increase in the reactive intermediate which is hepatotoxic

34

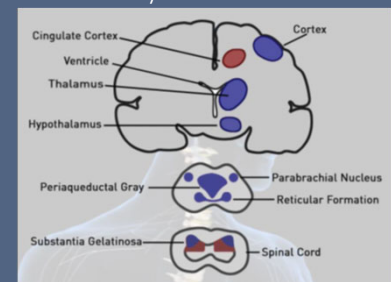
Centrally Acting Agents

- React with receptors in the CNS
- Interrupt the pain message AND the emotional response
- Opioids – e.g. morphine, oxycodone, codeine – mechanism is poorly understood
- Endorphins – naturally manufactured by the brain, they may block peripheral transmitters or hyperpolarize neurons

35

OPIOID RECEPTORS/PEPTIDES

- MU/Endorphins
- Kappa/Dynorphins
- Delta/Enkephalins



36

COMBINATION OPIATE ANALGESICS

• CODEINE +	APAP = Tylenol 1, 2, 3, 4
• HYDROCODONE +	APAP = Vicodin
• Oxycodone +	ASA = Percodan
• Oxycodone +	APAP = Percocet
• Tramadol +	APAP = Ultracet

43

Which Tylenol with Codeine is Best?

- All contain 5 grains (300mg) APAP
- Tylenol #4 = 1 grain (60mg) codeine
- **Tylenol #3 = ½ grain (30mg) codeine ***** MOST COMMONLY Rx**
- Tylenol #2 = ¼ grain (15mg) codeine
- Tylenol #1 = 1/8 grain (7.5mg) codeine

44

OXYCODONE: “The Big Gun”

- With ASA = Percodan
- With APAP = Percocet
- Schedule II = High abuse potential

45

SNAPSHOT OF OPIOID CRISIS HISTORY

- 1995:
 - Pain is declared the “5th vital sign”
 - Oxycontin FDA approved as “safe alternative to combination opioids”
- 1998:
 - FDA approves Fentanyl (50x stronger than heroin) for cancer breakthrough pain (patches and lollipops)
 - 10-point pain scale
 - JCAHO & Purdue Pharma team up: “There is no evidence that addiction is a significant issue when persons are given opioids for pain control”



46

OPIOID CRISIS HISTORY

- 1998-2002: Opioid prescriptions increase:
 - Oxycodone 402%
 - Morphine 73%
 - Hydromorphone 96%
- 2004: Federation of State Medical Boards recommend sanctioning doctors who under-treat pain
- **2007**: Purdue Pharma sued by FDA, fined \$634.5M for misleading advertising and misrepresenting the risk of addictive properties of Oxycontin
- 2009:
 - JCAHO removes requirement to assess all patients for pain
 - USA consumes 99% of world's hydrocodone and 81% of oxycodone



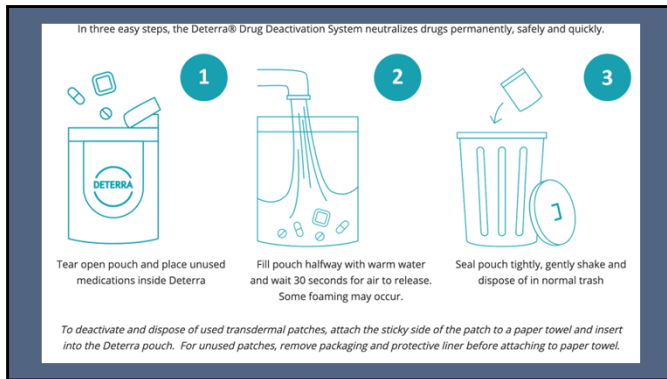
47

OPIOID CRISIS HISTORY

- 2011:
 - CDC declares that overdoses due to painkillers is an epidemic
- 2000-2014: Opioid overdose deaths increase by 200% in USA
- 2016:
 - AMA drops “pain as 5th vital”
 - Comprehensive Addiction Recovery Act passes
 - Expand education/prevention efforts
 - Expand availability of naloxone to law enforcement and first responders
 - Expand resources to ID and treat incarcerated addicts
 - Expand disposal sites
 - Launch evidence-based opioid and heroin treatment/intervention program
 - Launch medication-assisted treatment demonstration program
 - Strengthen prescription drug monitoring program to help states monitor and track drug diversion and to help at-risk people access services
- 2017: 116 Americans die each day from opioid overdose



48



55

Can we control pain without opioids?

- 500-1000mg Tylenol + 400-600 mg ibuprofen
 - Has been shown to have equivalent analgesia to opioids without the unwanted side effects and risk of dependence
- Have to remember contraindications/cautions of EACH drug
 - Pregnancy (ibuprofen)
 - Bleeding/GI (ibuprofen)
 - Renal disease (ibuprofen)
 - Liver disease (acetaminophen)

56

A special case of ocular pain

- Herpes Zoster Post-Herpetic Neuralgia
 - Pain that lasts 3 months or longer after the shingles rash has cleared
 - Burning, stabbing, deep, aching
 - Sensitive to touch
 - Itching and numbness
- Who's at Risk?
 - Older than 50
 - Severe rash and pain
 - Other chronic conditions (diabetes)
 - Face/torso location of rash
 - Delayed antiviral therapy

57

Manage Post-Herpetic Neuralgia

- **PREVENT:** Recognize HZ and prescribe oral antivirals ASAP
- **Treat:**
 - Oral antivirals
 - Zostrix crème to area 3-4 times per day
 - Low dose tricyclic antidepressants (amitriptyline 25mg/day)
 - Gabapentin (Neurontin) – huge dose range (100-5,000mg/day)
 - Start low, but must give enough
 - ?? Within OD scope of practice
 - 5HT Agonists ("triptan" drugs)
 - Inhibit trigeminal nerve

58

Summary

- Acute Ocular Pain is common
- Managing the underlying condition is essential
- Relief is often provided with local pharmaceuticals and non-pharmaceutical measures
- Oral analgesia is occasionally needed
 - Non-opioid and non-pharmacologic measures may be sufficient
 - Opioid analgesics may be prescribed with appropriate precautions in certain situations of severe acute pain

59

Thank You For Your Attention!

Questions?

Email me: dmarrelli@uh.edu

60