Non-Opioid Analgesic Options for Chronic Pain

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Learning Objectives

1) Define the role of non-opioid medications for analgesia in patients with chronic pain.
2) List the various categories of non-opioid pain medications.
3) Describe non-medication options for the management of chronic pain.

Multimodal Analgesia

Interventional
Nerve blocks
Neuraxial analgesia

Analgesics

Cognitive modalities
Deep breathing
Virtual reality
Distraction

Physical modalities
RICE
*Rest, Ice, Compression, Elevation

Medications affect pain differently

Descending Inhibitory Pathways (NE/5HT, enkephalins)

Central Sensitization

Peripheral Sensitization

CBZ
OXC
TCAs
TAMs
Lamotrigine
Lidocaine

Ca++: Gabapentin
Pregabalin
LVT
OXC
LTG
NMDA: Ketamine
Dextromethorphan
Memantine
Metamitine

Non-Opioid Medication Options

Treatment appropriateness based on severity of pain

**Range of Low Back Pain Pharmacotherapy**

- Beneficial
  - No definitive pharmacotherapy
- Likely beneficial
  - Opioids, antidepressants, NSAIDs, acetaminophen
- Trade-off's
  - SMRs
- Unknown
  - Epidural steroid injections, local injections

**Acetaminophen (APAP)**

- Inhibits central prostaglandin synthesis without affecting peripheral prostaglandin synthesis
- Additive analgesia with opioids
- IV product has comparable efficacy with oral, more expensive
- Single doses provided 4hrs of at least 50% relief in 37% of patients with post-op pain
  - ↓ opioid consumption by 30% in first 4hrs
  - No reduction in opioid-related adverse effects

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**NSAIDs – they aren’t all ibuprofen**

**NSAIDs** – the aren’t all ibuprofen

**NSAIDs – they aren’t all equal, either**

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**The 2007 Oxford league table of analgesic efficacy**

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Number of patients in comparison</th>
<th>Percent with at least 50 % relief</th>
<th>NNT</th>
<th>Lower confidence interval</th>
<th>Higher confidence interval</th>
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</table>
Anticonvulsants

Prototypical Agents:
- Gabapentin/Pregabalin
- Carbamazepine, Valproic acid, Topiramate
- Act by a reduction of neuronal irritability

Indications: Neuropathic pain
- Gabapentin/ Pregabalin: Postherpetic Neuralgia, Diabetic Peripheral Neuropathy, fibromyalgia
- Valproic Acid, Topiramate: migraine
- Carbamazepine: Trigeminal neuralgia

Gabapentinoids
- Modestly ↓ opioid requirement & pain scores post-op*
- Some data indicates ↓ in chronic post-op pain
  - Gabapentin: 100-1200mg pre-op, 600mg x1+ doses post-op
  - Pregabalin: 150-300mg pre-op, 150-400mg x1+ doses post-op
- Consider using for major surgeries and opioid-tolerant patients
- May cause additive sedation with opioids

Gabapentin
- Binds to the α2-δ subunit of presynaptic voltage dependent Ca** channels
- Reduces the release of pain neurotransmitters

Uses include:
- Fibromyalgia (off-label)
- DPN (off-label)
- PHN (approved)
Pregabalin

Pregabalin (Schedule V)

- Approved indications:
  - PHN, DPN, fibromyalgia, spinal neuropathic pain
- Better absorption, decreased somnolence (vs. gabapentin)
- Improvement in Non-REM sleep
- 150mg/d in divided doses...up to 600mg/d (maximum dosage dependent upon condition)
- Reduce dose by 50% if Clcr 30-60 mL/min

Adverse Effects

- Somnolence, dysphoria, euphoria
- Increased risk of angioedema—caution with ACEi
- Boxed warning: Increased risk of suicidal ideation

“Pearls”

- Don’t stop abruptly
- Don’t drink alcohol

Ketamine

- Adjunct to opioid therapy for:
  - Patients with inadequate relief or ADEs from opioids
  - Patients with opioid tolerance
- 0.5mg/kg IV bolus, then 10mcg/kg/min intraoperatively +/- continuous infusion post-operatively
**Local Anesthetics**

- Infiltration anesthesia
  - Prior to incision and at wound closure
- IV infusions intraoperatively
- IV regional anesthesia
  - Injection of local anesthetic into an extremity with a tourniquet on
- Peripheral nerve blocks
  - Individual nerves or plexus can be blocked
  - Most applicable for extremity surgeries
- Central neuraxial blocks (spinalis, epidurals)

**LDN in Chronic Pain**

| Table 3. Mechanisms of action and clinical use in regard to different doses of naltrexone used |
|---|---|---|
| Dose Range | Dose-Specific Mechanisms of Action | Clinical Use |
| Normal (50‐100 mg) | Opioid receptor antagonism | Alcohol and opioid abuse |
| Low-dose (15‐30 mg) | Tolerability, rapid dose, opioid receptor antagonism | Painful diabetic neuropathy, chemotherapy-induced pain, opioid detoxification, anorexia, weight loss |
| Very low-dose (0.1‐1 mg) | Pain or mood to low-dose | Addictive use/stabilizing effects |
| Ultra-low-dose (0.001‐0.1 mg) | Acting as a high-affinity dopamine (DA)1 and kappa-opioid receptor antagonist, also an opiate antagonist | Potentiating opiate analgesic |

**LDN in Chronic Pain**

- Complex Regional Pain Syndrome (CRPS)
  - In addition to a standard pain management, “considerably improved symptoms” in patients with LDN
- Fibromyalgia
  - 8 weeks of 4.5mg po LDN
    - 32.5% reduction in symptoms (vs. 2.3% placebo)
  - 20-week study
    - 57% LDN responders to 3mg po LDN
- Crohn’s
  - 4 weeks of 0.5mg po LDN
    - 75% response rate for pain free days and symptom relief

**SMR Overview**

- **Appear to ↓ discomfort & accelerate recovery in acute situations**
- Benefit with NSAID in acute situations
- Adverse effects problematic, esp. longer use
- Avoid carisoprodol.
- No good data or consensus on chronic use
Non-NSAID Topical Analgesics

- Lidocaine
  - Multiple concentrations
  - 5% patch approved for PHN; 4% OTC (same effect)
  - Also as ointment, cream and gel

- Camphor, menthol, methyl salicylate (Bengay)

- Capsaicin - may deplete substance P to inhibit transmission of pain signal

Capsaicin

- Many concentrations: (0.025% to 8%)
- Effective for: PHN, DPN, surgical neuropathic pain, osteoarthritis, neck pain
- Works at the vanilloid (temperature) receptor
- Chronic distal painful neuropathy


Herbal Medications for Pain

**Feverfew:** Tanacetum parthenium
- Migraine treatment and prophylaxis
- 50-100mg of dried leaves

**Butterbur:** Petasites hybridus
- Migraine prophylaxis
- Root extract Petadolex™ 150mg/d

**Alpha Lipoic Acid:**
- Diabetic peripheral neuropathy, other neuropathy
- 300-600mg daily

Chamberlin KJ, Salvo M. “Chapter 10: The Use of Dietary Supplements.” In: Taihly
Dendritic & Weiss’ Toward Healthy Aging, 10e. In press.

Non-Pharmacologic Pain Management

- Psychosocial Support and Counseling
  - Cognitive-Behavioral Therapy
- Physical Therapy
  - Heat/Cold Therapy
  - Exercise Therapy
  - Massage
  - TENS
- Spinal Manipulation

- Complementary Therapies:
  - Acupuncture
  - Hypnosis
  - Biofeedback
  - Meditation
  - Progressive Muscle Relaxation
  - Music Therapy
  - Yoga

Bed Rest

- Not necessary for most
- > 2 days of bed = worse outcomes

Bed Rest

“Time Organization Chart/Supplies” 8 by Jason MCH
Manipulation and Mobilization

- OMT
- Massage: effleurage, petrissage, tapotement, friction
- Graston
- Myofascial release
- Exercise
- TENS
- Electrical stimulation
- Traction (not a stand-alone treatment)
- Cupping

The Devil Is in the Details

- OMT – 2004 review said healthy patients derive more benefit
  - Techniques
    - Soft tissue applies pressure to the muscle area around the spine. It consists of rhythmic stretching, deep pressure, and traction.
    - Muscle energy: the patient is directed to use his or her muscles from a precise position and in a specific direction against a counterforce.
    - Thrust: uses high velocity forces to restore motion to a joint “cracking”
    - Counterstrain: where the patient is moved away from a position where motion is restricted to one of greater comfort.

Cryotherapy and Superficial Heat

- ICE = first few days
- HEAT = thereafter
- DON’T use in combo with rubs, i.e.:
  - Bengay® (trolamine salicylate)
  - Flexall 454® (menthol and methyl salicylate)
  - IcyHot® (capsaicin)

Things You Can Do

- Corrective posture
- Sleeping position
- Weight
- Exercise
- Proper lifting with KNEES, not back
- Stress reduction

Stretches

PELVIC TILT:
- Tighten abdominal muscles and tilt pelvis so curve of back is flat to floor

KNEE RAISE:
- Lie flat with knees bent up
- Bring one knee to chest and hug
- Repeat with other knee

PARTIAL PRESS-UP:
- Lie face-down on carpeted surface
- Arms bent alongside, raise upper body enough to lean on elbows
- Hold for 30 seconds; ▲ to 5 min

Cough & Sneeze Mast 2007; 9:27-28
And the elephant...

- Patients on chronic opioid therapy
- Tolerance, physical dependence
- Compared with opioid-naïve patients:
  - Severity of post-op pain is 3 times higher
  - Use 3 times more opioids post-op
  - Require epidurals for 3 extra days

Un- / Under-treated acute pain → chronic pain


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