Case Studies:
Acute pain management
in patients with opioid addiction

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Disclosure

- I have no financial relationships with industry to disclose

Objectives

- Misconceptions vs. Facts
- Case Studies:
  1. Prescription opioid abuse
  2. Methadone
  3. Buprenorphine

Misconception 1:
The maintenance opioid agonist (methadone or buprenorphine) provides analgesia

Facts:

Duration of analgesia from methadone and buprenorphine is about 4-8 hours while it's suppression of opioid withdrawal lasts 24-48 hours

Misconception 1:
The maintenance opioid agonist (methadone or buprenorphine) provides analgesia

Facts:

- Cross tolerance occurs within the opioid class
  - Respiratory Depression
  - Sedation
  - Analgesia
- (need for higher and more frequent doses)

Misconception 1:
The maintenance opioid agonist (methadone or buprenorphine) provides analgesia

Fact:

- Opioid induced hyperalgesia
- Evidenced by studies showing patients on maintenance methadone therapy tolerate cold-pressor pain only half as long as do matched controls

Misconception 2: Use of Opioids for Analgesia may result in Addiction Relapse

Facts:

- No clinical evidence that opioids for acute pain conditions triggers relapse
- Limited evidence suggests the opposite
- Unrelieved pain more likely to trigger relapse

Misconception 3:
The Additive Effects of Opioids for analgesia and maintenance therapy may cause respiratory depression and sedation

Facts:

- Patients on daily opioid agonist therapy have already developed tolerance to the respiratory depression and sedation
- Acute pain antagonizes respiratory depression

Misconception 4:
Reporting Pain May be a Manipulation to Obtain Opioid Medications or Drug-seeking, because of Opioid Addiction

Facts:

- Pain reports are always subjective
- Objective evidence to support the reports
  - Changes in vital signs with acute pain
  - Condition known to cause pain
- Maintenance opioid can block euphoria from other opioids

Misconception 4:
Reporting Pain May be a Manipulation to Obtain Opioid Medications or Drug-seeking, because of Opioid Addiction

Facts:

- Addicts are at risk for undertreatment of pain leading to the development of pseudoaddiction behaviors

Case Studies

Case 1: Prescription opioid abuse

- MS is a 21yom with a history of ADHD. He presents to the ED with gradual onset of jaundice, abdominal pain and bloating, white stools, nausea and vomiting. Diagnostic work up reveals a large Ewing's Sarcoma extending from the right lobe of the liver, through the right lung and into the heart.
- In the ED, the patient required 8 mg of hydromorphone IV over 4 hours before reporting pain relief to 5 out of 10.

Case 1: Prescription opioid abuse

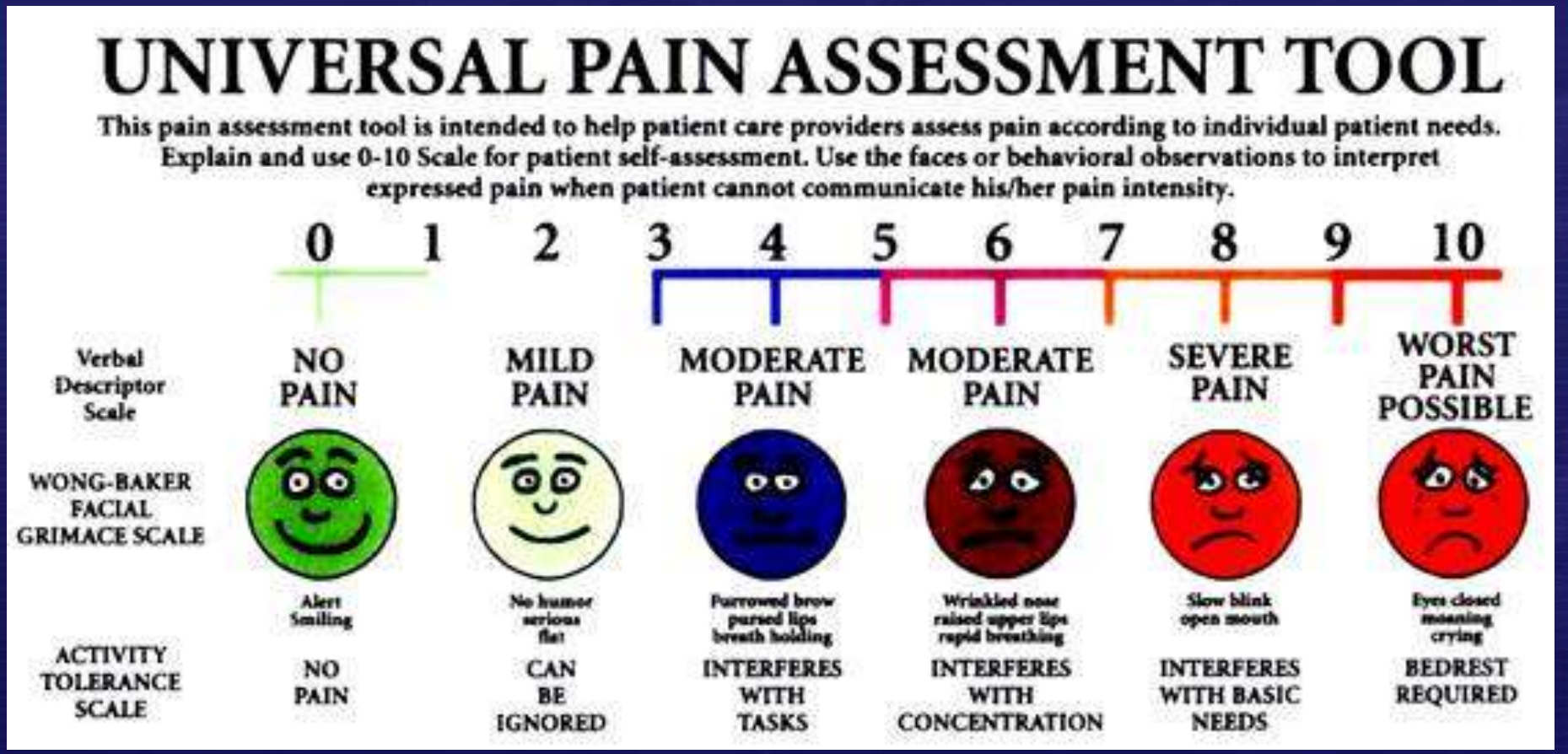
- Tox screen in the ED was + opioids (oxycodone) and + THC. Negative for amphetamines.
- On questioning of substance abuse history, the pt reports, “I mess around with percs and pot from time to time.”
- The pt’s girlfriend discloses that he buys OxyContin, Percocet and Vicodin on the streets. She is unclear how much he uses, but notes that he has been taking pills daily in recent weeks.

Case 1: Prescription opioid abuse

Where would you begin with managing his pain?

a) Start patient on methadone
b) Start the patient on a Morphine PCA pump with demand only doses
c) Start the patient on oral Morphine Sustained Release 45 mg po 2xd with morphine 15mg po q2h prn for breakthrough pain
d) Start the patient on Acetaminophen 650mg 4XD
e) Start OxyContin 80mg po 2xd with hydromorphone 2mg IV q2h prn for breakthrough

Example Pain Scale



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Case 1: Prescription Opioid Abuse

- Initial Pain Management Regimen:
  - Morphine Sustained Release 45mg po 2xd
  - Morphine Immediate Release 15mg po q2h prn BTP
  - Ibuprofen 400 mg po q6 h around the clock
  - Gabapentin 300 mg po 3xd
  - Hydromorphone 2mg IV one time orders before painful procedures
  - Maximize non-pharmacological treatments as well
    - Heat, ice, message, distraction, relaxation techniques, guided imagery, cognitive behavioral feedback,etc.

Case 1: Prescription Opioid Abuse

- Titrate as needed for pain relief
  - Opioid naïve or sensitive: 10-15% increase
  - Opioid tolerant: increase 25-33% or more
  - Titrate based on drug/route kinetics
  - Breakthrough opioid dose is 10-20% of the total daily opioid dose.
  - Don’t forget to titrate the short acting opioid

Case 1: Prescription Opioid Abuse

- MS's pain meds were titrated every other day until adequate analgesia was achieved.
- Discharge Regimen:
  - Morphine Sustained Release 180mg (60mgx3 caps) 2xd
  - Morphine IR 45mg (15mg x3) q4h prn breakthrough pain
  - Ibuprofen 600mg 3xd
  - Gabapentin 600mg 3xd

Case 2: Methadone

- DC is a 52yom on methadone maintenance for 18 years for prior heroin addiction. Confirmed dose is methadone 80mg po daily. He has herniated discs at L4-L5 and L5-S1. He has failed conservative treatment with PT, chiropractic spinal manipulations, epidural steroid injects and long-term NSAID use. Here for an elective laminectomy and spinal fusion.

Case 2: Methadone

Where would you begin to manage his post-operative pain?

a) Continue methadone
b) Stop the methadone
c) Oxycodone/acetaminophen 1-2 tabs q4h prn
d) Hydromorphone 1mg IV q2h prn
e) OxyContin 20mg po 2xd
f) Acetaminophen 650mg 4xd
g) Morphine PCA

Patients Receiving Methadone

- Continue the methadone maintenance dose
- Use additional opioids at doses needed to provide analgesia and given on a scheduled basis
- Maximize non-opioids as able
- Alternatively, for pain conditions that are expected to be prolonged, an increase in methadone dose given at divided intervals may be appropriate

Methadone

Mechanism of action:

- Opioid analgesic with activity at Mu and Delta opioid receptors
- Additionally acts as a NMDA receptor antagonist (like ketamine and dextromethorphan)
- Also a weak serotonin/norepinephrine reuptake inhibitor (like amitriptyline)

Methadone Pharmacokinetics

- Onset of analgesia
  - Oral: 30-60 minutes
  - IV: 10-20 minutes
- Peak
  - Oral: 3 to 5 days
- Duration of analgesia
  - Initially ~4 hours
  - Increases to 6-12 hrs with repeated dosing
- Half-life
  - 8-59 hours

Case 2: Methadone

- Typical recovery time and duration opioids are prescribed for pt's without addiction
- Scheduled opioids to prevent pain as able
- PRN opioids for breakthrough pain and in advance of incidental pain
- If eating oral diet then use oral pain meds
- Adjunct analgesics
- Wean off with healing/recovery from surgery

Case 2: Methadone

Initial Regimen:

- Methadone 80 mg 1xd
- Oxycodone Sustained Release 20mg 2xd
- Oxycodone Immediate Release 10 mg po q3h prn for breakthrough pain and a dose given 30-45min before physical therapy
- Acetaminophen 650mg 3XD scheduled
- Baclofen 5 mg 3xd scheduled

Case 2: Methadone

- Regimen on Day 3 (Discharge Day)
- Oxycodone Sustained Release 40 mg 2xd
- Oxycodone Immediate Release 15mg po q4h prn
- Acetaminophen 650mg 3xd
- Baclofen 5 mg 3xd

Case 2: Methadone

Planned wean:

- Wean Oxycodone Sustained Release by 10 mg every 1-2 weeks until off
- Wean Oxycodone Immediate Release by 5 mg every 1-2 weeks until off
- Use baclofen as a PRN for up to a month after surgery
- Continue acetaminophen as long as needed
- Inform methadone program of discharge date and current regimen with planned duration

Buprenorphine Nuances

Buprenorphine

- Brand Names:
  - Buprenex® or Subutex®
  - Butrans® (transdermal patch)
  - Suboxone®- buprenorphine combined with naloxone
- Mechanism of Action:
  - Mixed Agonist/Antagonist
  - Partial mu agonist activity
  - Kappa antagonist
  - High binding affinity with slow receptor dissolution rate
  - Half-life for SL in 37 hrs

Buprenorphine

- Concomitant opioid administration risks displacement of the buprenorphine or buprenorphine will block the additional opioid
- If therapy is interrupted, re-starting will displace other opioids leading to acute opioid withdrawal and pain
- Abrupt discontinuation of buprenorphine can lead to increased sensitivity to full opioid agonists, including respiratory depression and sedation

Approaches to Acute Pain while on Buprenorphine

1. Continue Buprenorphine and provide additional opioids as needed. (Treat through)
2. Split the daily dose of buprenorphine to 3-4 doses/day to treat acute pain.
3. Convert to methadone 30-40mg/day to manage addiction and additional opioids to manage acute pain. (hospitalized patients)
4. Stop buprenorphine. Treat acute pain for expected course. Resume buprenorphine after acute illness.

General Recommendations

- Early/aggressive use of opioids for acute pain
- Scheduled doses to prevent pain
- Titrate to response
- Maximize non-opioid adjuvants
  - Acetaminophen or NSAIDs/COX-2 Inhibitors
  - Gabapentin/Pregabalin
  - Antidepressants (TCA's, SNRI's)
  - Clonidine or dexmedetomidine
  - Ketamine
- Avoid the patient previous opioid of addiction

Case 3: Buprenorphine

- TJ is a 33yom presents to the ED with acute left flank pain, frequent painful urination with hematuria, n/v and fever to 102°F.
- Pt with a history of prescription drug abuse and has been on Buprenorphine 8mg/Naloxone 2mg SL 2xd for the last 18 months.
- Diagnosed with pyelonephritis and left kidney stone, being admitted for IV antibiotics, hydration, pain control and lithotripsy.

Case 3: Buprenorphine

Where would you begin to manage his acute pain?

a. Buprenorphine 0.3 mg IV q4h prn
b. Hydromorphone 1 mg IV q2h prn
c. Morphine 2 mg IV q2h prn
d. Naloxone 2mg IV x1 now, then morphine 6mg IV q2h prn
e. Oxycodone/acetaminophen 5mg/325mg 2 tabs q6h prn

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Case 3: Buprenorphine

Initial Treatment Regimen

- Continue Buprenorphine 8mg SL 2xd
- Add hydromorphone 1mg IV q2h prn until able to tolerate oral diet
- Transition to oral as soon as able
- Rapidly wean off over the next couple days

Case 4: Buprenorphine

TB is a 47yom helmeted driver involved in a motor cycle accident, resulting in:

- liver and renal laceration
- multiple rib fractures
- left lower extremity open tib/fib fx
- closed left distal humerus fx
- PMH: Hypertension, Chronic low back pain from spinal stenosis, L4-L5 laminectomy, depression and anxiety. No known drug allergies.

- SH: divorced, 2 teenage sons, employed truck driver. History of prescription drug abuse (Oxycontin® for back surgery) on buprenorphine/naloxone (Suboxone®) for the last 6 months. Former smoker.
- Home Medication Regimen:
  - Hydrochlorothiazide 25mg once a day
  - Sertraline 50mg once a day
  - Naproxen 500mg twice daily
  - Buprenorphine/naloxone 8mg/2mg sublingual twice daily
  - Epidural steroid injections

Hospital Course:

- Intubated in the ED for airway protection
- Exploratory laparotomy with repair of hepatic laceration and lower extremity washout and ex-fix on HD#1
- Extubated on HD#2
- Washout /wound vac placement of LLE and ORIF of LUE on HD#3
- I&D and ORIF of LLE on HD #6
- Cleared for d/c to rehab on HD#10

Case Study: Pain Management in the ED

- Opioids, intravenous
- Avoid mixed or partial agonists
- Aggressive dose titration (33-100% increases)
- Provide dose prior to tests/procedures anticipated to cause pain
- Re-assess routinely

Sedation usually precedes respiratory depression

Acute pain drives respiration

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Case Study: Pain Management in the ICU

- Buprenorphine has been stopped during recovery from acute trauma
- Continuous infusion of opioid used to “replace” buprenorphine with dose escalation to cover acute pain and sedation requirements
- Fentanyl is suggested because of it’s high binding affinity for the mu receptor and neutral hemo-dynamic profile

Case Study: Transitioning to the wards

- Use ICU opioid administration records to guide
- Consideration to acute issues while in the ICU
- Consult conversion charts, reduce by 50%
- Use long acting to prevent pain and manage opioid withdrawal (replace what is lost with d/c buprenorphine)
- PRN dose 10-20% of TDD of long-acting.
- Provide in advance of incident pain (PT, vac changes) and for breakthrough pain

Case Study: Long term plan

- Plan weaning strategy. Discuss in advance of initiating. Some flexibility to alter plan, but commit and follow through.
- Wean regardless of suboxone f/u plan
- Example: Pain course expected to be most intense for 2 weeks following injuries then improve over the next 6-8 weeks.
- Wean the long acting at weekly intervals on Monday
- Wean short acting at weekly intervals on Thursday

Case Study: Long-term plan

- Communicate with the suboxone prescriber when the re-initiation will occur
- Stop prescribing opioids once the suboxone is restarted or the suboxone prescriber assumes prescribing of opioids

General Recommendations

- Continue maintenance opioids
- Early/aggressive use of opioids for acute pain
- Maximize non-opioid adjuvants
  - Acetaminophen
  - NSAIDs/COX-2 Inhibitors
  - Gabapentin/Pregabalin
  - Antidepressants (TCA’s, SNRI’s)
  - Clonidine
  - Ketamine

Addiction Treatment Issues

- Reassure patients that addiction history will NOT prevent adequate analgesia
- Continue usual dose of maintenance opioid
- Confirm dose with clinic/prescriber and timing of last dose
- Notify addiction treatment program of admission and discharge from hospital, as well as medications received during admission