Case Based Management of Ocular Pain

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Pain is NOT a disease-It is a sign of a disorder that must be diagnosed in conjunction with the management of the pain.

What is Pain?

- **Any unpleasant sensory and emotional experience associated with actual or potential tissue damage.**
- **75 million suffer from chronic pain**
- **1/3- 1/2 require daily pain management**

Analgesia VS Inflammation

- Choose the proper agent
- Choose the proper dose
- Dosage for the management of inflammation is higher than that for analgesia
- Side-effects increase with higher dosages

Why??
Why do I Have Pain?

- Pain mechanisms are complex
- Peripheral VS Central Pain
- Direct nerve stimulation-Drop hammer on toe
- Inflammatory pain-Prostaglandins
- Tissue damage-Via infection or trauma

When?@@@@@

When Do I Need to Consider Pain Management?

- Listen to your patient…IT HURTS!
- Be aware of clinical procedures and ocular disorders that are associated with significant

Acute Pain

- ~ specific and obvious cause (e.g. trauma, surgery)-ALWAYS FIND CAUSE
- ~ limited duration
- Resolves when the source of pain is detected and treated
- ~ requires topical/local treatment
  - Fewer side effects/complications

Physiologic Effects of Pain

- Tachycardia
- Systemic hypertension
- Tachypnea
- Can exacerbate pre-existing cardiovascular disease

Psychological Effects of Pain

- Poor sleep patterns
- Anxiety
- Uncooperativeness

Analgesia

- The removal of pain
- Peripheral Agents: NSAID's
- Central Agents: Opiates
- Acetaminophen

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**

Topical Lidocaine is a BETTER anesthetic

- **BENEFITS:**
- **NO CROSS SENSITIVITY**
- **EFFICACY ON VASCULAR TISSUE**
- **NO LOCAL METABOLISM**
- **LONGER LASTING**

Analgesic Indications

FIRST, TX the primary condition, however, don’t ignore pain management

Indications

- Abrasions
- Lacerations
- Thermal and Chemical injury
- Dacryocystitis
- Bacterial corneal ulcers
- Cryo therapy
- Micropuncture

Prokera

- Amniotic membrane on a scaffold ring
- Functions as a bandage lens
- Healing properties?
- COST = $900
- REIMBUSEMENT = $1,400

SECOND: KEEP IT HEALED

- **PEARL: Think Doxycycline (50mg BID)**
- **Watch out for smokers-Vitamin C (1-2gm/D**
- **SALT OINT, NOT SOLUTION**

PAIN MGT OPTIONS: Oxycodone, The "BIG GUN"

- With ASA = Percodan
- With APAP = Percocett
- Schedule II drug = High abuse
- Vicodin now schedule ll
- Tramadol (Ultram)
- 50mg, up to 400mg max/D
- Usual 1-2 tabs QID PO

Watch Out for those Air Bags

- **Blunt trauma to cornea produces a concussive trauma**
- **Abrasive surface can denude the epithelium completely**
- **Temporary to permanent stromal edema and hazing-de-compensation due to endothelial shock**
- **Often an associated uveitis/hyphema and other forms of blunt ocular traumatic injuries**

Analgesia VS Anti-inflammatory Therapy

- NSAID's are both analgesic and anti-inflammatory agents
- Anti-inflammatory dose is higher thyan analgesic dose
- Higher dosages = greater side-effects

Analgesic Pharmacology

- Tylenol/Acetaminophen/(N-Acetyl-P-aminophenol)/APAP
- Unknown central mechanism
- Anti-pyretic: Hypothalmus
- No anti-inflammatory effect@@@@
- No inhibition of platelets@@@@

Acetaminophen is a Safe Drug?

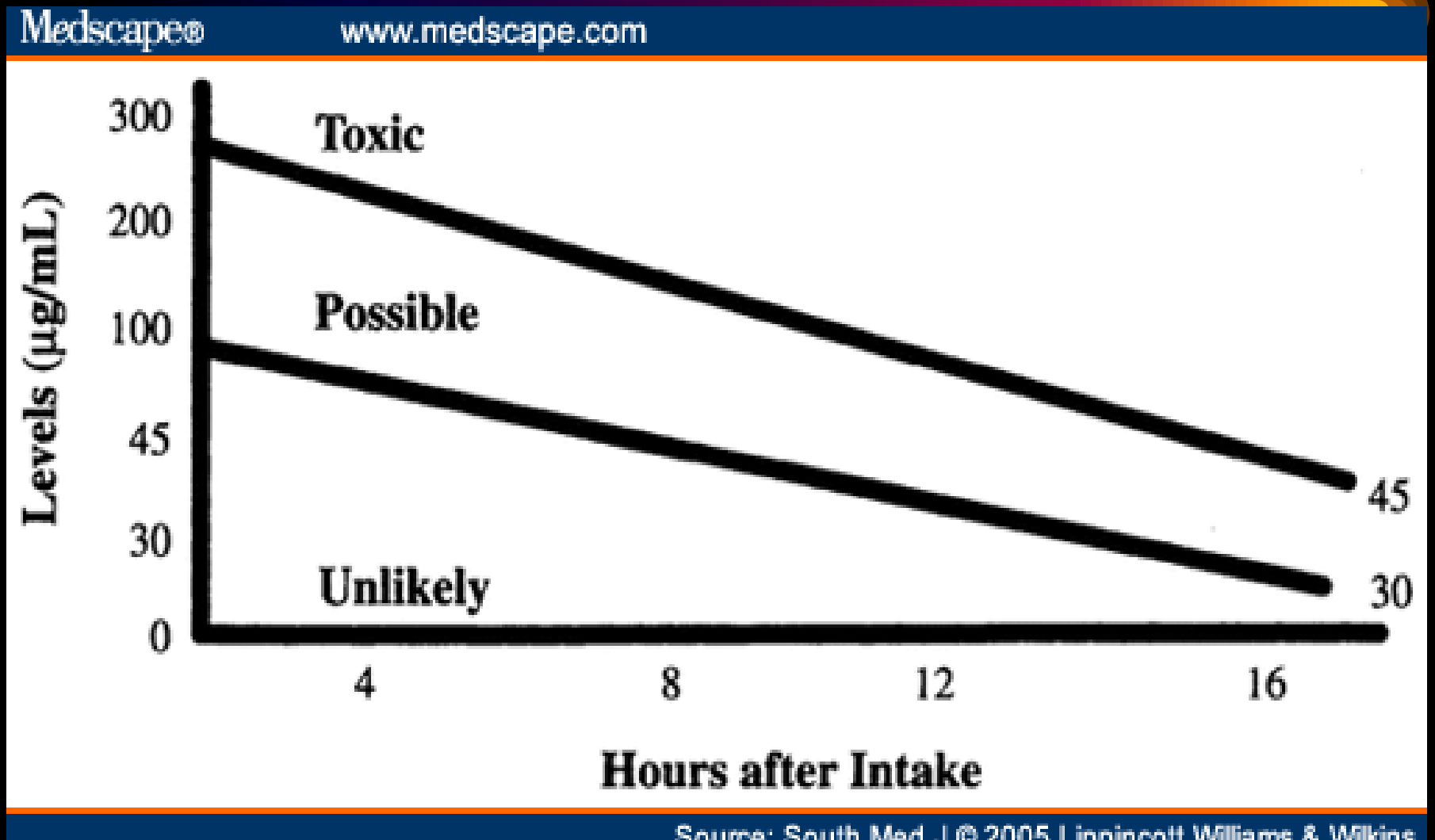
Drug of Choice (DOC) in:

- **Children**
- **Viral induced fever**
- **Pregnancy@@@@**
- **Nursing mothers**
- **No GI distress**
- **No Increase in Bleeding?@@@@**

If They Like to Drink, Think Twice About Acetaminophen

- Acetaminophen associated with liver failure in alcoholics (>3 drinks/d)
- Liver failure = decreased drug metabolism = overdose
- Reduced vitamin K clotting factors = increased bleeding
- Max adult dose = 4gm/D = 8 extra-strength Tylenol per 24 hours (2.6gms?)
- 5% of metabolites hepatotoxic

Acetaminophen toxicity



MU Opioid receptors

- **Classic morphine receptor**
- **Located in brain and spinal cord**
- **Stimulated by endogenous endorphins**
- **Binding of drug to these receptors produces analgesia/sedation/decreased BP/itching/nausea/euphoria/decreased respiration/**
- **Effects decline as drug tolerance develops**
- **Narcotic antagonists block these receptors**

Kappa Opioid receptors

- Novel receptors
- Stimulation relieves pain, but produces nausea and sweating (dysphoria)
- Endogenous transmitters are dynorphins
- Located in the periphery by pain neurons

Delta Opioid receptors

- Stimulated by endogenous enkephalins
- Produces "ischemic preconditioning"
- Stimulation induced protective increase in blood flow to tissues surrounding an ischemic area
- May have cardioprotective effect

Opiate Analgesics

- Block central pain receptors, reduce perception of pain-They feel pain, but don’t care
- Allergic to one opiate, allergic to all opiates
- Know your schedules
- Schedule II, high abuse, V= low abuse
- Know your side-effects/autonomics

Side-effects

- Respiration-sleep apnea/COPD
- Urinary tract/the big prostate/incontinance TX
- GI Tract: The food stops here
- Interaction with other anticholinergics/
- DRY/DROWSINESS/GLC

COMBINATION OPIATE ANALGESICS

- Propoxyphene +
- Propoxyphene +
- Codeine +
- Hydrocodone +
- Oxycodone +
- Oxycodone +

- ASA = Darvon cmpd
- APAP = Darvocett
- Tylenol 1,2,3,4
- APAP = Vicodin
- ASA = Percodan
- APAP = Percocett

PROPOXYPHENE = DARVON

- Relatively poor analgesia
- Lots of sedation
- Neurological side-effects
- Use if you want them to sleep a lot
- Darvocett N 50 and 100 are the best of group = propoxypene napsylate with acetaminophen

GONE

Which Tylenol with Codeine Should You Use?

All contain 5 grains of APAP (325mg) WITH:

- **Tylenol #4 = 1 grain (60mg) codeine**
- **Tylenol #3 = 1/2 grain (30mg) codeine@@@@**
- **Tylenol #2 = 1/4 grain (15mg) codeine**
- **Tylenol #1 = 1/8 grain 7.5mg) codeine**

A CLINICAL MOMENT

36 Y/O construction worker suffers an orbital blow-out fracture, complains about severe pain, requests pain reliever

Write him a prescription for acetaminophen with codeine-give him the maximum pain relieving dosage of the drug

John Doe 7/20/00

100 Low Life Ln.

Acetaminophen with Codeine #3

#20 (Twenty)

SIG: i-ii tabs q 4-6H prn pain

Refills: Zero

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Oxycodone, The "BIG GUN"

- **With ASA = Percodan**
- **With APAP = Percocett**
- **Schedule II drug = High abuse**
- **Better alternative with a schedule III drug?**

5mg/325mg
Schedule II

Ibuprofen/acetaminophen

- Incredible synergism@@@@@@
- Non-narcotic drugs
- Non RX drugs
- Inexpensive
- Monitor for sensitivity to either drug
- No motrin in pregnancy/with blood thinners/GI problems/renal disease/CHF

Ibuprofen/Acetaminophen Indication/dosage forms

- Indications:
- Mild to severe pain
- Dosage forms
- 400-600mg motrin with 500-1000mg acetaminophen (Do not exceed 4 gms acetaminophen/day)
- No acetaminophen for persons that regularly consume daily alcohol

HOW ABOUT ULTRAM?

- A synthetic opiate with slightly reduced opiate side-effects
- NOT for opiate allergics
- Not for addicts-Induce withdrawal
- Has produced addiction
- 50-100mg QID prn-max 400mg/D
- >65, then 300mg/D max
- Ultracet, like Tylenol #3

Who gets Post-herpetic Neuralgia

- Immunocompromised folk
- The elderly
- Best treatment is prophylactic TX

Manage Potential Post-herpetic Neuralgia

- Oral acyclovir 800mg 5X daily
- Valacyclovir 1000mg TID
- Famcyclovir 500mg TID
- Zostrix creme 3-4 times daily
- Low dose tricyclic antidepressant-amitryptyline 25mg/day

Anti-depressant for pain relief?

- **Very good neural pain relief**
- **“GOOD” anticholinergic side-effects**

Rheumatoid disease

- A disease of inflammation and autoimmunity
- Affects joints-localized to the synovial membrane

Cause of RA

- **Genetic predisposition: Rheumatoid factor**

An IgM antibody (auto-immune) against IgG

Present in most RA patients

Produced by B-cells (humoral anti-body) in synovial fluid

Progression

- RF factor/IgG complex triggers complement = tissue damage
- Damage attracts cellular response- PMN's and macrophagees
- Pannus formation in joint : PMN's (+) macrophages (+) fibroblasts form scar tissue in joint
- IL-1 and TNF alpha produced by pannus stimulate osteoclasts from macrophages and produce bone reabsorption = joint damage

Meet the DMARD's

- D – Disease
- M – Modifying
- A – Anti-
- R – Rheumatic
- D - Drugs

Indications

- Relieve or reduce pain
- Improve function
- Reduce joint inflammation (swelling, tenderness & reduced ROM
- Prevent joint damage and deformity
- Prevent disability
- Improve quality of life
- More toxic than NSAIDS

Categories of DMARD's

- **FIRST GENERATION**

Gold compounds: aurothioglucose

Action: Inhibit macrophage migration and phagcytosis

Toxic: Colitis and reduced immunity

Required weekly IM injections

Categories of DMARD's

- **ORALS: 2nd generation**

Hydroxychloroquine
Leflunomide
Methotrexate
Sulfasalazine
Azathioprine
Cyclophosphamide
Cyclosporine
Minocycline
Penicillamine

Methotrexate and leflunamide

- Cytotoxic B/T cell inhibitors
- Block pyramidines (Inhibits DNA synthesis)
- **Prevent B and T cell proliferation and therefore prevent formation of RF**

Hydroxychloroquine/Plaquenil

- Inhibits lymphocytes and IL-1 production
- Dose : 200-400mg/D
- Monitor for maculopathy
- Occurs rarely/increased risk after cumulative dose of 700gm (>5yrs TX)

Categories of DMARD's

- **BIOLOGICALS (Injectables)**
- **3rd generation TNF alpha antagonists**

Abatacept : Orencia

Adalimumab : Humira

Anakinra : (Kineret)

Inflixamab : Remicade

Rituximab : Rituxan

Biologicals

- Prevent bone absorption and joint deformation
- Protein compds-must be injected
- Cost: $10K/yr
- **Adverse effects:**

Liver toxic

Opportunistic infections

Death

RA TX

OLD WAY

- Tx conservatively
- With NSAIDS-DMARDS only if severe

NEW WAY

- TX aggressively with DMARDS ASAP-”window of opportunity is early in TX
- Combination TX is common

Steroids and RA

- Block production of IL-1
- Dramatic , rapid suppression of inflammation
- Short term, intermittent use only –due to SE's
- Used until DMARDS take effect
- Local joint injections can produce degeneration of cartilage