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Practical Issues in Chronic Non Cancer Pain: Managing Opioid/Non-opioid Analgesia in the Primary Care Setting

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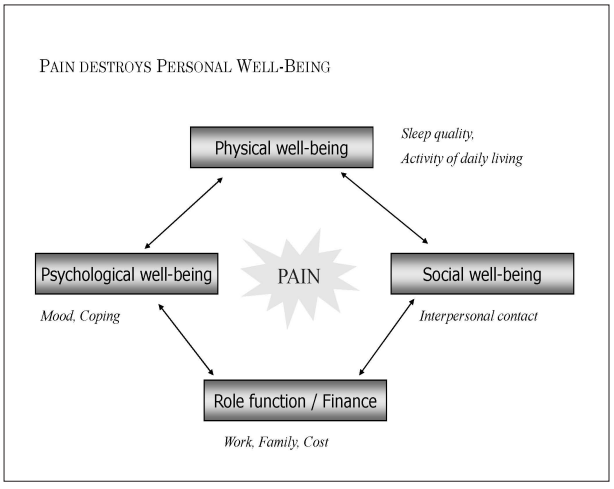
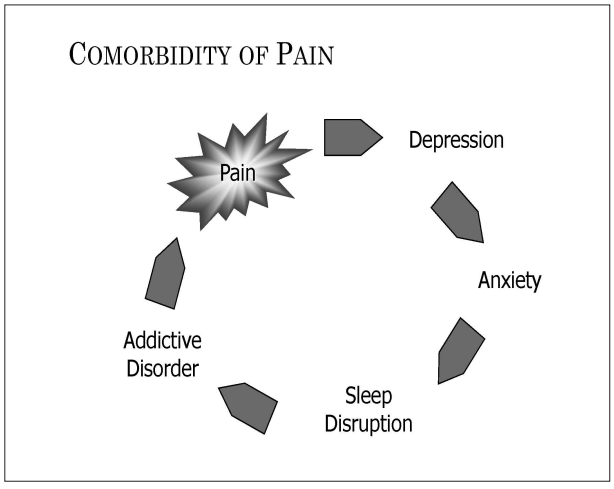




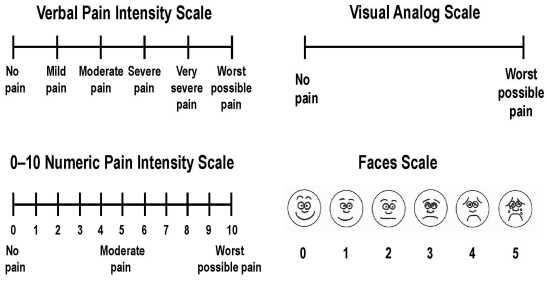
TYPES OF PAIN

1. Acute
2. Cancer, acute or chronic
3. Chronic non-malignant

ACUTE VS CHRONIC PAIN

Characteristic	Acute Pain	Chronic Pain
Cause	Generally known	Often unknown
Duration of pain	Short, well-characterized	Persists after healing, ≥3 mo
Treatment disease approach	Underlying disease	Underlying and pain disorder

Assessment of Pain Intensity



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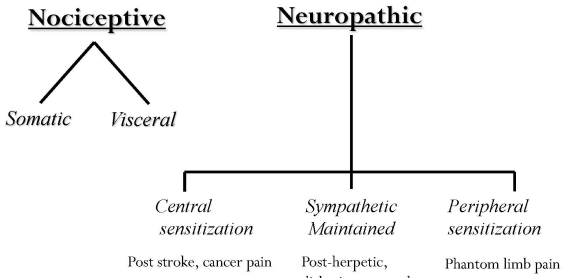
Types of Pain



www.themegallery.com

Potential Descriptions of Chronic Pain

- Sensations
  - burning
  - paresthesia
  - paroxysmal
  - lancinating
  - electriclike
  - raw skin
  - shooting
  - deep, dull, bonelike ache
- Cardinal signs/symptoms
  - allodynia: pain from a stimulus that does not normally evoke pain
    - thermal
    - mechanical
  - hyperalgesia: exaggerated response to a normally painful stimulus

Most Common Chronic Pain Syndromes

- Low Back
- Headaches
- Neck
- Facial
- Arthritides
- Fibromyalgia
- Cancer

Treatment of Pain

Options:

- **Non-pharmacologic**
-
- **Medications**
  - **NSAIDs**
  - **Acetaminophen**
  - **Antidepressants & anticonvulsants**
  - **Adjuvants**
  - **Opioids**

Invasive procedures

Non-Pharmacologic (Chronic Pain)

- Cognitive Behavioral Therapy:
  Yes, 'A', Cochrane

"Cortical plasticity related to chronic pain can be modified by behavioral interventions that provide feedback to the brain areas that were altered by somatosensory pain memories." H. Flor, 2002 & 03

"Individuals can gain voluntary control over … specific brain region… these effects were powerful enough to impact severe, chronic clinical pain." de Charms, 2005, Nat'l Acad Sci

- Meditation: Yes, 'A', Cochrane
  - Strong evidence for the use of relaxation & hypnosis in reducing pain in a variety of medical conditions

Music Therapy: Yes, 'A', Cochrane

- Pre-Op counseling: Yes, 'B', Cochrane
- Ice: Yes, "B", Cochrane
- Chiropractic: No, 'B', Cochrane
- Lumbar fusion for low back pain after prior surgery for disc, No, 'B'; Brox, Pain, May 2006
- Massage: Yes for cancer, low back

& OA pain, 'B', Cochrane

Exercise : Yes; 'B'; Burleson. Family Practice News. April 1, 2008; p 50.

- Magnets: Don't Know 'I', Cochrane
- Spinal Cord Stimulation: Don't know, 'I', Cochrane
- Acupuncture: Don't Know, 'I', Cochrane
- TENS: Don't Know, 'I', Cochrane

Non-Opiate Pharmacotherapy

- NSAIDs/Cox-2
- Acetaminophen
- Antidepressants
- Anticonvulsants
- Oral local anesthetics
- Alpha adrenergic agents
- Neuroleptics
- NMDA receptor antagonists
- Muscle relaxants
- Topical analgesics
- Emerging Agents

NSAIDS

Use in selected pts with good indications

- bone pain
- inflammatory pain
- somatic pain with poor response to other analgesics

- Be aware of absolute & relative contraindications
- PRESCRIBE FOR LIMITED DURATION

Using Acetaminophen Effectively

- First-line agent for OA
- Safe alternative to NSAID's for non-inflammatory pain
- Safe given q4H to max 4000 mg/day
- Caution with liver disease or heavy EtOH
- Rapid onset (20-30 mins)

ANTIDEPRESSANTS*

Tricyclic	SSRI	Other
Amitriptyline (Elavil®)	Fluoxetine (Prozac®)	Nefazodone (Serzone®)
Desipramine (Norpramin®)	Paroxetine (Paxil®)	Venlafaxine (Effexor®)
Doxepin (Sinequan®)	Sertraline (Zoloft®)	Trazodone (Desyrel®)
Imipramine (Tofranil®)	Fluvoxamine (Luvox®)	Bupropion (Wellbutrin®)
Nortriptyline (Pamelor®)	Citalopram (Celexa)	

*Partial list
SSRI = selective serotonin reuptake inhibitor

COMMONLY USED DRUGS FOR THE TREATMENT OF NP

Medication	Index	Benefit	Maximum dose	Duration for initial observation	Major side effect	Precautions
Secondary TCA	+	Depression, insomnia	150mg/d	6~8 week	Sedation, dry mouth, blurred vision, urinary retention	Cardiac disease glaucoma
Duloxetine	++	Depression	60mg bid	4 week	Nausea	Hepatic dysfunction Renal insufficiency
Gabapentin	++	Sleep disturbance little drug interaction	3600mg/d	3~8 week	Sedation, dizziness, peripheral edema	Renal insufficiency
Pregabalin	++	Sleep disturbance, anxiety little drug interaction	600mg/d	4 week	Sedation, dizziness, peripheral edema	Renal insufficiency
Topical lidocaine	++	No systemic side effect	3 patches/d	3 week	Local erythema, rash	None
Oxycodone	+	Rapid onset	180mg/d	4~6 week	Nausea, vomiting, constipation, dizziness, drowsiness	History of substance abuse driving in initiation
Tramadol	+	Rapid onset	400mg/d	4 week	Nausea, vomiting, constipation, dizziness, drowsiness, seizure	History of substance abuse seizure disorders, with TCA or SNRI

(Minn YK, Kim SM, 2008)

NMDA-R ANTAGONIST PROPERTIES

- Dextromethorphan
- Ketamine
- d-Methadone
- Amantadine
- Memantine
- Amitriptyline

OPIOID EBM

- Short-term efficacy good for musculoskeletel and neuropathic pain
- No conclusions about long-term efficacy, tolerance nor addiction

Cochrane review, 2004

OPIOIDS FOR CHRONIC PAIN: GENERAL PRINCIPLES

- Use WHO pain ladder to select analgesic
- Around-the-clock, q. 3-4 hr.
- Assess frequently, adjust dose
- Add up total opioid taken q. 24hr.
- Select long-acting opioid q. 12 hr.
- Use short-acting opioid for breakthrough pain prn.

RCTs

- Efficacy of opioids in chronic noncancer pain established in a number of randomized, controlled trials, including placebo-controlled trials of:
  - codeine
  - tramadol
  - oxycodone
  - morphine
  - fentanyl
- Comparative trial of transdermal fentanyl and sustained-release oral morphine

Opiate Dosing Equivalence

Analgesic	Equianalgesic Oral Dose	Equianalgesic Parenteral Dose
Codeine	200 mg	N/A
Hydrocodone (Vicodin)	30 mg	
Oxycodone	20 mg	N/A
Morphine	30 mg	10 mg
Hydromorphone (Dilaudid)	7.5 mg	1.5 mg
Fentanyl	N/A	0.1 mg
Methadone	20 mg	10 mg

What is the Maximum Dose?

- There is no "ceiling effect" with the pure opioids (except codeine).
- Keep titrating until the pain is controlled or the dose is limited by adverse effects.

How Much Should I Increase the Dose?

- Mild Pain- increase by 25%
- Moderate Pain- increase by 50%
- Severe Pain- increase by 100%

How Should I Treat Breakthrough Pain?

- Offer an immediate release opioid.
- Give 10-15% of the 24 hour dose or 1/3 of the 12-hr. dose.
- Extra breakthrough doses:
  - Q 1-2 hrs for po route
  - Q 30 minutes for SC or IM route
  - Q 15 minutes for IV route.

Opioid Tapering

- 50% of dose X 2 days, then reduce by 25% q 2 days until equivalent of 30 mg/day of morphine.
- Then D/C
- Explain withdrawal Sx to patient
- Manage with Clonidine, Imodium, Tramadol, Anticonvulsants

What About Patients with Hepatic or Renal Disease?

- Opioids 90-95% renally cleared
- Renal Disease
  - *Morphine* - 2 metabolites: M6G is active and has a longer half-life than morphine. As a result– **decrease the dose, widen the interval, use PRN or not at all**.
  - Safer to use hydromorphone, fentanyl but still consider starting w/ half the usual dose and/or increasing the interval.
- Less of an issue w/ liver disease but with severe hepatic dysfunction increase the dosing interval or decrease the dose.

Management of Opioid Side Effects

- Nausea and vomiting
  - switch opioids; anti-emetics
- Sedation
  - lower dose if possible; add co-analgesics; add stimulants
- Constipation
  - treat prophylactically with stool softeners, bowel stimulants, and nonpharmacologic measures; switch opioids

OIN: Treatment

- Opioid rotation
- Reduce opioid dose
- Hydration
- Circadian modulation
- Psychostimulants
- Other Rx

Tolerance

- Diminished drug effect over time due to ongoing drug exposure- i.e. **takes higher dose to get relief**.
- Desirable in the case of side effects.
- * Which side effect do patients NOT develop tolerance to?
- Tolerance does NOT cause addiction.

Relative Contraindications to Opioid Use

- Hx of substance abuse
- Severe personality disorder
- Risk of suicide or overdose
- Chaotic home
- High stress
- Significant renal impairment
- Very poorly-characterized pain

Chronic non-cancer pain

- Chronic pain is complex and pain perception is altered by social, psychological and cultural context
- Chronic pain is common at all ages but is more common in older people
- Chronic pain can become entrenched biologically and psychologically
- Drug treatment is only a small component of management
- Strong opioids have a place but must be used with caution and under careful supervision
- Psychological interventions are advocated but good evidence is lacking
- Acupuncture is often used but evidence is also weak
- Formal recording of pain scores should be the norm.