Acute Pain Management in the Opiate-Exposed Patient

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DISCLOSURES

• Speaker has no known or real conflicts of interest to declare
LEARNING OBJECTIVES

• Describe the neurological changes that underlie addiction and discuss how these changes play a role in altering pain perception.

• Describe the clinical presentations of acute pain in opioid dependent patients.

• Describe various principles in managing acute and chronic pain in hospitalized opioid dependent patients.
FURTHER OBJECTIVES

- Addictions, not pain expert
- Rational approach, not empirical (protocol driven)
TERMINOLOGY

- Addiction = Substance Dependence
- Substance Misuse and Abuse
- Physiological dependence
- Tolerance
- Pseudo-Addiction
ADDICTION = SUBSTANCE DEPENDENCE

- DSM V
- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

ASAM 2011
ADDICTION

• Control – inability to predict
• Compulsion – pushes other realms aside
• Consequences – 8 realms
• Continued Use – despite above
• Craving/Preoccupation – time thinking
ADDICTION

• Primary chronic brain disease
• Loss of insight occurs early
• Predictable prevalence
• Identified risk factors - genetic, psych, social
• Predictable natural history
• Predictable morbidity and mortality
• Good treatment efficacy
• Potential for prevention
WHAT DOES ADDICTION LOOK LIKE?

• 7 to 15% life time prevalence (excl. nicotine)
• Often unable to see neg. impact on quality of life
• Denial, minimization, rationalization defense mechanisms prominent
• Affective component
• Poor relationship with self, other, life...
MISUSE AND ABUSE

• Misuse – using the medication for something for which it was not intended, but little or no consequences
• Abuse – recurrent or continued use causing impairment or distress
PHYSIOLOGICAL DEPENDENCE

• Tolerance and Withdrawal
• Tolerance = neuro-adaption
• Withdrawal – stopping abruptly, rapid dose reduction, using an antagonist, reduced bioavailability
• Expected
• Can occur rapidly – continuous use for days or weeks
• Does not mean Addiction
PSEUDO-ADDICTION

• Inadequate treatment of pain or withdrawal causing "drug seeking" behaviors
• Should resolve with management of pain or withdrawal state
ADDICTION VS PSEUDO-ADDICTION

- Addiction diagnosed **prospectively**
  - Aberrant behavior gets worse with rational treatment plan
- Pseudo-Addiction diagnosed **retrospectively**
  - Aberrant behavior normalizes with rational plan
WHAT CAUSES ADDICTION?

"The next few days are critical. We're going to slowly reintroduce her to cash."
c.3400B.C. Lower Mesopotamia

It is known that the poppy was cultivated by the Sumerians who called it "Hul Gil" the "joy plant" who would pass it on & it’s euphoric effects to the Assyrians, Babylonians and finally the Egyptians.
Thebes Egypt c. 1300B.C.

- Famous poppy fields.
- Reign of Thutmose IV
- Akhenaton
- King Tutankhamen
- c.400 A.D. opium thebaicum is introduced to China via Arab trade routes
Alexander the Great

- 330 B.C.
- Introduces opium to the people of Persia and India
- For hundreds of years used by the Arabs, Greeks, and Romans used as as a sedative and soporific
...AND MORE RECENTLY


These graphics vividly establish that deaths and addictions from prescription opioids have
THEORY ON ADDICTION

- Concept that reward/pleasure systems existed as discrete neurological areas foreign until 1950
- fMRI (neuroimaging) allowed human research
- Naturally self regulating system with neg. feedback
- Reinforcing effects of all MAD have final common pathway – Mesolimbic Dopamine Reward system (MLDR)
ADDICTION – REWARD AND INHIBITION

• Reward Tone:
  • Mediated thru Mesolimbic Dopamine Reward System
  • Present in all animals
  • Mediates pleasure for survival behaviors – eat/sex/nurture
  • Sensitization – repeated same doses result in increased D release
  • Increased D binding causes down regulation (reduced sensitivity and number) of D sites (and others)

• Allostasis or neuro-adaptation occurs
  • Reduced reward tone – negative emotional/physiological state and increased use – downward spiral

• MLDR system fully developed by adolescence
Opioids Decrease D2 Receptors

OVERVIEW – REWARD AND INHIBITION

• Inhibitory Tone:
  • Medicated by Frontal Lobes (prefrontal cortex) control for inhibitory tone and executive functioning
  • Planning, attention, working memory, problem solving, multitasking, relations with concrete and abstract/animate and inanimate-spirituality
  • Reduced activity with active substance use
• Fully developed age 20 – 25
• Size and function related to risk – poor impulse control strong predictor of addiction
ADDICTION

• Dysregulation of motivational and inhibitory systems
• Reward system high jacked by drug/behavioral reinforcer
• Renders inhibitory and connecting system ineffective
• Role of genetics
• Role of Epigenetics
  • Factors that determine whether a gene will be expressed
  • How non-genetic influences impact on gene expression – how genes are switched on and off
• We are not Just Our Genes
THE FEMALE BRAIN

FOOTNOTE: The "Put Oil into the Car" and "Be Quite During the Game" glands are active only when the "SHINY THINGS AND DIAMONDS" Olfactory has been satisfied or when there is a shoe sale.

THE MALE BRAIN

FOOTNOTE: the "Listening to children cry in the middle of the night" gland is not shown due to its small and underdeveloped nature. Best viewed under a microscope.
ADDICTIONS AND PAIN COMMON FEATURES
Pain is the most highly modulated sensory experience

- Central Modulation
- Inhibitory and facilitatory processes in spinal cord (ascending) or brain (descending)
NEURAL MODULATION OF PAIN

- Opioid, Serotonin and Norepinephrine
- Substance P
- NMDA Receptor
- Excitatory and Inhibitory systems
- On-off cells
- Endocannabinoid system
CONUNDRUMS

- Opioids initially enhance descending inhibition
- May facilitate later (hyperalgesia)
- Possible peripheral effects
- Mu receptor alterations
- Pain and opioid spiral
  - Repeated cycle of pain contingent dosing with SA opioid causing tolerance and dependence and poorer analgesic effect
- Addiction alters pain perception via multiple mechanisms
- Addiction may predispose to altered pain perception
COMMON CO-MORBIDITIES

Secondary Discomforts

Sleep Disturbance

Drug Dependence

Pain

Addiction

Depression

Anxiety

Increased Stresses

Functional Disability
PREVALENCE OF CHRONIC PAIN

• Growing public health problem
• 1 in 10 Canadians aged 12 to 44 years of age\textsuperscript{1} and 1 in 5 Canadians overall.\textsuperscript{2}
  • Pain lasting several months or persisting after the injury has healed

PREVALENCE OF ADDICTION IN CHRONIC PAIN?

- 3 to 26% of patients receiving chronic opioid therapy will meet criteria for an Opioid Use Disorder\(^1\)
- Caseload increase from 9.4 to 15.7% between 4/2004 – 3/2009 for Prescription Opioid treatment admissions (DATIS).\(^2\)


\(^{2}\) Changes in and characteristics of admissions to treatment related to problematic prescription opioid use in Ontario, 2004-2009.
CHARACTERISTICS OF PATIENTS REFERRED TO PAIN MANAGEMENT

- Report high level of psychological distress
- Display high levels of psychopathology
- Report high levels of functional impairment
- Have work/MVA/accidental injuries
- Frequent use of health care resources
- Complain of constant pain
- Multiple prior surgeries/procedures
- Are using multiple narcotic medications
CHARACTERISTICS OF PATIENTS SEEN BY ADDICTION MEDICINE SERVICES

- Report high level of psychological distress
- Display high levels of psychopathology
- Report high levels of functional impairment
- Have work/MVA/accidental injuries
- Frequent use of health care resources
- Complain of constant pain
- Multiple prior surgeries/procedures
- Are using multiple narcotic medications
PRESENTATIONS

- Illicit opioid addiction with acute pain
- Polydrug dependence with acute pain
- MAT (Medication Assisted Therapy) – methadone or Bup/Nal and acute pain
- COT (Chronic Opioid Therapy) and acute pain
MOST HAVE CHRONIC PAIN

- Chronic pain occurs in 22 to 58% of addictions populations depending on study
- Highest in MAT (Meth and B/N-Suboxone®) populations
- Hospitalization may also select for this co-morbidity
Doverty et al (Pain 2001;90 91-96) – 16 OD stable MMT vs 16 control. Electrical vs Cold Pressor test. Measured detection for onset of pain and tolerance at trough and peak MMT levels. MMT detected early and less pain tolerant. NOT same for electrical stimulus.
Figure Legend:

MMTP indicates methadone maintenance treatment program. MMTP patients with any pain (313/390 [80%]) and inpatients with any pain (412/531 [78%]) include chronic severe pain as well as any pain in the past week. Pain severity was measured on the Brief Pain Inventory item "pain at its worst" in the past week.
Figure Legend:

MMTP indicates methadone maintenance treatment program. Data are patients reporting a score of 5 or higher on the Brief Pain Inventory "interference" item, scored from 0 (does not interfere) to 10 (interferes completely).
**From: Prevalence and Characteristics of Chronic Pain Among Chemically Dependent Patients in Methadone Maintenance and Residential Treatment Facilities**


**Figure Legend:**

MMTP indicates methadone maintenance treatment program.
ASSESSMENT
• How many days in the last month have you used alc/bzo/opi/mmt/coc/meth/thc/OTC?
• Longest abstinent of all substances
• History of withdrawal
• Treatment history
  • ie: I/P, O/P, 12 step, counseling, EAP, addictions assessment
ADDICTIONS ASSESSMENT

- Social
  - Legal consequences - DUI, 24h suspension, arrest, charges pending or probation
  - Housing
  - Relationships and supports
  - Income
- Screening for mood and anxiety disorders
- Current/past suicidal ideation
ADDICTIONS ASSESSMENT

- PharmaNet
  - Amount prescribed vs patient’s report of use
  - Number of prescribers
  - Frequency of prescriptions
- Examination – pain type and generator
- Old records
- Collateral information
- Labs
  - UDT, Preg test, CBC, INR, E7, LFTs, Mg and Ca
PAIN ASSESSMENT

• Locus, duration, initial cause and character
• radiation, worse and better factors, daily worst and best,
• how much opioids relieve
• how long on daily opioids
• treatments (non-opioid meds, non-pharm tx), investigations (CT/MRI/labs/pain or other specialist), who prescribes, how often seen and regular or prn, UDT?
ABERRANT BEHAVIORS

More predictive of addiction

• Selling prescription medications
• Prescription forgery
• Stealing or “borrowing” drugs from others
• Injecting, chewing or snorting oral formulations
• Getting prescription drugs from non-medical sources
• Concurrent use of alcohol or illicit substances
• Multiple dose escalations or other therapeutic non-compliance despite warnings
• Multiple episodes of prescription loss
• Covertly seeking prescriptions from other MD/ER after warnings
• Reduced work/family/social LOF related to drug use
• Resistance to therapeutic change despite adverse drug consequences
ASSUMPTIONS

- Polydrug dependence
- Ongoing, individualized process
“We can give you enough medication to alleviate the pain but not enough to make it fun.”
PRINCIPLES

• Manage pain and opioid debt
• Manage other dependencies and withdrawal
• Physiological issues – sleep etc
• Psychosocial issues
• Medication rationalization
• Behavioral issues
• Outcomes
  • Objective pain reduction
  • Improved functionality
GENERAL ISSUES

• Define roles early – “informed consent”
  • With patient and treating team
  • Assign on MRP

• Provide a clear treatment plan and goals
  • Addiction history ≠ poor pain management
  • “treatment agreement”

• Begin with clear boundaries and expectations
  • The 10% that will clearly benefit from it

• Start discharge planning on day one

• Base analgesic decisions on objective outcomes
RATE PAIN ON OBJECTIVE OBSERVATIONS

Analogue Pain Scale

Pain scales tend to refocus on pain
Look at Dynamic and functional measures
Sleep, mobility, independent observation on ward,
nursing report, deep breath, cough, candy wrappers
MULTIMODAL MANAGEMENT

• Pharmacological
  • Opioids, non-opioid, SSRI, TCA, anti-convulsants, Adjunctives – clonidine, ketamine etc

• Non-Pharmacological
  • Interventional - regional block or analgesia

• Psychiatric

• Physio and OT

• Social work
PREEXISTING OPIOID DEPENDENCE

Replace Opioid Debt

• Assess thirty day history

• PharmaNet provides daily **maximum**
  • Heroin:Morphine=2-3:1, but 10 – 30% pure
  • IV>potency than smoke/snort

• Replace 50 to 100% - split q4h po>sq, not iv,
  • **hold if drowsy**

• Continuous and “hold is drowsy” vs prn only
PREEXISTING OPIOID DEPENDENCE

Analgesia
• Shorter frequency and higher dose – cross tolerance
• Higher affinity opioid?
• Regular vs prn dosing
• Aggressive early analgesia
• Taper to sq and po rapidly
• Consider MMT in Opioid Dependence
• Avoid mixed agonist/antagonist analgesics
OTHER DEPENDENCIES AND WITHDRAWAL

- Alcohol dependence
  - CIWA
  - HOB>30°, sat monitor, review regularly
  - High risk

- Benzodiazepine dependence
  - Assess thirty day history
  - PharmaNet provides daily maximum
  - Replace 50 to 100% - depending on history
  - Give majority at hs
  - Taper as outpatient
OTHER DEPENDENCIES AND WITHDRAWAL

• Stimulants
  • Generally not clinically significant withdrawal
  • Beware of withdrawal crash
  • Quetiapine for agitation
  • Some altered pain perception

• Chronic marijuana use
  • Variable effect
Physiological Issues

- What is the pain generator?
- Reassess commonly for medical issues
  - Manage and stabilize underlying medical issues
  - Chaotic patients – easy to miss serious problems
  - Pain means pathology
- Sleep
  - Avoid prolonged use of bzo
    - Cognitive impairing, depressing, impaired mobility
  - Consider sedating typical or novel anti-psychotic or TCA
PSYCHOSOCIAL ISSUES

- Focus on rehabilitation and discharge planning not pain
- Patient centered and self responsibility
- Speed bump in the same direction or opportunity to change direction
- Address psychiatric co-morbidities
- Opportunity for smoking cessation
  - Defocuses from pain
  - Promotes other healthy behaviors
MEDICATION RATIONALIZATION

• All medication is started on a trial basis
• Discontinue if no objective benefit
• Discontinue or taper if no rationale for use
BEHAVIORAL ISSUES

- Establish mutual trust/honesty at outset
- Establish boundaries and consequences early
  - Unable to provide opioids/narcotics in setting of illicit drug use – safety issue
  - Medical model (outcomes) focus not moral model
  - Contingency management
    - No parenteral opioids if can leave ward
- Establishing a hospital pattern of practice
DISCHARGE CONCERNS
DISCHARGE GOALS

• Attainable
• Reduced likelihood of readmission
DISCHARGE PLANNING

- Treatment referral
  - MMT Clinic
  - Outpatient counseling
  - Inpatient facility
  - In hospital mutual help meetings
- Communicate with community providers
- Controlled Prescriptions
  - Transition to community
  - Tapering
  - Q 1-2 day pickup to reduce self risk
DISCHARGE PLANNING

• Is the patient leaving addicted to something they weren’t on prior to admission?
CASE 1

- 38 yo F, necrotizing fasciitis right limb
- Extensive resection and debridement
- Bup/Nal (Suboxone) 24 mg/d
- Clonazepam 2mg bid
- Needing bid dressing changes
- Hx depression and anxiety disorders
PRINCIPLES

• Manage pain and opioid debt
• Manage other dependencies and withdrawal
• Physiological issues – sleep etc
• Psychosocial issues
• Medication rationalization
• Behavioral issues
• Outcomes
  • Objective pain reduction
  • Improved functionality
MISCONCEPTIONS

Treatment of acute pain in patients on MAT

1. Maintenance dose provides analgesia
2. Use of opioids for analgesia may result in addiction relapse
3. Additive effect of analgesia and MAT may cause respiratory and CNS depression
4. Pain reporting is manipulation or drug seeking
Effects of Buprenorphine Maintenance Dose on μ-Opioid Receptor Availability

BUP/NAL (SUBLUXONE) AND ACUTE PAIN

• Continue B/N and titrate short acting opioid (short duration of pain only)
• Divide B/N dose qid
• D/C B/N and use opioid regime and convert when pain gone
• D/C B/N and provide methadone (20-40 mg) and use opioid regime
• Reduce B/N to 2-4 mg and use high dose, high affinity regime
CASE 1

• Analgesia
  • Stop B/N – dissociation curve
  • MSO4 then HM then Fentanyl and how
  • Regular Tylenol, NSAID, no block, elevation of leg
  • Gabapentin on day 5
  • Single prescriber

• Bzo dep, sleep, mood and anxiety issues
• Clear tx plan – everyone saying the same thing
ISSUES

• What happens on discharge
  • Patient is in relapse with pain
  • Community MDs role
  • Risk to patient
Appendix A: The University of Michigan Protocol for the Management of Sublingual Buprenorphine (Suboxone and Subutex) in the Acute Perioperative Setting for Elective Surgery

**Elective Surgery**

- Minimal to no pain
  - Ask the patient if they are still taking their buprenorphine
    - Yes: Still taking buprenorphine
      - Surgeons ensure that the physician writing the buprenorphine is aware of surgery
      - Continue the buprenorphine for post-op pain
      - Do not routinely prescribe supplemental opioids
      - Consider adjuncts- Acetaminophen and/or NSAIDs
    - No: Off buprenorphine
      - Assess the amount of time since the last dose of buprenorphine
      - If ≥ 5 days off buprenorphine, treat with traditional opioids
      - Surgeons should contact the physician prescribing buprenorphine and ensure that they are aware of surgery
      - After post-op pain normalizes, the patient may work with their physician to Reinstitute buprenorphine therapy
- Moderate to severe pain
  - Ask the patient if they are still taking their buprenorphine
    - Yes: Still taking buprenorphine
      - Cancel surgery
      - Patient should return to the physician that prescribes their buprenorphine; coordinated by surgical team
      - Should be taken off of buprenorphine and transitioned to short-acting opioids for ≥ 5 days prior to surgery by physician prescribing buprenorphine
      - Coordinate follow-up post-operatively with buprenorphine provider
    - No: Off buprenorphine
      - Anticipate patient’s course will be similar to opioid tolerant patient
      - Surgeons should ensure appropriate outpatient follow-up
Appendix B: The University of Michigan Protocol for the Management of Sublingual Buprenorphine (Suboxone and Subutex) in the Acute Perioperative Setting for Emergent Surgery

Still taking buprenorphine
- Surgeons should ensure that the physician writing their buprenorphine is aware of surgery
- Continue the buprenorphine for post-op pain
- Do not routinely prescribe supplemental opioids
- Consider adjuncts- Acetaminophen and/or NSAIDs

Off buprenorphine
- Assess the amount of time since the last dose of buprenorphine
- If ≥ 5 days off buprenorphine, treat with traditional opioids
- Surgeon should contact the physician prescribing buprenorphine and ensure that they are aware of surgery
- After post-op pain normalizes, the patient may work with their physician to reinstitute buprenorphine therapy

Urgent/ Emergent Surgery

Preoperatively:
Surgical team should assess anticipated post-operative pain and opioid requirements

Ask the patient if they are still taking their buprenorphine

Minimal to no pain

Moderate to severe pain

Still taking buprenorphine
1. Discontinue buprenorphine
2. Start PCA - Will likely require high doses; may require some continuous opioid infusion, however, would avoid high-dose continuous opioids and instead allow the patient to use PCA. PCA to be managed by Acute Pain Service (APS).
3. Patient should be in a monitored setting with close nursing monitoring (ICU or BD only)
   - Duration of ICU/monitored setting time will vary
   - Half-life of buprenorphine will vary by patient and dose (24-60 hours); anticipate decreased opioid requirements after buprenorphine clears
4. Regional Anesthesia - Consider continuous catheters
5. Maximize Adjuncts
   - Dexmedetomidine for ICU patients used according to ICU protocols
   - Acetaminophen ATC
   - Consider gabapentin or pregabalin
6. Continue traditional opioid therapy for post-op pain after discharge - Coordinate follow-up with pain physician prescribing buprenorphine for eventual opioid wean and reinstitution of buprenorphine therapy

Off buprenorphine
- Anticipate patient’s course will be similar to opioid tolerant patient
- Surgeons should ensure appropriate outpatient follow-up
CASE 2

• 28 yo M admit with MVA multitrauma
  • # right femer IM nail
• IVDU heroin 5 pts per day
• Crack eight ounce per day
• No tx exposure, homeless, no supports, social asst, pending courts, hx ADHD/BAD
• HCV positive
Universal Precautions in Pain Medicine

1. Diagnosis with appropriate differential
2. Psychological assessment including risk of addiction
3. Informed consent (written)
4. Treatment agreement (written)
5. Pre-treatment assessment of function/pain
6. Appropriate trial of opioid therapy +/- adjuvants
7. Reassessment of pain score and level of function
8. Regularly assess the “Four A’s” of pain medicine
9. Periodic review of diagnosis and comorbid conditions, including addiction
10. DOCUMENT, DOCUMENT, DOCUMENT

Gourlay D, and Heit H. Pain Medicine 2006, 6(2) 107-112
CHRONIC PAIN SYNDROME

- Greater than 6 months intractable pain
- Marked functional impairment
- Marked behavioral impairment
- Excessive medication/medical service use
- No clear relationship to organic disorder after thorough investigation