Chronic Pain Management Primer

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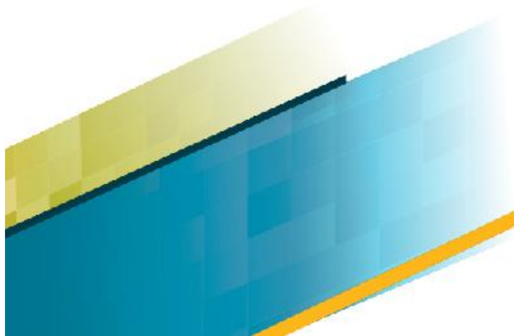

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Learning Objectives

1. Discuss pain pathophysiology as it relates to selecting pain management therapy choices
2. Outline monitoring plans for chronic pain management
3. Recognize risks and benefits of opioid medication utilization

What is pain?

- Take the next 1-2 minutes to write a definition of pain

Food for thought

Are you satisfied with the definition you came up with?

- Yes
- No

Why is it easy or difficult to define pain?

- Yes
- No

How can we prove if one of us is in pain or not?

- Yes
- No

Prevalence of Chronic Pain

- Pain Incidence
  - More than 30% of Americans have some form of acute or chronic pain
  - Among older adults, the prevalence of chronic pain is more than 40%.2
- Opioid analgesics are now the most commonly prescribed class of medications
  - In 2014, U.S. retail pharmacies dispensed 245 million prescriptions for opioids
    - 65% were for short-term therapy (<3 weeks)
    - 3 to 4% of the adult population (9.6 million to 11.5 million persons) were prescribed longer-term opioid therapy

Etiology of Pain

- Changes in body structure
  - Physical or chemical damage
- Preexisting pain
- Viral illness
- Cancer
- Cardiovascular illness
- Neurologic illness/damage
- Unknown

Chronic Pain Etiologies

- Arthritis
- Back Pain
- Chronic Fatigue Syndrome
- Cancer
- Regional Pain Syndromes
- Restless leg syndrome
- Fibromyalgia
- Sciatica
- Headache
- Spinal Stenosis

Definitions of Pain

- Somatic pain
  - “dull, sharp or aching”
  - responsive to typical analgesics
- Neuropathic pain
  - “burning, radiating, shooting, tingling”
    - also allodynia, parasthesias
  - poorly responsive to typical analgesics
- Bone pain
  - “sore, aching”
  - responsive to anti-inflammatory agents

Barriers to Adequate Pain Relief

- Not believing patient is in pain
- Fear of being on opiates
- Fear of addiction
- Fear of legal action
- Fear of overdose

"Will the patient become **addicted**?"

"Not likely, but you may become tolerant and dependent."

- Tolerance
  - requiring increasing doses to achieve the same effect
- Dependence
  - over time an opioid user will have withdrawal upon discontinuation of the opioid
- Addiction
  - using immoral or unethical means to obtain drugs for illicit use

Risk for Opioid abuse/addiction

- Data from VA system on >15,000 chronic users of opioids from 2000-2005
- Non-opioid substance abuse
  OR = 2.34, $p < 0.001$
- Mental health disorders
  - OR = 1.46, $p = 0.005$
- Prevalence of mental health disorders was much higher than the prevalence of non-opioid substance abuse disorders
  - 45.3% vs. 7.6%
- Males, younger adults, and individuals with greater days supply of prescription opioids dispensed

Edlund MJ et al. Pain 2007.

Risk for Opioid Abuse

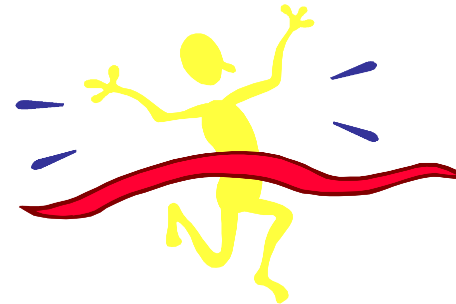
- Evaluation of Arkansas Medicaid and Private insurance claims from 2000-2005
  - Prevalence of opioid abuse diagnosis ~3%
  - Risk of abuse was higher in patients < 50 years of age versus over 50 years old
  - Back and headache pains had a higher risk as compared to joint and neck pain patients
  - Diagnosis of 2 or more mental health disorders increased risk
  - Use of > 120 mg daily morphine equivalents as compared to less
  - Schedule III or IV use only had baseline risk as compared to patients using short and long acting Schedule II medications
  - Prescription days supply > 160 days had an increased risk of abuse

Edlund MJ et al. 2010

Factors affecting risk of Addiction & Overdose

- Factor Risk Medication-related
  - Daily dose >100 MME — Overdose & addiction
  - Long-acting or extended-release formulation — Overdose
  - Combination of opioids with benzodiazepines — Overdose
  - Long-term opioid use (>3 mo)† — Overdose & addiction
  - Period shortly after initiation of long-acting froms (< 2 weeks) — Overdose
- Patient related risk factors
  - >65 yr — Overdose
  - Sleep-disordered breathing‡ — Overdose
  - Renal or hepatic impairment — Overdose
  - Depression — Overdose & addiction
  - Substance-use disorder (including alcohol) — Overdose & addiction
  - History of overdose — Overdose
  - Adolescence — Addiction

Clinical Presentation of Acute Pain



- Subjective!
  - Sweating
  - Facial expression of pain
  - Crying, Grimacing
- Positive association
- Objective
  - Hypertension
  - Tachycardia
- Goal: pain relief & "cure"

Clinical Presentation of Chronic Pain

- Subjective
  - Lacks positive meaning
  - Depression
  - Anhedonia
  - Loss of Appetite
  - Insomnia
- Objective
  - Lacks changes in vital signs
- Goal is pain relief & "rehab"

Problems in Pain Patients

- Acute pain in patient with chronic pain
- Terminal pain
- Assessing/relieving pain in patients with communication difficulties
- Treating pain in patients with histories of drug abuse

Patient Assessment

- Communication issues
- Past experiences of pain & analgesics
- Medical history
- Allergy/intolerance/drug interactions
- Concurrent medical problems
- Issues with abuse
- Financial issues
- Family support

Pain Assessment - PQRST

- **P** = palliative/provocative factors
  - e.g. "What makes it worse or better?"
- **Q** = quality
- **R** = radiation
- **S** = severity
- **T** = temporal factors
- Ask appropriate ***FOLLOW-UP*** questions!

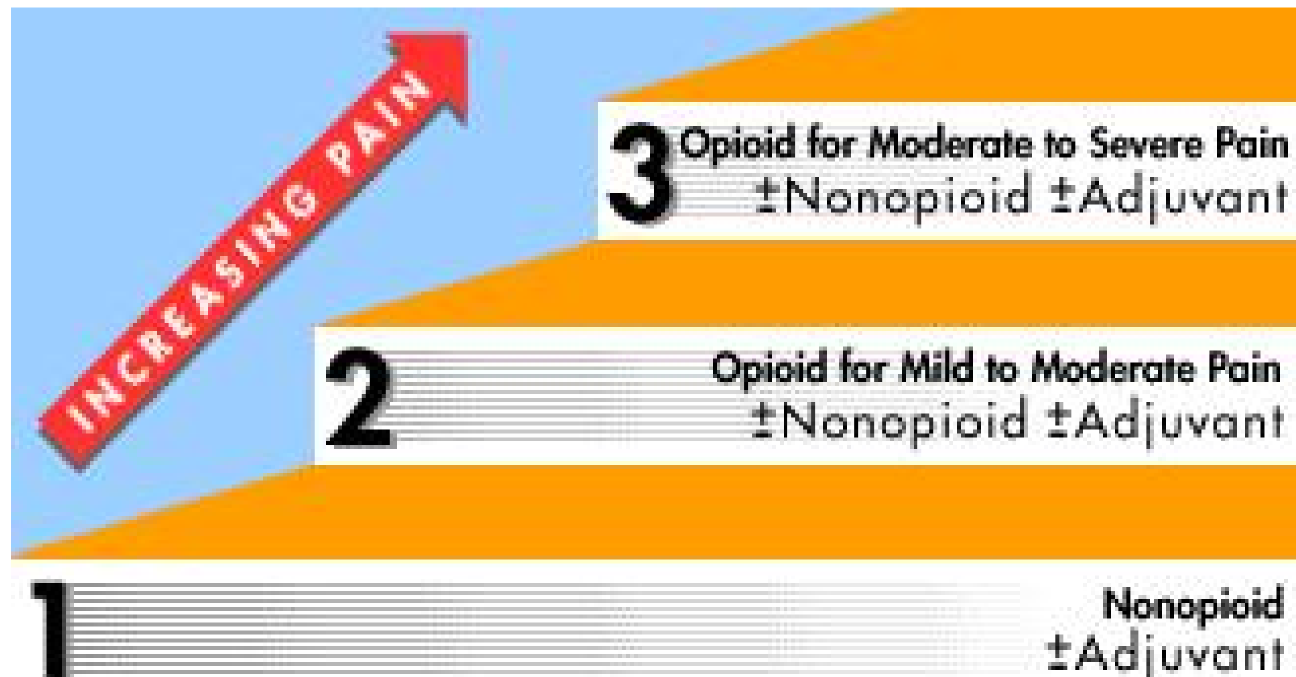
Pain Assessment Scales

- 0-10 scale
  - 0 is no pain, 10 is worst pain possible
- Visual analog scale (VAS): 100 mm line
  - No pain (0)___________ Worst pain (100)
- When to assess pain:
  - Now
  - Over past 24 hours
  - Before and after triggers
  - Last week
  - Last month

Assessment of Regimen

- Total daily dose of analgesics
- Appropriate route?
- Appropriate drugs?
- Appropriate frequency?
- Appropriate doses?

WHO Ladder Approach to Pain



Selecting appropriate agents

- WHO step 1
  - Pain levels 1-4
  - Typically use acetaminophen or NSAIDS +/-adjuvant interventions
- WHO step 2
  - Pain levels 4-6
  - Typically use weak opioid combination products, acetaminophen combinations, or NSAIDs
    - Typically hydrocodone, oxycodone in combination
    - May use Morphine or hydromorphone
- WHO step 3
  - Pain levels 7-10
  - Typically use pure opioid formulations
  - Typically fentanyl, morphine, oxycodone, hydromorphone, methadone

Developing a management plan

- Use single agent if possible
  - Incorporate pharmacology of drug to design optimal schedule
  - Use appropriate route for patient
- Evaluate need for adjuvant therapy
- Develop monitoring plan
  - Include plan to manage side effects
- Provide patient counseling

Opiate Side Effects

- Constipation
  - Use stool softeners & stimulant laxatives
- Nausea
  - tolerance usually develops
- Sedation
  - tolerance usually develops
- Respiratory depression
  - Rarely occurs, treat with naloxone
- Orthostatic hypotension
- Urinary retention
- Others: myoclonus, hallucinations

Opiate sedation

- Usually tolerance develops
- May require addition of stimulant agents
  - Dextroamphetamine
    - 2.5-5 mg po daily or twice daily
  - Methylphenidate
    - 2.5-5 mg po daily or twice daily
  - Modafinil (Provigil)
    - 100-200 mg po am

NSAID's in Pain

- Very helpful for bone pain("opiate sparing" effect) & are 1st step of ladder
- Caution:
  - significant renal impairment, oncology
  - GI bleeding or thrombocytopenia
- SE: GI intolerance, allergy, effect on platelets, masking of fever, CNS SE
- "Ceiling effect" prevents dose escalation in some patients

Steroids in Pain

- Useful for bone pain
- Dexamethasone, prednisone
- SE often limit long-term use
- Use GI prophylaxis with H_2 blocker or PPI
- Short term SE
  - hyperglycemia, CNS effects, ↑ appetite, insomnia, weakness
- Long-term SE
  - osteoporosis, cataracts, moon-face

Bisphosphonates in Pain

- Effective in patients who have osteolytic lesions in bone – e.g. breast cancer, prostate cancer, multiple myeloma
- Shown to ↓ pain and ↓ fractures
  - Pamidronate 90 mg IV over 3 hours q 4 weeks
  - Zoledronic acid (Zometa) 4 mg IV over 15 min. q 4 weeks

Treatment of Neuropathic Pain

- Signs and symptoms
  - Numbness and tingling in hands, feet, or legs
  - Shooting pains or electrical type pain
- Often resistant to opiates and NSAID's

- First line therapy-Antiepiletics
  - Gabapentin (Neurontin®)
    - 100 mg TID (up to 3600 mg/day)
  - Pregabalin (LYRICA®)
    - 75 mg BID (up to 300 mg/day)
  - Levetiracetam (Keppra)
    - 500 mg BID-TID (up to 3000 mg/day)
  - Topiramate
    - 25-50 mg daily (up to 400 mg/day)
  - Lamotrigine
    - 25 mg QOD (Up to 400 mg/day)
  - Zonisamide
    - 100 mg hs (Up to 400mg/day)
- Second/Third line agents
  - Carbamazepine
    - 100 mg BID (Up to 800 mg/day)
  - Phenytoin
    - 300 mg daily (Up to 300-400 mg/day)
  - Valproate
    - 125 mg tid (Up to 3000mg/day)

Treatment of Neuropathic Pain

- Antidepressants
  - SSRI's – 1st line
    - Sertraline 50-150 mg daily
    - Duloxetine 20-60 mg daily
    - Venlafaxine 75-225 mg daily
    - Fluoxetine 20-40 mg daily
- Tricyclic antidepressants
  - Amitriptyline 10-100 mg hs
  - SE: anticholinergic effects, sedation, orthostatic hypotension
    - Avoid in closed angle glaucoma, BPH, urinary retention, significant CV disease
- Local therapy
  - Lidocaine patch 5% (Lidoderm): excellent responses seen in some patients
    - lidocaine 5% patch up to 3 for 12h/d

Muscle pain/spasticity

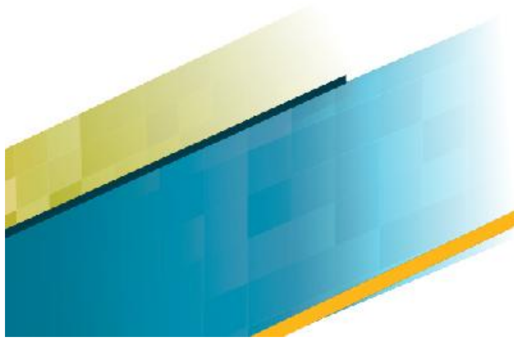
Often utilized in chronic back pain

- Baclofen
  - 5-20 mg TID
- Orphenadrine
  - 100 mg BID
- Cyclobenzaprine
  - 5-10 mg TID
- Tizanidine
  - 2-4 mg po BID-TID
- Carisoprodol
  - 250-350 mg po TID x 2-3 weeks
- Metaxalone
  - 800 mg po TID-QID
- Diazepam
  - 2-10 mg po TID-QID

Alternative Therapies

- Behavioral therapy
- Massage therapy
- Music therapy
- Acupuncture
- Hypnosis
- TENS (Transepidermal neuro stimulation) therapy
- Exercise
- Heat therapy
- Cryotherapy
- Occupational therapy
- Physical therapy
- Biofeedback

Back to Opioid Therapy



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Opioid Duration of Analgesia

- Morphine
  - 3-5 hours
- Hydromorphone
  - 3-4 hours
- Oxycodone
  - 4-6 hours
- Methadone
  - 4-12 hours
- Oxymorphone
  - 4-6 hours

Opioid Conversion Tables

Drug	PO/PR	SQ/IV
Morphine	30 mg	10 mg
Oxycodone	20 mg	NA
Hydrocodone	20 mg	NA
Hydromorphone	7.5 mg	1.5 mg
Fentanyl	NA	100 mcg
Oxymorphone	10 mg	1 mg

Pain Management Tables & Guidelines 2007, Dana Farber Cancer Institute/Brigham & Women's Hospital

Fentanyl Patch Conversions

Hydromorphone PO (mg/day)	Morphine PO (mg/day)	Oxycodone PO (mg/day)	Fentanyl Patch
12.5	50	30	25
25	100	65	50
37.5	150	100	75
50	200	130	100
62.5	250	165	125
75	300	200	150
87.5	350	230	175
100	400	265	200

Pain Management Tables & Guidelines 2007, Dana Farber Cancer Institute/Brigham & Women’s Hospital

SR Versus IR

- SR = sustained release
  - Use scheduled dose to prevent pain
  - Only in opiate tolerant patients
- IR = immediate release
  - Use prn to control breakthrough pain
  - DO NOT schedule around the clock

How to Calculate an SR Dose

Scenario: You have a patient using immediate release opioids on a regular basis and you do not expect to be able to manage pain without opioids any time soon.

- Calculate total daily dose (TDD) of opiates used
- Use ~ 80% of dose and divide into appropriate dosing intervals
- Reassess as needed

How to Calculate an SR Dose:

KD uses oxycodone 20mg po q3h (5-7 x/d) w/ acceptable relief, but wants to take fewer doses

- Plan to use oxycodone hydrochloride **extended-release** (Oxycontin) + oxycodone
- TDD = 100-140 mg po oxycodone/day
  - 80% = 80-112 mg
- Will dose q 12h, so divide by 2 = 40-56 mg q 12h
  - Based on availability recommend oxycodone hydrochloride **extended-release** (Oxycontin) 40 mg po q 12h + oxycodone prn
- Reassess as needed

How to Calculate an IR Dose:

- What about the prn oxycodone dose?
- KD's dose of oxycodone hydrochloride **extended-release** (Oxycontin) is 40 mg po q 12h
  - Plan to use oxycodone IR
  - TDD = 80 mg oxycodone SR/day
  - About 60% (50-70%) = 48 mg (40-56 mg)
  - Will dose q4h prn based on pharmacology, so divide dose above by 6, which is total possible doses in 24-hour period, and dose is 8 mg q 4h
  - Based on availability
    - recommend oxycodone 10 mg po q 4h prn
  - Reassess as needed

Switching Opiates

Potential reasons to switch therapy:

- Side effects
- Low potency
- Cost
- Available routes of administration

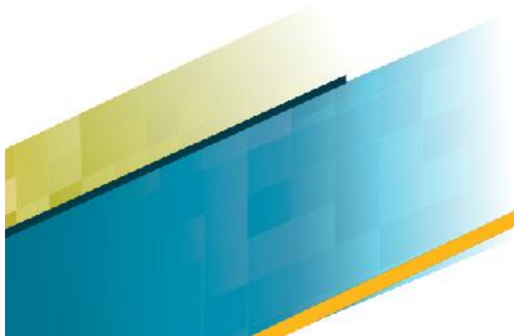
How to Switch Opiates

- Cross-resistance is incomplete between analgesics
- Use total daily dose of opiates to convert
- Use conversion table to convert & usually use 80% of new dose
  - If patient still in pain on previous regimen, use 100%, as it isn't enough anyway
- Divide dose into appropriate dosing schedule with available doses and routes of administration

GR on Fentanyl 200 mcg/hr patch q72h & oxycodone 20mg po q4h prn pain (5-6 x/d) with incomplete relief

- Plan to switch to morphine sulfate **extended-release** tablets (MS Contin) and MSO4
- Fentanyl 200mcg/hr =400 mg of oral morphine daily
- oxycodone 100-120 mg/d = 150-180 mg po MSO4/d
- TDD = 550-580 mg po MSO4 day
  - Will use 100% of dose to convert, because still has pain on this TDD so recommend:
    - Recommend: morphine sulfate **extended-release** tablets (MS Contin) 280 mg po q 12 h
- The prn morphine order
  - New TDD is 560 mg, take 60% (336 mg) & dose q 4h, so divide into 6 doses (56 mg)
    - Recommend: morphine sulfate 50-60 mg po q4h prn pain
- Always double check your calculations

Applying the Information



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Practice Case #1

TV 45 year-old man with chronic low back pain is in the pharmacy with two new prescriptions for Oxycodone/APAP (Percocet) 5/325 mg 1-2 tablets po q 6 hours prn pain #100 and baclofen 10 mg po three times daily #90 with 4 refills.

He has had multiple prescriptions for Oxycodone/APAP (Percocet), cylobenzaprine, carisoprodol, and diazepam. He says that the pain is constant and severe over the last 12 months since he hurt his back at work.

Which of the following is the most appropriate action?

A. Call the physician office to discuss the use of a pain contract for this patient
B. Call the physician office to verify the prescription first
C. Discuss addiction with the patient
D. Initiate the patient encounter by planning on dispensing the medications

Practice Case #2

MJ 67 year old woman with long standing diabetes in complaining to you about severe shouting pains in her legs over the last month and numbness and tingling.

She is currently on metformin, glipizide and NPH insulin as well as other cardiovascular and lipid lowering agents.

You are the pharmacist at her regular store, what to you suspect her pain etiology is?

A. Somatic pain
B. Neuropathic pain
C. Bone pain
D. Psycho-somatic pain

Practice Case #3

Based on the WHO pain management ladder.

You have a patient with abdominal pain associated with pancreatic cancer.

Which of the following would be an initial appropriate choice of medications for someone rating their pain a 7 of out 10?

A. Hydrocodone/APAP (Vicodin) 5/500 1-2 tablets po every 4-6 hours
B. Amitriptyline 50 mg po daily
C. Gabapentin 100 mg po three times daily
D. Pregabalin 100 mg po twice daily

Practice Case #4

JH a 58 year old woman with metastatic breast cancer has been receiving multiple prescriptions over the last 8 months for MS extended release 200 mg PO q8-12 hours.

She is now in the pharmacy with a prescription for methadone 10 mg PO three times daily and relates her pain is severe and 9 out of 10.

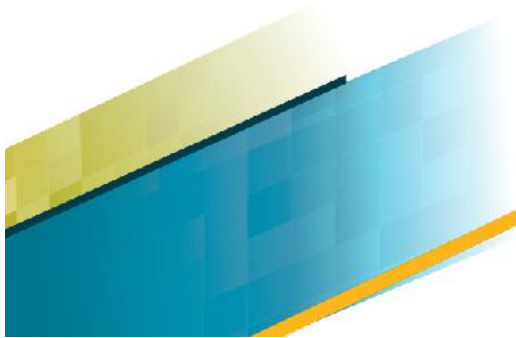
Which of the following would be the most appropriate to do?

A. Utilize the PQRST method to assess her pain
B. Discuss the issue of addiction with the patient
C. Discuss the issue of withdrawal symptoms with the patient
D. Call the physician office to verify the prescription first

Summary

- Pain management is complex
  - Have a Plan
  - Educate patients on use of pain medications
  - Monitor for adverse effects
  - Re-evaluate the plan
- Addiction is a concern
  - Understand patients factors that enhance risk
- Develop a patient care relationship

Resources



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WHO resources and position statements

- WHO cancer pain guideline
  - https://www.who.int/ncds/management/palliative-care/cancer-pain-guidelines/en/
- WHO other pain guidelines under-revision
  - Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines (2011)
  - WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses (2012)
- WHO cancer pain ladder
  - https://www.who.int/cancer/palliative/painladder/en/
- https://www.who.int/news-room/detail/22-05-2020-who-guideline-on-ensuring-balanced-national-policies-for-access-and-safe-use-of-controlled-medicines