

Ongoing Resources List

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- <https://iecho.unm.edu/sites/uidaho/download.hns?i=51>

ECHO IDAHO



ECHO Idaho: Opioid Addiction and Treatment

Managing Pain in Patients with Opioid
Use Disorder

May 14, 2020

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The speaker has no relevant financial relationship(s) to disclose.

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Learning Objectives

1. Determine appropriate pain pharmacotherapy based on the pain mechanism.
2. Safely manage and prescribe medications for central pain disorders.
3. Discuss pain management in patients on MAT
4. Review the data around cannabis for pain (if time)

Acknowledgments

Select slides adopted from Dr. Daniel Clauw (Univ. of Michigan) and Dr. George Comerici, Jr. (UNM)

Different Categories of Pain

	Nociceptive	Neuropathic	Centralized
Cause	Inflammation or damage	Nerve damage or entrapment	CNS or systemic problem
Clinical features	Pain is well localized, consistent effect of activity on pain	Follows distribution of peripheral nerves (i.e. dermatome or stocking/glove), episodic, lancinating, numbness, tingling	Pain is widespread and accompanied by fatigue, sleep, memory and/or mood difficulties as well as history of previous pain elsewhere in body
Screening tools		PainDETECT	Body map or FM Survey
Treatment	NSAIDs, injections, surgery, ? opioids	Local treatments aimed at nerve (surgery, injections, topical) or CNS-acting drugs	CNS-acting drugs, non-pharmacological therapies
Classic examples	Osteoarthritis Autoimmune disorders Cancer pain	Diabetic painful neuropathy Post-herpetic neuralgia Sciatica, carpal tunnel syndrome	Fibromyalgia Functional GI disorders Temporomandibular disorder Tension headache Interstitial cystitis, bladder pain syndrome

Treat Based on the Mechanism

	Nociceptive	Neuropathic	Centralized
NSAIDs	+	-	-
Opioids	+/-	+/-	-
Surgery/ Injections	+	+	-
Tricyclics	+	+	+
SNRIs	+	+	+
Gabapentinoid	-	+	+
Cannabinoid	-	+	+

Pharmacological Therapies for Centralized Pain

Strong Evidence	<ul style="list-style-type: none">■ Dual reuptake inhibitors such as<ul style="list-style-type: none">■ Tricyclic compounds (amitriptyline, cyclobenzaprine)■ SNRIs and NSRIs (milnacipran, duloxetine, venlafaxine)■ Gabapentinoids (e.g., pregabalin, gabapentin)
Modest Evidence	<ul style="list-style-type: none">■ Older less selective SSRIs■ Low dose naltrexone
Weak Evidence	<ul style="list-style-type: none">■ Cannabinoids
No Evidence	<ul style="list-style-type: none">■ Opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, benzodiazepine and nonbenzodiazepine hypnotics

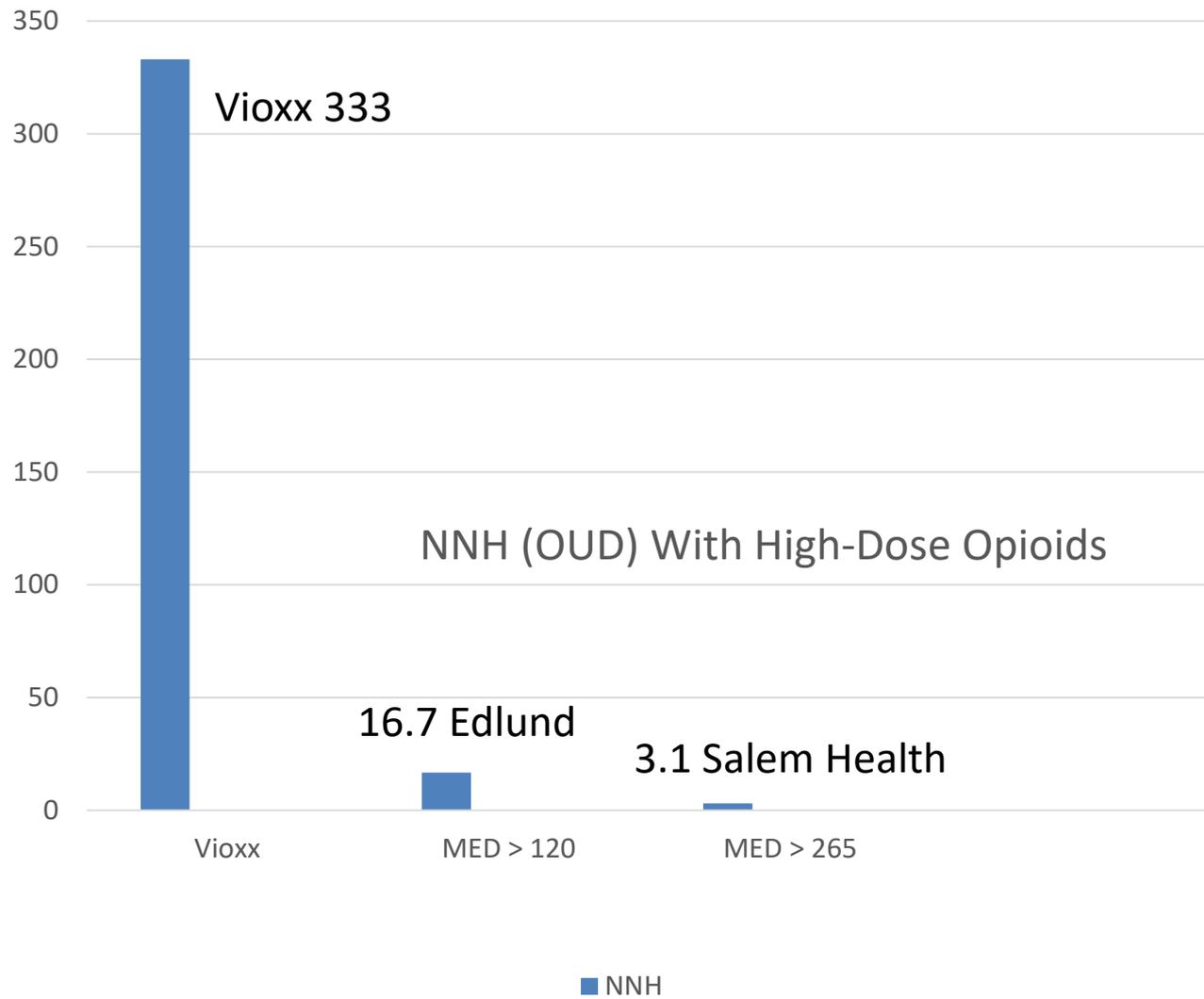
ASA, APAP and NSAIDs

Prototypical Drugs: *Ibuprofen, Celecoxib, ASA and APAP (acetaminophen)*

- inhibition of COX-1/2/3 enzymes which convert arachidonic acid to prostaglandins

Indications and efficacy:

- nociceptive pain
- NNT 2-4 patients for a 50% reduction in moderately severe pain (combination APAP + ibuprofen NNT 1.5 in one study [see *Swift* in references])
- All NSAIDs are probably equal in analgesic efficacy



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Slide from Dr. Paul Coelho, Salem Health, with permission



Anticonvulsants

Prototypical Agents:

- **Gabapentin/Pregabalin Carbamazepine, Valproic acid, Topiramate**
 - Act by a reduction of neuronal irritability

Indications: Neuropathic pain

- **Gabapentin/ Pregabalin** : Postherpetic Neuralgia (PHN), Diabetic Peripheral Neuropathy (DPN), fibromyalgia
- **Valproic Acid, Topiramate**: migraine
- **Carbamazepine**: Trigeminal neuralgia

Anticonvulsants

Gabapentin

- Binds to the $\alpha 2$ - δ subunit of presynaptic voltage dependent Ca^{++} channels
- Reduces the release of pain neurotransmitters
- Uses include:
 - Fibromyalgia (off-label)
 - Diabetic Peripheral Neuropathy (off-label)
 - Post-herpetic Neuralgia (approved)

Anticonvulsants

Gabapentin

Dosing: *start low, go slow*

- Strive for a dose of 1800-3600 mg/day
- Stack doses at nighttime
- Adjust for renal function

Adverse Effects

- Somnolence
- Falls
- Rare: angioedema, leukopenia, thrombocytopenia
- **Black Box:** increased suicidal thinking
- Needs a taper to stop

Contraindications

- Renal failure

GABAPENTIN (NEURONTIN) FOR CHRONIC NEUROPATHIC PAIN

Number needed to treat / number needed to harm = 8

Benefits

Harms

1 in 6 was helped
(diabetic neuropathy)

1 in 8 was harmed (developed dizziness)

1 in 8 was helped
(postherpetic neuralgia)

1 in 11 was harmed (developed somnolence)

1 in 13 was harmed (developed ataxia)

1 in 21 was harmed (developed edema)

Anticonvulsants

Pregabalin

- Approved indications:
 - PHN, DPN, Fibromyalgia, spinal neuropathic pain
- better absorption, decreased somnolence
- Improvement in Non-REM sleep
- 150mg/d in divided doses...up to 600mg/d (maximum dosage dependent upon treated condition)
- Reduce dose by 50% if Clcr 30-60 mL/min

Risks/Benefits of Pregabalin

- NNT for at least 50% pain relief over baseline for 600 mg pregabalin daily compared with placebo:
 - 3.9 (95% confidence interval 3.1 to 5.1) for postherpetic neuralgia
 - 5.0 (4.0 to 6.6) for painful diabetic neuropathy
 - 5.6 (3.5 to 14) for central neuropathic pain
 - 11 (7.1 to 21) for fibromyalgia.
- 600 mg pregabalin:
 - somnolence typically occurred in 15% to 25%
 - dizziness occurred in 27% to 46%
 - treatment was discontinued due to adverse events in 18 to 28%

Antidepressants: TCA

Indications and Efficacy

- Neuropathic pain *
 - Diabetic Peripheral Neuropathy, Postherpetic Neuralgia
- Other chronic pain:*
 - Fibromyalgia, Low Back Pain
 - HA syndromes
- NNT (TCA) = 2-4 for 50% reduction in pain. (Cochrane Review 2010)

*non-FDA approved

TCA_s

- Start with nortriptyline, imipramine, and desipramine (less sedation, fewer anticholinergic effects)
- Start at low doses at night, increase slowly
- Don't expect antidepressant/anxiolytic effects

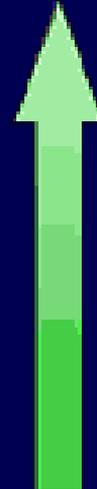
Tricyclic Antidepressants: Adverse Effects

- Commonly reported AEs (generally anticholinergic):

- blurred vision
- cognitive changes
- constipation
- dry mouth
- orthostatic hypotension
- sedation
- sexual dysfunction
- tachycardia
- urinary retention

AEs = adverse effects.

Fewest
AEs



Most
AEs

- Desipramine
- Nortriptyline
- Imipramine
- Doxepin
- Amitriptyline

Antidepressants: SNRIs

Duloxetine

- *Diabetic peripheral neuropathy*
 - 60mg/d resulted in 50% pain reduction: NNT: 6
- *Fibromyalgia (FDA approved!)*
 - 60mg day: NNT:8
- *Chronic Musculoskeletal Pain (FDA approved!)*
 - 60mg day: NNT:8
- Use in doses up to 60mg-90mg/d. Lower doses not effective (Cochrane 2014 reviewed doses up to 120mg—more minor adverse effects, serious AEs rare)

Duloxetine

Side Effects

- N/V most common reason for discontinuation
- Transaminitis is not uncommon - Do not use in patients with liver disease
- Adjust dosage for severe renal insufficiency
- *Serotonin syndrome*: especially with >2 other drugs that increase serotonergic activity
- **Black Box**: increased suicidal thinking

Muscle Relaxants

Antispasticity Drugs

- Spasticity: loss of descending inhibition to spinal motor neuron due to upper motor neuron disease
- *cyclobenzaprine, tizanidine, baclofen, diazepam*

Antispasmodics:

- methocarbamol (Robaxin™), orphenadrine (Norflex™), metaxalone (Skelaxin™), dantrolene
- Act by relieving muscle spasm caused by local tissue trauma from acute muscle damage or strain

Generally, should be used short-term

Muscle Relaxants

Cyclobenzaprine (Flexeril™)

- Think “TCA”: anticholinergic, prolongs QTc
- Potentiates norepinephrine and binds to serotonin receptors reducing spasticity (centrally acting)
- Seems most efficacious for short term usage

Others: methocarbamol (Robaxin™), orphenadrine (Norflex™), metaxalone (Skelaxin™)-mode of action not well understood

Do NOT use carisoprodol (Soma)

Managing Pain in Patients on Buprenorphine

ONLINE FIRST AUGUST 21, 2019—CHOOSING WISELY®: THINGS WE DO FOR NO REASON™

Things We Do for No Reason™: Discontinuing Buprenorphine When Treating Acute Pain

Lawrence A Haber, MD^{1*}; Triveni DeFries, MD, MPH²; Marlene Martin, MD¹

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Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy

Daniel P. Alford, MD, MPH; Peggy Compton, RN, PhD; and Jeffrey H. Samet, MD, MA, MPH

More patients with opioid addiction are receiving opioid agonist therapy (OAT) with methadone and buprenorphine. As a result, physicians will more frequently encounter patients receiving OAT who develop acutely painful conditions, requiring effective treatment strategies. Undertreatment of acute pain is suboptimal medical treatment, and patients receiving long-term OAT are at particular risk. This paper acknowledges the complex interplay among addictive disease, OAT, and acute pain management and describes

4 common misconceptions resulting in suboptimal treatment of acute pain. Clinical recommendations for providing analgesia for patients with acute pain who are receiving OAT are presented. Although challenging, acute pain in patients receiving this type of therapy can effectively be managed.

Ann Intern Med. 2006;144:127-134.
For author affiliations, see end of text.

www.annals.org

Perioperative Considerations for the Patient with Opioid Use Disorder on Buprenorphine, Methadone, or Naltrexone Maintenance Therapy

Thomas Kyle Harrison, MD^{a,*}, Howard Kornfeld, MD^b,
Anuj Kailash Aggarwal, MD^c, Anna Lembke, MD^{d,e}

Efficacy of Full μ -Opioid Receptor Agonists is not Impaired by Concomitant Buprenorphine or Mixed Opioid Agonists/Antagonists – Preclinical and Clinical Evidence

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Clinical Review & Education

Teachable Moment

Acute Pain Management in Patients Treated With Buprenorphine A Teachable Moment

Rachel Cooper, MD; Rahul Vanjani, MD, MSc; M. Catherine Trimbur, MD, MPH



Perioperative Management of Non-Pregnant Patients on Maintenance Therapy for Opioid Dependence

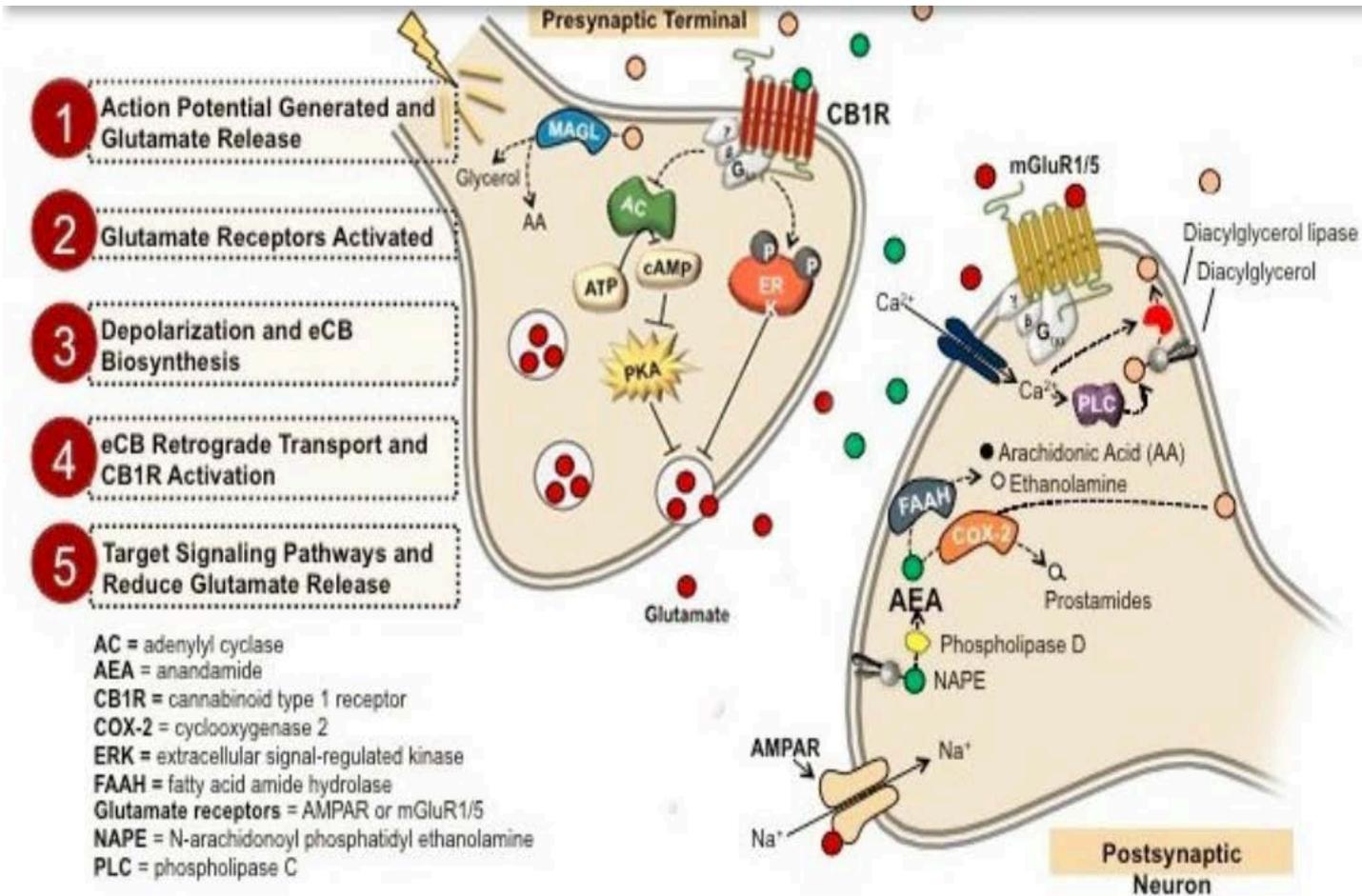


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Revised:
Section: Pharmacy

Perioperative Management of Non-Pregnant Patients on Maintenance Therapy for Opioid Dependence

Buprenorphine, methadone, and naltrexone are pharmacologic therapies indicated for maintenance treatment of opioid use disorder. The appropriate treatment of acute pain in patients on buprenorphine and methadone maintenance includes continuing the patient's baseline opioid requirements to avoid increased pain sensitivity associated with opioid withdrawal. Thus, daily opioid maintenance treatment requirements must be met before attempting to achieve analgesia. These patients have also been shown to have increased pain sensitivity and cross-tolerance to opioid analgesics, therefore adequate pain control will often necessitate higher opioid doses at shorter dosing intervals. All patients on buprenorphine and methadone maintenance should be co-managed with their buprenorphine or methadone provider during the pre- and post-procedure period. Addiction medicine is available for consultation to assist with recommendations for opioid use disorder management in the postoperative period.

Cannabis for Pain



Medical Marijuana: A View Beyond the Smoke

Mark P Brady, MS, PA-C; Michael E Schatman, PhD April 27, 2016

Benefits of Cannabis

NEJM October 18, 2018

- Anti-inflammatory and neuroprotective effects that may alleviate chronic pain in a dose-dependent manner
- Low risk of lasting illnesses from use; at worst, temporary discomfort from excessive use
- Prevalence of addiction and risk of overdose are low
- May lower opioid doses (some reversal of hyperalgesia)
- For 50% reduction in pain, NNT 20*
- For 30% reduction in pain, NNT 11*

* Cochrane March 2018 (and JAMA 2015)

Risks of Cannabis

NEJM October 18, 2018

- Commonly reported side effects: sedation, dizziness, dry mouth, dysphoria, increased appetite, short-term memory loss
 - NNH for adverse CNS effects: 3*
 - NNH for psychiatric disorder: 10*
- Long-term exposure associated with psychotic disorders, including exposing latent schizophrenia
- Inability to establish a safe dose
- Delivery is problematic– oral bioavailability ranges from 13-19% and can take up to 3 hours to reach peak concentration; smoking is risky

* Cochrane March 2018 (and JAMA 2015)



Recommendations

- Canadian Pain Society: third-line therapy for chronic neuropathic pain syndromes if established therapies (e.g. anticonvulsants, antidepressants) had failed (Moulin 2014)
- The Special Interest Group on Neuropathic Pain (NeuPSIG): weak recommendation against use of cannabis-based medicines (Finnerup 2015)

Thank you!

Resources

- Clauw DJ. JAMA. 2014;311:1547-55.
- Hijacking the endogenous opioid system to treat pain: who thought it would be so complicated? Clauw, DJ, Pain. 158(12):2283–2284, Dec 2017
- Swift A. Non-opioid analgesia is as effective as opioid management in acute pain and supports a change in prescribing practice to help address the ‘opioid epidemic’ *Evidence-Based Nursing* 2018;21:50.
- <https://www.medscape.org/viewarticle/498353>
- Cannabis-based medicines for chronic neuropathic pain in adults; Martin Mücke, Tudor Phillips, Lukas Radbruch, Frank Petzke, Winfried Häuser, 07 March 2018

Resources

- Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ. Pregabalin for acute and chronic pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 3.
- Medical Marijuana for Chronic Pain. N Engl J Med October 19, 2018. 379; 16
- Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. Whiting, PF et al. JAMA.2015 Jun 23-30;313(24):2456-73



ECHO Idaho: Opioid Addiction and Treatment

Join us for our next session

For information, please visit uidaho.edu/echo