

*Opioid Agonist Therapy 101:
An Introduction to Clinical Practice Workshop*

**Special Considerations: Acute, chronic and perioperative
pain in the context of Opioid Agonist Therapy**

Slide development - Kulvir Badesha MD, FRCPC

And Nicole Nakatsu B.Sc. Pharm, BCPS, EPPh

Faculty/Presenter Disclosure

- * **Faculty:** Nicole Nakatsu
- * **Relationships with commercial interests: (list None if no disclosures)**
 - * **Grants/Research Support:** None
 - * **Speakers Bureau/Honoraria:** Fresenius Kabi
 - * **Consulting Fees:** None
 - * **Other:** None
- * **Mitigating potential bias: (delete this section if no disclosures above)**
 - * Fresenius Kabi at the time I gave the talk sold no narcotics. The talk was on Opioid Stewardship and they had no input on the content

Learning Objectives

- * Review definitions, pathophysiology, and classification of pain
- * Understand the epidemiology and management of chronic pain
- * Outline rational pharmaceutical options for pain management
- * Review current guidelines for Opiate Replacement Therapy (OAT) with respect to patients with concurrent pain
- * Discuss management of pain for patients on OAT with acute and chronic pain through case-based learning

Case 1: Jim

- * 52 year old male
- * Long standing history of alcohol use disorder
- * Introduced to opiates via his wife
- * Stabilized on methadone for a few years with a few minor relapses only
- * No other medical history or medications

Case 1: Jim

- * Jim's wife leaves for 2 weeks to visit with family
- * Jim takes the opportunity to indulge in a few beer
- * Unfortunately, while on a ladder, Jim falls and has an acute navicular fracture for non operative management
- * He is having considerable pain, what do you do?

Case 2: Kathy

- * Kathy is a 33 year old female
- * She has a positive family history of substance abuse
- * She herself has a long standing history of an opiate use disorder for which she is on 120 mg of methadone
- * She also has known Crohn's Disease which is currently in remission
- * She is transferred your clinic with the following....

Pyoderma Gangrenosum



Case 2: Kathy

- * Kathy presents in crisis
- * She is receiving Infliximab and prednisone and is being followed by a gastroenterologist as well as a dermatologist. She has had a poor response to therapy thus far
- * She is in pain. How do you proceed?

Pain Overview

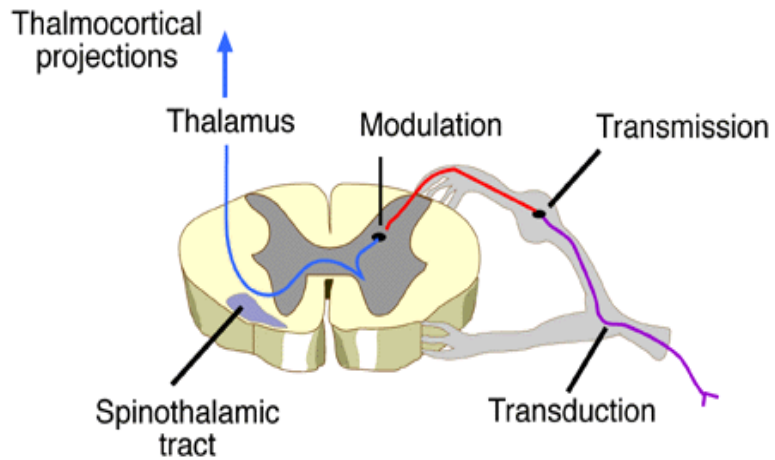
Definitions

- * Nociception
 - * The process by which information about a noxious stimuli is conveyed to the brain. It is the total sum of the neural activity that occurs **prior to the cognitive processes** that enable human to identify a sensation as pain
- * Pain
 - * An unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage...it is always subjective.

A picture is worth.....

* Nociception

* Pain



Classification of Pain

- * Type: nociceptive, neuropathic pain
- * Temporal: acute pain, chronic pain
- * Location: soft tissue, bones/joints, visceral pain

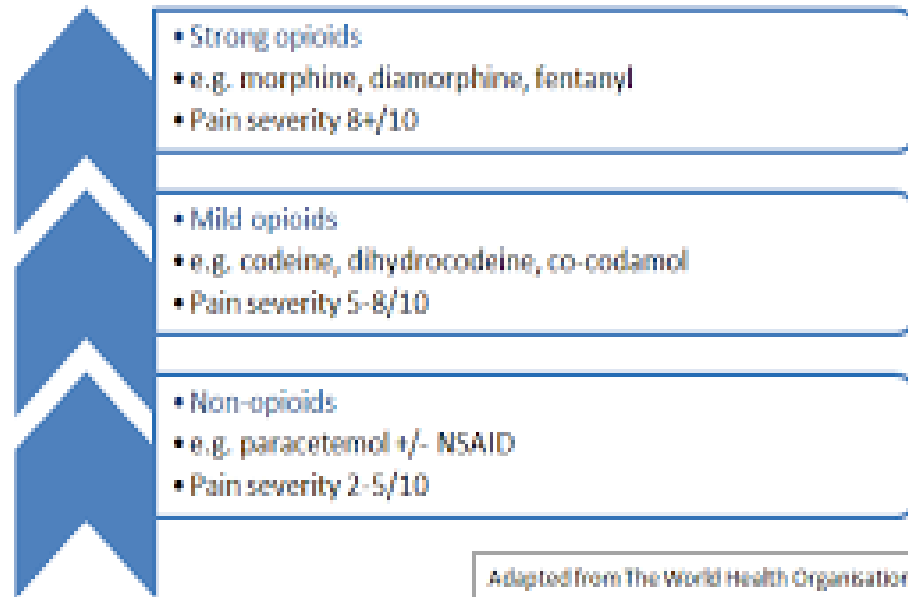
Goals of Chronic Pain Management

- * Focus visits on function
- * Identify complex interactions that may be driving or enhancing the pain experience
- * Collaborative care models

Pain Overview

Pharmaceutical Options

Acute Nociceptive/Perioperative Pain



Adapted from The World Health Organisation pain ladder¹

But what about the methadone/buprenorphine?

- * Continue OAT
- * OAT dose is baseline for preventing withdrawal and once daily dosing will not provide significant pain relief
- * Split dosing may be an option for those eligible for carries
- * People on OAT may have a lower pain threshold, increase pain sensitivity
- * If using opioids start with dosing similar to that used for a person not on OAT
 - * Caveat: may need to be larger and/or more frequent doses
- * Avoid using person's abuse drug of choice if possible
- * Shared decision making should always be sought
- * Consideration of regional anaesthesia for perioperative pain

Buprenorphine hmmm...

- * Buprenorphine binds tightly to the mu-opioid receptor as a partial agonist



ELSEVIER

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

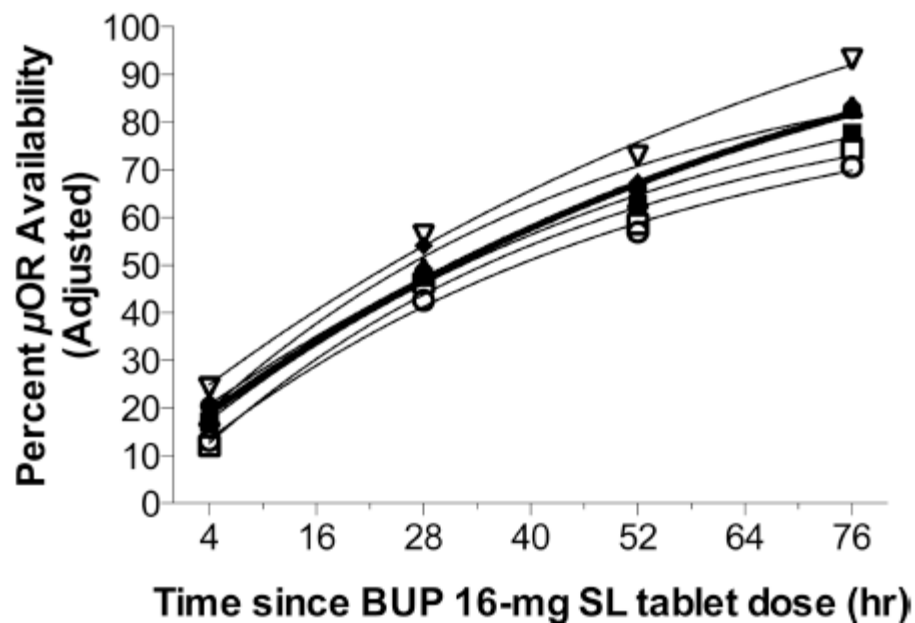
Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs[☆]

Donna A. Volpe^{a,*}, Grainne A. McMahon Tobin^a, R. Daniel Mellon^b, Aspandiar G. Katki^a,
Robert J. Parker^a, Thomas Colatsky^a, Timothy J. Kropp^c, S. Leigh Verbois^c

Drug	K _i (nM)	Drug	K _i (nM)	Drug	K _i (nM)
Tramadol	12,486	Hydrocodone	41.58	Butorphanol	0.7622
Codeine	734.2	Oxycodone	25.87	Levorphanol	0.4194
Meperidine	450.1	Diphenoxylate	12.37	Oxycodone	8.4955
Propoxyphene	120.2	Alfentanil	7.391	Hydromorphone	0.3654
Pentazocine	117.8	Methadone	3.378	Buprenorphine	0.2157
		Nalbuphine	2.118	Sufentanil	0.1380
		Fentanyl	1.346		
		Morphine	1.168		

Buprenorphine maintenance and μ -opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy

Mark K. Greenwald^{a,*}, Sandra D. Comer^b, and David A. Fiellin^c



The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain

Main editor

Jason Busse

2017 Canadian Guidelines for CNCP

Recommendation 3: For patients with chronic noncancer pain with an active substance use disorder

Strong Recommendation

AGAINST

We recommend against the use of opioids

2017 Canadian Guidelines for CNCP

Recommendation 5: For patients with chronic noncancer pain with a history of substance use disorder, whose nonopioid therapy has been optimized, and who have persistent problematic pain

Weak Recommendation

We suggest continuing nonopioid therapy rather than a trial of opioids

Other considerations

- * Referral to a reputable pain clinic regarding pharmacological non opioid pain alternatives and non pharmacological alternatives
- * Employ non opiate alternatives when possible
- * Ensure patient is aware of short term nature of opiate prescribing when necessary
- * Single prescriber
- * Limited dispensing
- * Close monitoring
- * Split dosing?

Pain Overview
Pharmaceutical Options
What about my patient with acute pain on OAT?

Clinical Application

Case 1: Jim

- * Jim's wife leaves for 2 weeks to visit with family
- * Jim takes the opportunity to indulge in a few beer
- * Unfortunately, while on a ladder, Jim falls and has an acute navicular fracture for non operative management
- * He is having considerable pain, what do you do?

Case 2: Kathy

- * Kathy is a 33 year old female
- * She has a positive family history of substance abuse
- * She herself has a long standing history of an opiate use disorder for which she is on 120 mg of methadone
- * She also has known Crohn's Disease which is currently in remission
- * She is transferred your clinic with the following....

Pyoderma Gangrenosum



Case 2: Kathy

- * Kathy presents in crisis
- * She is receiving Infliximab and prednisone and is being followed by a gastroenterologist as well as a dermatologist. She has had a poor response to therapy thus far
- * She is in pain. How do you proceed?

Take Home Messages

- * Appreciate the pain experience in the context of each individual patient
- * Manage expectations early and set realistic goals
- * Be aware of awakening the addiction circuitry and be ready to tighten treatment parameters for safety
- * More research is needed regarding sub-populations of patients with chronic pain
- * More research is needed regarding treatment of pain in patients with concurrent opiate use disorders
- * Return to first principles, understand the type (s) of pain that you are attempting to palliate, and then choose medications appropriately

References

- * <http://www.iasp-pain.org/>
- * College of Physicians and Surgeons of Manitoba 2015. Manitoba Methadone and Buprenorphine Maintenance: Recommended Practice.
- * College of Physicians and Surgeons of Ontario 2011. Methadone Maintenance and Treatment Program: Standards and Clinical Guidelines.
- * Center for Addictions and Mental Health 2011. Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guidelines.
- * Greenwald MK et al. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. *Drug Alcohol Depend.* 2014 Nov 1; 0: 1-11.
- * National Opioid Use Guideline Group 2010. Canadian Guideline for Safe and Effective use of Opioids for Chronic Non Cancer Pain
- * Crewe K.R. et al. Clinical Pharmacogenetics Implementation Consortium guideline for cytochrome P450 2D6 genotype and codeine therapy; 2014 update. *Clinical pharmacology and therapeutics.* 2014; 95:376-382.
- * Rosenblum, A. et al. Prevalence and Characteristics of Chronic Pain among Chemically Dependent Patients in Methadone Maintenance and Residential Treatment Facilities. *JAMA.* 2003; 289: 2370-2378.
- * Katz, J. Chronic Pain, Psychopathology, and DSM-V Somatic Symptom Disorder. *Can J Psych.* 2015; 60 (4): 160-167.
- * Moulin, DE. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. *Pain Res Manag;* 2014: 328-335.
- * Moulin, DE. Chronic Pain in Canada – Prevalence, treatment, impact and the role of opioid analgesia . *Pain Res and Manag;* 2002: 179-184.
- * Turk D et al. Treatment of chronic non-cancer pain. *Lancet.* 2011; 377: 2265-35.
- * Volpe DA et al. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. *Regulatory Toxicology and Pharmacology* 59 (2011) 385-390.

Questions ???