

UW PACC Psychiatry and Addictions Case Conference UW Medicine | Psychiatry and Behavioral Sciences

MANAGING ACUTE PAIN in PATIENTS on NALTREXONE

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SPEAKER DISCLOSURES

 \checkmark No conflicts of interest

 Other disclosures: I'm an addiction psychiatrist, not a card-carrying pain specialist



PLANNER DISCLOSURES

The following series planners have no relevant conflicts of
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SO...YOUR PATIENT BROKE HER CLAVICLE?



A CASE:

Julie is a 35yo woman with OUD on XR-NTX who suffered a midshaft clavicular fracture after fall during a sporting event.

After discussing risk/benefits with the surgeon, she's leaning towards surgery, which can be scheduled for early as the following day.

She and the surgeon reach you (her PCP) in clinic, with a couple of "quick questions."

Any special planning/considerations if she opts for surgery?

And, either way, broken bones hurt! How on earth are we going to manage my/her pain?



OBJECTIVES

For patients on XR-Naltrexone as MOUD requiring acute pain management we will:

- 1. Appreciate pain as a complex phenomenon.
- 2. Identify challenges related to pain management in the setting of Naltrexone for MOUD.
- 3. Outline treatment strategies in different clinical contexts.



BACKGROUND



PAIN: IT'S COMPLICATED

All pain's not the same!

- Etiology
 - Nociceptive
 - Neuropathic
 - (other?)
- Chronicity:
 - Acute
 - Chronic
- Severity, tolerability can be shaped by:
 - Central Sensitization
 Syndrome
 - Hyperalgesia (eg, w/chronic opioids)
 - Comorbid anxiety/affect
 - Other medical conditions
 - Pain modulating agents, techniques



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ACUTE NOCICEPTIVE PAIN









https://www.uptodate.com/contents/images/PC/60488/Primary_pain_pathways.gif

ACUTE NOCICEPTIVE PAIN

In Summary:

- The hard truth: Pain is complicated
- A positive reframe:
 Because it's
 complicated, there are
 multiple potential sites
 for intervention





PAIN IN OPIOID USE DISORDER – A SPECIAL CASE

- Chronic opioid exposure:
 - Tolerance, physiologic dependence
 - Hyperalgesia, alterations in pain thresholds and experience
- Addiction's psychological and social valences
 - Patients' & Providers' prior experiences, preconceptions, & anxieties
 - Ineffective pain management 个 risk of disengagement from care, relapse to use
- Impacts of treatment (e.g., Naltrexone)
 - Alters Sensitivity to Opioids
 - ↓ Sensitivity (blocks receptors)
 - ...but also can ↑ Sensitivity (loss of tolerance; upregulation of μreceptors)

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NALTREXONE as **MOUD**

- Indications:
 - OUD & AUD
- MOA:
 - competitive antagonist at opioid receptors
 - high receptor *affinity* (for mu esp)
- Formulations & dosing:
 - PO: 50-100mg/day
 - IM: 380mg Q4wks
- Duration of Effect:
 - Oral: 50 mg: 24 hours (100 mg: 48 hours)
 - IM: 4 weeks
- Metabolism:
 - Extensive non-cytochrome-mediated dehydrogenase
 → 6-beta-naltrexol (primary metabolite)
 - Oral: Extensive first-pass effect
- Excretion:
 - Primarily urine (metabolites, minimal unchanged drug)
- Half-life :
 - Oral: NTX 4 hours; 6-beta-naltrexol 13 hours;
 - IM: naltrexone and 6-beta-naltrexol: 5 to 10 days (dependent upon erosion of polymer)
- Time to peak, serum:
 - Oral: ~60 minutes
 - IM: Biphasic: ~2 hours (1st peak), ~2-3 days (2nd peak)





XR-NALTREXONE & ACUTE PAIN – COMMON CONCERNS

– Pragmatically, how will we manage my pain?

- If I need opioids: will I be given any; will they work?
- Under what circumstances should I stop, continue, modify naltrexone dosing?
- What about unanticipated acute pain (e.g., trauma)?
- Stigma, shame:
 - Addressing pain in setting of OUD
- Fear
 - Unmanageable pain
 - Risk of relapse w/opioid re-exposure, changes in MOUD



PLANNING & ASSESSMENT



PLAN AHEAD!

- When to discuss acute pain management?
 - *Prior to* XR-NTX induction: MOUD education & consent
 - Pts are already thinking about pain get it out in the open
 - *Ongoing*: ask about upcoming procedures, current pain symptoms
- Consider the context of Pain:
 - Timeframes
 - Urgent/emergent
 - Future/anticipated event
 - Anticipated/experienced Severity & Duration



ENGAGE, ASSESS, EDUCATE, COLLABORATE, COORDINATE CARE

- Empathetic, non-judgmental, and open approach
- Take patient's concerns & symptoms seriously
- Provide a thorough assessment
- Develop shared & reasonable tx goals, expectations
 - Pain management (not elimination)
 - Focus on function & recovery
 - Anticipate pain-illness course (reduce uncertainty)
- Review treatment options & their rationales
 - Outline the components and value of a multimodal approach
- Commit to ongoing coordination with patient and other providers



ANTICIPATING PAIN:

- Identify & Normalize concerns while addressing unhelpful thinking
- Promote agency, selfefficacy
- Develop shared & reasonable tx goals, expectations
- Put plan into action
- Continue coordination with patient and other providers

Pain Catastrophizing Scale (Copyright 1995, 2001, 2004, 2006, 2009 Michael JL Sullivan, PhD) Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feeling that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at	To a	To a moderate	To a	All the
	an	degree	degree	degree	time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

ASSESSING EXISTING PAIN

Pain (QISS-TAPED)

- Q = Quality
- I = Impact
- S = Site
- S = Severity
- T = Temporal Characteristics
- A = Aggravating & Alleviating Factors
- P = Past Treatment & Response,Patient Preferences
- E = Expectations, Goals, Meaning
- D = Diagnostics, physical exam

Approach

- Establish rapport
- Listen to the patient's story
- Use open ended questions in non-judgmental fashion
- Anticipate anxiety, fear
- Discuss prior experiences
- Listen for & reflect concerns about bias, stigma, problems with medical care



... AND ONGOING RE-ASSESSMENTS



С

Choose the word that best describes your pain:

- None
- Mild
- Moderate
- Severe

D

TREATMENT

IN ALL CASES, AIM FOR A BALANCED, MULTI-MODAL ANALGESIA

TCAs=tricyclic antidepressants; SSRIs=selective serotonin reuptake inhibitors; SNRIs=serotonin-norepinephrine reuptake inhibitors; LAs=local anesthetics; NSAIDs=nonsteroidal anti-inflammatory drugs; ASA=aspirin.

Slide adapted from presentation by Deb Gordon, DNP (Harborview Acute Pain Service) Kehlet H, Dahl JB. *Anesth Analg.* 1993;77:1048-1056

NON-PHARMACOLOGIC STRATEGIES

- □ Treat underlying cause(s) of pain!
- Physical techniques (e.g., Cold, Heat, TENS, Massage, PT):
 - Can provide comfort, reduce inflammation, correct physical dysfunction, and alter physiologic responses
- Cognitive/behavioral strategies (e.g., mindfulness, CBT-pain techniques, psychoeducation, distraction, relaxation, music, hypnosis):
 - Can help patients understand pain, alter pain behavior, enhance coping skills, change perception of pain

BENEFITS OF NON-PHARMACOLOGIC STRATEGIES

- Reduced anxiety
- Improved mood
- Increased sense of control over pain
- Improved sleep

- Decreased fatigue
- Improved function
- Restored hope
- Improved quality of life

ORAL PHARMACOLOGIC STRATEGIES (NON-OPIOID)

- Acetaminophen
 - APAP 325-1000mg PO Q4-6hr (max dose 4 g/day)
- NSAIDs
 - Nonselective NSAIDs
 - Ibuprofen (400mg Q4-6hr); Diclofenac (50 mg three times daily)
 - (Preoperative PO NSAIDs for elective minor surgery ↓ postoperative pain; post-op NSAIDs decrease PRN morphine requirement)
 - COX-2 inhibitors In Cochrane reviews of placebocontrolled randomized trials of postoperative pain control, use of
 - Celecoxib (200-400 mg PO), etoricoxib (120mg PO)
 - Delays and decreases use of opioids for breakthrough pain
 - Several trials suggest > analgesic effect & tolerability than opioids, were similar to nonselective NSAIDs for postoperative pain management
 - (Note: "black-box" warning regarding CV risk, appears associated with long-term use.)

ORAL PHARMACOLOGIC STRATEGIES (NON-OPIOID), CONT.

- Gabapentinoids:
 - <u>Gabapentin</u> (300-600mg PO X1 pre-op) or <u>Pregabalin</u> (75-150mg PO X1 pre-op)
 - And can schedule and titrate as tolerated BID/TID for ongoing acute/subacute pain.
 - SEs: sedation and dizziness, possible respiratory depression in older pts or in combo w/other meds
 - Note: stronger evidence for chronic, neuropathic pain than acute pain; *may* reduce risk of chronic post-op pain, duration of PRN opioids (in **non-dependent pts)**
- Alpha-2 receptor agonists
 - <u>clonidine</u> 0.1-0.2mg BID, as tolerated (analgesic effect enhanced w/concurrent opioid)
 - <u>tizanidine</u> 2-4 mg TID-QID PRN
- SNRI/TCAs:
 - Early analgesic effects ~1wk, w/maximum benefit delayed weeks/months
 - Consider for pt's with comorbid anxiety/depression and/or pre-existing chronic pain
- Muscle relaxants (baclofen 5mg TID; methocabamol 750mg q8h prn)
- Local/topical anesthetics (lidocaine patches; capsaisin, diclofenac, other topicals)

KETAMINE

- N-methyl-D-aspartate (NMDA) antagonist that can inhibit induction and maintenance of central sensitization ("wind-up") after painful stimuli
 - Pain Reduction
 - Analgesic opioid sparing (5-20mg MED/day)
- Concerns about mind-altering effects rarely problematic (RR 1.27)
- Bolus dose not to exceed 0.35mg/kg infusions without ICU not to exceed 1mg/kg/hr

Snijdelaar DG et al, *Anaesthesia* 2004;59(3):222-228. Unlugenc H et al, *European Journal of Anaesthesiology* 2003;20:416-21. Wang L, et al, *Canadian Journal Anaesthesia* 2016;63(3):311-325. Schwenk ES et al. *Regional Anesthesia and Pain Medicine* 2018;43(5):456-466

Slide adapted, with permission, from presentation by Deb Gordon, DNP (Harborview Acute Pain Service)

NEURAXIAL AND REGIONAL ANALGESIA

• Epidural

Peripheral Nerve Block

Slide adapted, with permission, from presentation by Deb Gordon, DNP (Harborview Acute Pain Service)

4% LIDOCAINE SOLUTION PRE-DRESSING CHANGE

- Lidocaine 1mg/kg applied topically without impairment of healing
- Wound size limits volume used due to potential systemic toxicity
- Normal saline may dilute making less effective
- Apply 20-30 minutes prior
- >50% may report stinging
- Short half-life allows for reapplication

FULL AGONIST OPIOID

- Can be used, if needed, for inadequately managed pain with special attention in the setting of NTX
 - NTX blockade is still in full/partial effect:
 - Consider use of Higher-Affinity full agonist Opioids:
 - » Hydromorphone (PO/IV/PCA), fentanyl (IV/lozenge)
 - May require high doses (10-20X if blockade in effect) & close monitoring
 - NTX is sub-therapeutic
 - Consider use of Higher-Affinity full agonist Opioids:
 - » Hydromorphone (PO/IV/PCA), fentanyl (IV/lozenge)
 - Care with dosing—sensitivity variable and increasing over time!
- Titrate for analgesia, monitoring for side effects.
- Use for short duration (rarely indicated >2 wks, even after major surgery), taper w/close follow-up & clear MOUD plan

OK, OK BUT WHAT DO WE DO WITH & ABOUT THE NALTREXONE?

OUTLINE OF TREATMENT STRATEGIES: NALTREXONE & PAIN MANAGEMENT (GENERAL)

Mild/Moderate pain:

- Non-pharm treatments
- NSAIDs (save time-limited Ketorolac for moderate to severe pain).
- APAP
- Some of the other Rxs already discussed

Emergency management of high moderate/severe pain:

- regional anesthesia
- conscious sedation w/benzodiazepines or ketamine
- Non-opioid options in general anesthesia.
- Opioids (short-acting only) at 10-20X nl doses can overcome NTX blockade, requires careful monitoring

OUTLINE OF TREATMENT STRATEGIES: NALTREXONE IN ELECTIVE SURGERY

- Ensure surgical team is aware of pt's NTX.
- Determine if opioids will be required
- If Opioids are required:
 - XR-NTX: dc >30 days before surgery (switch to PO NTX if needed to bridge)
 - PO NTX: dc >48-72hrs before surgery *if* anticipated need for opioids.
 - Plan for re-induction of XR-NTX: short-acting opioid washout 3–7 days; provide naloxone challenge.

SO, YOUR OTHER PATIENT, JOHN, HAS AN UPCOMING PROCEDURE...

ANOTHER CASE:

John is a 55yo M planning for a non-emergent/elective ortho surgery. He has been stable on XR-NTX for OUD for years prior to admission.

Prior to surgery, what should you do?

- Begin dialogue w/pt, explore near and long-term options, goals, concerns.
 - Wants to cont XR-NTX, concerned about pain management
- Communicate with his surgical/anesthesia team regarding NTX plan, their anticipated intra- and post-op pain severity and their expected management.
 - They anticipate need for Opioid rx, post-op for ~1wk (which you think is reasonable)
- Develop plan w/pt & team (informed by the info above)

What would be a reasonable perioperative plan?

- What will you do with his XR-NTX?
- Other interventions?

CASE, CONT – PRE-OP PLAN

NTX:

- Stop XR-NTX min 1mo before surgery
- If longer than 1mo, begin PO NTX, holding 48-72hrs prior to surgery

Other Interventions:

- Pain Catastrophizing Scale (anticipate & address distress)
- Mindfulness training, CBT
- Review multimodal pain management plan

Other Planning:

- Relapse prevention-planning
- Plan XR-NTX re-induction

Intra-operative Options:

- Regional anesthesia
- Conscious sedation (benzo or ketamine)
- General anesthesia

Perioperative Interventions:

Regional Anesthesia

Acetaminophen and NSAIDs

Gabapentinoids

Alpha-2 Agonists

Ketamine & Magnesium

See Harrison et al (2018). Perioperative considerations for the patient with opioid use disorder on buprenorphine, methadone, or naltrexone maintenance therapy. Anesthesiology Clin 36 pgs 345-359.

Promote calm and comfort

Anxiety, fear, depression are common: Instill sense of control, provide education on self-management techniques such as mindfulness meditation. Reduce noise, uncertainty, confusion. Positioning, splinting, and physical comfort should be maximized. Minimize unnecessary NPO status.

TREAT UNPLEASANT SYMPTOMS:

Diphenhydramine 25-50mg PO q8h prn insomnia/anxiety Tizanidine 2-4mg q6h prn muscle spasms Ondansetron 4mg PO q6h prn nausea Trazadone 50mg PO qhs prn insomnia Melatonin 3mg PO qhs prn insomnia Lorazepam 0.5-1mg PO prn anxiety Antipsychotics prn psychotic disorder symptom control Nicotine replacement prn tobacco dependence

Regional Anesthesia

Peripheral nerve blocks: superficial cervical plexus, brachial plexus, radial/median/ulnar, PECS, erratus plane, TAP, femoral, sciatic, posterior tibial.

Spinal and Epidural anesthesia

Acetaminophen and NSAIDs

Acetaminophen and NSAIDs, when not contrainidicated, should are the foundation of a multimodal analgesic strategy.

Gabapentinoids

In opioid depenent patients, the calcium channel inhibitors, gabapentin and pregabalin reduce postoperative pain and reduce opioid consumption. Gabapentin 300-600mg PO TID.

Alpha-2 agonists

Clonidine and Dexmedetomidine are anxiolytic and analgesic with significant opioid sparing affects. e.g. **Clonidine** 0.1-0.3mg PO q6-8h prn pain or anxiety (NTE 1.2mg/day, hold if BP <100/70).

Ketamine & Magnesium (NMDAR antagonists)

Ketamine is the most potent non-opioid analgesic for opioid tolerant patients. A brief infusion of 0.3mg/kg IV over 15min is followed by 0.3-1mg/kg/hr as needed.

Magnesium is also an NMDAR with analgesic and opioid sparing effect. eg. 30-50mg/kg bolus followed by 10-mg/kg/hr.

IV Lidocaine (Na channel antagonist)

Opioid sparing analgesic. A bolus of 1-1.5mg/kg is followed by 1.5-3 mg/kg/h. Contraindications include cardiac dysrthymias. Must monitor serum levels after 24hrs.

$\bullet \bullet \bullet$

55yo M was stable on XR-NTX, transitioned to PO NTX then dc-ed prior to non-emergent surgery, now on multimodal analgesia that includes a PO hydoromorphone PRN, tapering. He returns to your care in the outpt setting where you and Jouhn continue collaborative planning regarding his pain management and MOUD:

Pt's Goal: Get back on XR-NTX

<u>Plan</u>:

- Optimize non-opioid pain management
- Optimize support, follow-up
- Opioid → NTX induction when and how?
 - 1. Traditional induction:
 - > 7 day washout followed by naloxone challenged & XR-NTX induction
 - 2. What about a rapid induction?
 - Consideration: No/minimal physiologic dependence after 1-2 wks exposure; but, elevated risk return-to-use (and OD) prior to MOUD.
 - Complete morphine (half-life ~3hrs) taper, wait >5 half-lives (e.g., 24hrs) and give naloxone challenge + XR-NTX

DISCUSSION AND QUESTIONS

- What experience have you had treating patients with acute pain who are on naltrexone?
- What challenges & strategies for success have you run across (or might anticipate) for your clinic and patients?

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