Outpatient Pain Management Updates and Guidelines
Spring COP CE Program 2019
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Objectives
• Discuss the mechanisms and benefits of adjunctive and off-label medications for pain management
• Incorporate evidence-based pain management guideline recommendations into individual patient care plans
• Educate patients and prescribers regarding methods shown to appropriately provide individual patients adequate pain management

The International Association for the Study of Pain
Definition:
PAIN is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".

As Learning- It is nice to categorize patients pain
• Acute Pain:
  – Tissue damage pain
    • Strain sprains
    • Overuse syndromes
    • Cuts
    • Surgery
  – Confined tissue damage pain
    • Malignancy
    • Bone pain
    • Dental pain
    • Fascial sheath pain
  – Headaches
    • Multiple covered elsewhere
    • Visceral vs cutaneous
• Chronic Pain
  – Malignant pain
    • Spreads other organs
  – Nerve pain
    • Parasthesias
    • Neuropathic pain
    • Post herpetic neuralgia (PHN)
    • Phantom limb
    • Wind up
  – Non-malignant chronic pain
    • Complex Regional Pain Syndrome

Disclosures
• The planners and presenter of this presentation have disclosed no conflict of interest, including no relevant financial relationships with any commercial interests

Nociception:
An unpleasant sensation occurring in varying degrees of severity as a consequence of injury, disease, or emotional disorder.

How Do you Quantitate Pain?

• Visual Analog Scales
  – What is the most accurate?

• Functionality:
  • Improvement in Quality of Life

Measures of Analgesia

Western Ontario McMasters Osteoarthritis (WOMAC)

• 24 items divided into 3 subscales:
  – Likert 0-4 or Visual analog 0-100
  – Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing
  – Stiffness (2 items): after first waking and later in the day

Measures of Anaglesic Efficacy

Comparative Drug Studies

• Pain Intensity Reduction
  – Total Pain Reduction 4, 8 hours (TOPAR)
  – Sum of Pain Intensity Differences (SPIRD)

• Functionality

• Other medication sparing effects

Dosing Dental Extraction Model
Options of Analgesia

• Before we get to options let’s consider the routes:
  – Topical
  – Systemic
    • Injectable: IM vs IV
      – Oral
        – IR
        – SR
  • Nasal
  • Buccal
  – Spinal
• Duration of therapy:
  – WHO Pain Ladder
  – “Guidelines”
  – Simple Analgesics:
    – APAP, NSAIDS
  – Weak Opioids:
    – Tramadol, Codeine
  – Strong Opioids:
    – Morphine, Oxycodone
  – Adjuncts:
    – Everything else

Pharmacologic Options of Analgesia:

Recent “Guidelines” for Pain Management:

• CDC: 2016
  – Guideline for prescribing Opioids for Chronic Pain
  – https://www.cdc.gov/drugoverdose/prescribing/guideline.html
• FDA:
  – Responding to patient advocates—at present creating own “Guidelines”
• Veterans Administration: 2017
• Fibromyalgia Treatment Guidelines: 2017
• Pharmacy Benefits Managers:
• Individual Chain Initiatives:

CDC Guidelines: 2 Page pdf

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC’s Guideline for Prescribing Opioids for Chronic Pain is intended to improve communication between physicians and patients about the risks and benefits of opioid therapy for chronic pain. Improving the safety and effectiveness of pain therapy, and reducing the risks associated with long-term opioid therapy, including opioid use disorder and suicide. If you have any questions, contact your local or respective pharmacy benefit manager for assistance.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

• Clinicians should provide nonpharmacologic therapy, including nonopioid analgesics, and consider opioids in patients with severe pain.

CDC Guideline: 12 main points

• 1- Nonpharmacologic and non-opioid preferred in chronic pain
• 2- Establish treatment goals
• 3- Discuss risks and benefits
• 4- Immediate should be prescribed not LA/SR
• 5- Prescribe lowest dose possible (Avoid >90 MME/day)
• 6- Long-term use begins with tit of acute pain
• 7- Evaluate at 1-4 weeks
• 8- Before continuing establish plans to mitigate risk (naloxone)
• 9- Review PMP for use every 3 months
• 10- Consider urine drug testing
• 11- Avoid benzos with opioids
• 12- Offer txt for patients with opioid use disorder

Opioid Deaths

Drugs Involved in U.S. Overdose Deaths, 1999 to 2017

The Pendulum of the 2019

- “If everyone is in agreement that the use of opioids is excessive:............
- It is our responsibility to know the additional options of therapy that have shown benefit-
- And recognize the situations when one class may be more beneficial than another class!”  
  — rgh
Application of Superficial Heat
• Heating pad
• Whirlpool
• Menthol/Camphor Irritants
  – Bengay®
  – IcyHot®
  – Tiger Balm®
• “Non-smell”
  – Salicylate (methyl)
  • Absorbed work from inside out
  – Lidocaine:
    • 5% Lidoderm® Rx
      – Patch and Generic
    • Now up to 4% OTC
Substance P Decreasing agents
• Capsaicin
• Low to high concentrations
  • TID-QID to affected areas

BIGGEST thing to happen to class:

First Line Therapy: Acetaminophen/Paracetamol
• Acetaminophen
  • = Tylenol®
• Scheduled improves pain
• Does not relieve swelling
  – Minimal peripheral actions
  – Central PG analgesic
• Hepatic Toxin
  • NMT 4 Grams Total/day
    – 3 grams ETOH/Liver dx
    – 2 Grams Soon?- rgh
• Blood Pressure?
  • Coumadin- > 2 Grams/day
• Overdose

“Think Pair Share”
• Which of the following conditions would be most appropriate to suggest a topical camphor/menthol preparation?
  – A. Dental abscess
  – B. Post surgical pain
  – C. Neuropathic pain
  – D. Muscle overuse strain

Rationale for Opioid Plus APAP

Tissue Damage Pain: Confined Space Pain:
• Activation of
  – “Must know physiologic cascade number Three”- rgh
• Arachidonic Acid Metabolism
  – Bone
  – Injury
  – Dental pain
  – Osteoarthritis
  – Rheumatoid Arthritis
  – Back Pain?
Acute Pain

- Most times Acute pain is tissue damage pain:
  - Steroids or Non-Steroids

Arachidonic Acid Inhibitors:

- Systemic Steroids:
- Pharmacologic doses:
  - Prednisone
    - 1 mg/kg
  - Methylprednisolone
    - 1 mg/kg
  - Dexamethasone
    - 5-10 mg PO
- Use as DIAGNOSTICS

Examples Intra-Articular

- Triamcinolone Acetonide: Kenalog-40
  - Large Joints:
    - 20-40 mg q 1-2 weeks
  - Small Joints:
    - 5-10 mg q 1-2 weeks
  - Tendon Sheaths:
    - 5-10 mg q 1-2 weeks
  - Soft tissue infiltration:
    - 10-40 mg q 1-2 weeks
  - Bursae:
    - 20-40 mg q 1-2 weeks

- Dexamethasone Acetate: Decadron LA-
  - Large Joints:
    - 4-16 mg q 1-3 weeks
  - Small Joints:
    - 1-4 mg q 1-3 weeks
  - Tendon Sheaths:
    - 1-4 mg q 1-3 weeks
  - Soft tissue infiltration:
    - 2-8 mg q 1-3 weeks
  - Bursae:
    - 2-4 mg q 1-3 weeks

Acute Pain NSAID

Recommendations:

- Ketorolac Toradol®
  - 10 mg 5ID x 5 days (4 days)
- Indomethacin Indocin®
  - 50 mg TID
- Naproxen Sodium Anaprox®
  - 550 mg BID
- Ibuprofen Motrin®
  - 800 TID
- Sulindac Clinoril®
  - 200 mg BID

- Diclofenac Potassium
  - Cataflam®
  - 50 mg TID

- SCHEDULE for first week
- Then back down to lowest dose best tolerated agent
- Not everyone needs COX-2 walking in door!

Adverse Events NSAIDS

- Cardiovascular:
  - Hypertension
    - How to identify?
  - Heart Failure
    - How to identify?
  - Renal Failure
- Hepatic Toxins
  - How to identify?
  - Bone Marrow Supp
    - How to identify?
- Worsen Asthma
  - Must know physiologic cascade three
    - Why?
    - How to identify
Adverse Events NSAIDS

- Gastrointestinal
- Upper:
  - Gastroitis
- Stomach:
  - Decrease PG
  - Decrease Bicarb
  - Decrease Mucus
  - Peptic Ulcer Disease
- Lower:
  - Abdominal Distress

“Think Pair Share”

- Which of the following conditions would be most appropriate to suggest a medication that has inhibition of arachidonic acid metabolism characteristics?
  - A. Dental abscess
  - B. Post surgical pain
  - C. Neuropathic pain
  - D. Muscle overuse strain

Must need NSAIDS and Bleed

- Add Prostaglandins
- Misoprostil
  - Cytotec® 100 200 mcg
  - TID to QID
  - To any of them
- Or
- Arthrotec® 50/200, 75/200
  - Diclofenac + Misoprostil

Nambumetone
  - Relafen®
  - 500-2250 mg q day
  - Cox-2
  - Celecoxib Celebrex®
  - Meloxicam Mobic®

Or:
- Treat while causing
- Proton Pump Inhibitors
- H2 Blockers

And when we run out of oral routes:

Rx- Diclofenac Topical

| Table 5: Efficacy Outcomes of Voltaren® Gel in Studies 1 and 2 |
|-------------|-------|-------|
|            | Volume® Gel | Placebo (Vehicle) | Adjusted Difference (Volume® Gel) |
| Study 1 | Week 1 | 20° * | 10° |
| Study 2 | Week 6 | 10° * | 10° |

4 grams QID
100 Gram Tube = 6.25 Days
5 Tubes = 1 month
AWP: $199.01

Voltaren Gel

Neuropathic Pain: Fibromyalgia:

Table 6: Pharmacokinetics, efficacy and side effect profile of agents for the treatment of fibromyalgia syndrome

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pharmacokinetics</th>
<th>Efficacy Profile</th>
<th>Side Effect Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voltaren</td>
<td>Topical treatment</td>
<td>Pain reduction</td>
<td>Skin irritation</td>
</tr>
<tr>
<td>Diclofenac Sodium</td>
<td>Oral treatment</td>
<td>Pain reduction</td>
<td>Gastrointestinal side effects</td>
</tr>
</tbody>
</table>

Update on Treatment Guideline in Fibromyalgia Syndrome with Focus on Pharmacology

SNRIs/TCAs
ARIs Amine Reuptake Inhibitors
- TCAs
- Tetracyclics
- “SSRI’s”
- “SNRI’s”
- Miscellaneous
- MAO Inhibitors

“Old Pharmacology New Spin”
- “Depression Hurts”
- “SNRI”
  - Duloxetine Cymbalta®, Gen
  - Venlafaxine Effexor®, Gen
  - Desvenlafaxine Pristiq® Gen
  - Milnacipran Savella® Gen
  - Levomilnacipran Fetzima®

Alpha2-Delta Subunit Calcium Channel
- Neurontin® Gabapentin
- Lyrica® Pregabalin

Gabapentin
- Though the mechanism of action of gabapentin in the treatment of neuropathic pain is not clear, it does not influence the same pathways as opioids or tricyclic depressants. Current evidence indicates that gabapentin affects voltage-gated calcium channels in the CNS.
- Gaba pentin binds to the α2δ subunit of the voltage-dependent calcium channel, regulating the action of the calcium channels and neurotransmitter release
Pregabalin Efficacy DPN
Diabetic Peripheral Neuropathy

**Figure 1:** Patients Achieving Various Levels of Pain Relief - Study DPN 1

- Pregabalin: 50% reduction for DPN

Fibromyalgia: 20% patients will get 50% reduction

**Membrane Stabilizing Works Well**

“BIG 4” Keppra may also be tried

- Barbiturates:
  - Phenobarbital
  - 30-90mg a day
- Valproic Acid
  - Depakene®
  - Depakote®
  - Depakote ER®
    - Liver
    - BM
    - Weight Gain
    - Hyperammonemia
- Carbamazepine:
  - Tegretol®, Generics
  - XR®, Carbatrol®
    - Liver
    - BM
- Phenytoin:
  - Dilantin
    - Liver
    - BM
    - Gingival Hyperplasia
    - Skin Warnings 11/2008

Everything else is a “me too”: Mesantoin, Zarontin, Celontin, Benzos, Trileptal, Felbatol, Lamictal, Zonagran, Topamax, Keppra, Gabitril

“Think Pair Share”

- Which of the following conditions would be most appropriate to suggest a medication that has both NE and Serotonin increasing properties?
  - A. Dental abscess
  - B. Post surgical pain
  - C. Neuropathic pain
  - D. Muscle overuse strain

**Muscle Relaxants: Role?**

- Chlorzoxazone:
  - Parafon Forte®
  - 500 mg TID-QID
- Carisoprodol:
  - Soma®
  - 350 mg TID-QID
- Cyclobenzaprine:
  - Flexeril®
  - 10 mg TID-QID
  - Please never:
    - Flexeril® 5 mg
    - SR Amrix® 15 mg
- Carbamazepine:
  - Tegretol®, Generics
  - XR®, Carbatrol®
    - Liver
    - BM
- Metaxalone:
  - Skelexin®
  - 400 mg TID-QID
- Methocarbamol:
  - Robaxin®
  - 500, 750 mg TID-QID
- Orphenadrine:
  - Norflex®
  - 100mg BID-TID
- Tizanidine
  - Zanaflex®
  - 4-8 mg TID-QID

Muscle Relaxants

- Carisoprodol Better than Diazepam at 7 days
  - 70% improvement VAS vs 45%
- Carisoprodol Equal to Cyclobenzaprine at 8 days
  - VAS Improvement 30mm vs 28 mm
- Tizanidine Better than Diazepam on Pain at 7 days
  - 77% improvement vs 47%
  - No difference in functionality 87% vs 93%

**GABA Receptor Agonists/Benzos**

Strong Guideline recommendations to NOT use with opioids:

Deaths dramatically increased with the combination!

<table>
<thead>
<tr>
<th>Brandname</th>
<th>Route</th>
<th>Generic</th>
<th>Brandname</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Oral</td>
<td>Xanax®</td>
<td>Lorazepate</td>
<td>Oral</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Oral</td>
<td>Rivotril®</td>
<td>Zaleplon</td>
<td>Generic</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Intramuscular</td>
<td>Haldol®</td>
<td>Audax®</td>
<td>Oral</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Oral</td>
<td>Maxolon®</td>
<td>Audax ER</td>
<td>Oral</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Oral</td>
<td>Inderal®</td>
<td>Inderal®</td>
<td>Oral</td>
</tr>
</tbody>
</table>
“Narcotics”

“Med Chem is Important”

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Dose Available</th>
<th>Oral</th>
<th>IV Dose</th>
<th>IM Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydromorphone</td>
<td>Hydromorphone</td>
<td>10mg</td>
<td>10mg, 5mg</td>
<td>10mg</td>
<td>10mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Oxycontin</td>
<td>5mg, 10mg, 20mg</td>
<td>5mg, 10mg, 20mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Opana</td>
<td>10mg</td>
<td>10mg, 30mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Duragesic</td>
<td>20mcg</td>
<td>20mcg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

“Non-phenanthrenes”

“Abuse Potential”

- “Once you get Hydromorphone Dilaudid®- you never go back!!!- rgh
- Oxycodone-
  - Sustained Release Oxycontin®
  - Immediate Release, Ir
- Oxymorphone- Opana®
  - Sustained Release Opana ER®
  - Immediate Release
- REMS- Abuse Deterrent Tablets

Naloxone:
- IM:
  - 0.4mg SDV AWP $18.00
- IV:
  - Establishing Access- lay person?
- Nose Spray:
  - 4 mg AWP $150.00/ 2 pack

“Cutting Edge”

Prior to the Procedure

- What has been shown when given pre-operatively or pre procedure to decrease post procedure analgesic requirements?
- Dexamethasone
- Ibuprofen
- Diclofenac
- Celecoxib
- Acetaminophen
- Gabapentin

Study:
Nanzawa A, et al
Anesth Prog 2018 65:24-29
Dental Extraction Population
APAP 1000 mg Group A
Placebo Group P
Celecoxib 400 mg Group C
Diclofenac 50 mg Group D
Hanzawa Results Pre-operative drug with post operative analgesia


Low Dose Naltrexone: Fibromyalgia Pain:

Low Dose Naltrexone for the Treatment of Fibromyalgia

Naltrexone for the treatment of Fibromyalgia

Figure 1. Outline of the study protocol.

Figure 1. Box plots for visual analog scale (VAS) scores at 4, 5, and 6 hours after administration of study drug. Data are expressed as medians, percentiles, and range. A: all patients; B: patients with chronic pain; C: patients with non-chronic pain. The difference was compared with the placebo group by non-parametric Kruskal-Wallis test and Mann-Whitney U test with Bonferroni correction.

Low Dose Ketamine: Pain Syndromes

ER: Acute Pain Interventions
- 0.3mg/kg Ketamine IV
- 0.1mg/kg MSO4 IV

Ketamine - Faster acting yet shorter duration
= Another potential option

Cannabinoids:
- Can of worms but it works

Best marijuana strains for chronic pain

- Cannabis indica
- Cannabis sativa
- Hybrids

There is limited research available on the use of specific marijuana strains for pain and other symptoms. As a result, strain-specific recommendations are not medically proven.

The results of an online survey, comprising 95 participants, featured in the Journal of Alternative and Complementary Medicine in 2014.

Newer Pain Buzz

- Vitamin D
- Correlations:
  - Efficacy?
- Natraceuticals:
  - Kratom
  - Turmeric
  - Glucosamine
  - Dozens others

Chronic Pain Patient’s Self Perception:
The End