

**MAT TRAINING**

**PROVIDERS' CLINICAL SUPPORT SYSTEM**  
For Medication Assisted Treatment

# The Naltrexone Conundrum: Naltrexone's Impact on Pain Management in the Perioperative Period

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## Disclosures

- Brian A. Mirante, MD has no financial relationships to disclose.

*The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.*

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- The Council on Continuing Medical Education (CCME) has been delegated authority by the AOA Board of Trustees to monitor osteopathic CME and award Category 1 and Category 2 accreditation status to osteopathic CME sponsors.
- The purpose of the AOAAM's continuing medical education program is to continually improve the quality of patient care, through the growth of knowledge, the improvement of skills, and physician-to-physician interaction.

# Designation Statement

- The American Osteopathic Academy of Addiction Medicine (AOAAM) designates this educational activity for a maximum of **1 (one) Category 2B Credit by the AOA CCME** (*pending all requirements are met*). Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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# System Requirements

- In order to complete this online module you will need Adobe Reader. To install for free click the link below:
  - <http://get.adobe.com/reader/>

# Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.



# Educational Objectives

At the conclusion of this activity participants should be able to:

- Be able to discuss the therapeutic challenges that naltrexone may pose in the treatment of acute pain
- Gain familiarity with non-opioid modalities of pain management in the perioperative period
- Learn the appropriate preoperative recommendations for a patient on naltrexone therapy presenting for elective surgery

# Naltrexone – the good...

- Discourages the use of some of the most commonly abused substances currently in the U.S.- mainly opiates and alcohol
- Offers an approach to abstinence that differs from other current therapies
- Utilizes a purely antagonistic approach, thereby foregoing the side effects of chronic opioid agonism (i.e. potential for withdrawal, constipation, tolerance, etc.)
- Extended release formulations now available may help improve patient retention in rehabilitation programs

# ... the bad...

- Imperative that a clinician does not initiate therapy in the patient recently abusing opiates, this can obviously lead to an acute withdrawal syndrome
- Side effects- occasionally nausea, depression, allergic reaction and, very rarely, liver damage (which resolves upon discontinuation of therapy)
- Potential risks include a subsequent loss of tolerance and, a potential nightmare for caregivers in the perioperative setting, difficulty in the management of...

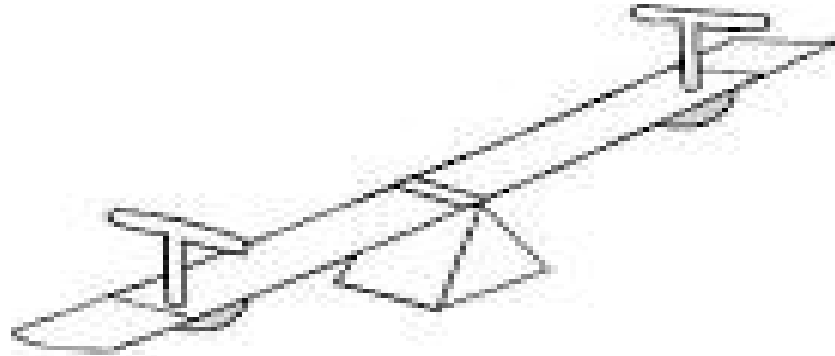
# PAIN

# Naltrexone's Effect on the Opioid Receptor

- Naltrexone is a cyclopropyl derivative of oxymorphone similar in structure to naloxone. It acts as a pure competitive antagonist at opioid receptor sites, showing the highest affinity for mu receptors.
- Clinical studies indicate that 50 mg of Naltrexone hydrochloride will block the pharmacologic effects of 25 mg of intravenously administered heroin for periods as long as 24 hours. Other data suggest that doubling the dose of Naltrexone hydrochloride provides blockade for 48 hours, and tripling the dose of Naltrexone hydrochloride provides blockade for about 72 hours.
- Great! Right?! Keep in mind that blocking the effects of heroin may be good for patients in rehabilitation... but... this also means blocking the effects of other opioids.

# Taking a ride on the see-saw

**BENEFITS**



**RISKS**

*As with every clinical scenario, the physician must weigh the risks and benefits for their individual patient*

# The Ideal Patient

- *I have a highly motivated patient that has a long history of relapsing into opioid abuse. He says “The temptation of getting a ‘high’ is too much sometimes”. He has unsuccessfully been through psychosocial treatment and complained of constipation with Methadone.*

*What about Naltrexone?*

# Naltrexone Therapy Guidelines

- Oral Naltrexone:
  - Can be started 3-6 days after last dose of short acting opiates and 7-10 days after last dose of methadone. Doses are 50 mg oral tablets Qdaily.
- XR-Naltrexone:
  - Can initiate in patients 3-4 weeks after last dose of opiates. Can be started conservatively by first giving 12.5 mg orally on the first day followed by 380 mg injection the next. Subsequent injections should be scheduled Q3-4 weeks.

# The “perfect storm”

- A patient on naltrexone that needs opiates...



# Case #1

- A 35 year old mother of 3 with a history of being a 3 year survivor of breast cancer and in active recovery from an opiate use disorder for a year. She is currently receiving monthly injections of naltrexone for medication assisted treatment of her opiate use disorder. She has been very successful and remains active in her opiate dependence recovery. Her last injection was two weeks ago. She was playing with her youngest daughter, 3 y/o, on a slide in a local park and came off the slide with her daughter in her arms landing awkwardly on her ankle. She was evaluated for the pain in her left lower extremity at the emergency department and was found to have a compound fracture of her left tibia.

*How can we treat her pain?*

# Our Options

- Nonopioid therapies:

- Acetaminophen
- NSAIDs
- NMDA antagonists  
(ex. Ketamine)
- Alpha-2 agonists  
(ex. Clonidine)
- Antispasmodics  
(ex. Baclofen)
- Antineuropathic agents  
(ex. Gabapentin)

- Nonpharmacologic therapies:

- Peripheral nerve block
- Centroneuraxial block
- Local anesthetic infiltration

# An Appropriate Pain Management Regimen for this Patient

- Left popliteal peripheral nerve catheter with an infusion of 0.2% Ropivacaine at 10 mL/hr
- Ketorlac (NSAID) 15 mg IV Q6H with Tylenol 500 mg PO Q6H

***Such a patient, as in this description, would likely have her pain completely treated in a non-opioid manner- resulting in minimal impact of naltrexone on her perioperative pain control.***

*But that isn't always the case...*

# Case #2

- A 25 year old opiate dependent male in recovery for the past 6 months was involved in a motor vehicle accident resulting in right T4-7 rib fractures, bilateral pulmonary contusions, left clavicle fracture, and a right femur fracture. He last had an injection of naltrexone one week before the accident.

***What can this patient expect in terms of pain management?***

# Case #2, *continued*

- Peripheral nerve block catheters are tremendous adjuvants to perioperative pain control, however, it is impractical to insert several different catheters for multiple injuries and furthermore, one would likely approach the toxic dose of local anesthetic.
- In order to effectively utilize a neuraxial catheter, one would likely have to use such a high dose and high dermatomal level that it would result in an apneic and comatose patient
- Low dose ketamine infusion, NSAIDs, acetaminophen and antispasmodics would all be reasonable therapies, but, would likely still insufficiently control the patient's pain...

# Case #2, *continued*

- In the event that a patient treated with long acting naltrexone experiences acute pain, nonopioid and nonpharmacologic strategies should be maximized. If the pain is severe, high doses of an opioid analgesic can overcome the naltrexone blockade of opioid receptors. However, upregulation of opioid receptors and increased receptor sensitivity is a possibility and therefore this is most safely done in a monitored setting due to the fear of a potential exaggerated response, in particular, life-threatening respiratory depression.
- **In addition to the nonopioid (NSAIDs, acetaminophen) and nonpharmacologic therapies (Right T5 paravertebral catheter, Right femoral catheter), this patient would likely require high dose narcotic in an ICU setting.**

# So, can it be done?

- Yes, but, it's kind of like going up the creek without a paddle. You'll probably make it- it will be more difficult and you'll have to use just about everything else you can think of besides a paddle... but you'll make it.



*So if I decide to put my patient on naltrexone and they end up requiring elective surgery, how can I optimally prepare them?*

# Case #3

- A 39 year old female in naltrexone rehabilitation program for history of alcohol and heroin abuse presents for a preoperative evaluation for her upcoming robotic assisted radical hysterectomy for uterine cancer.

***What are the appropriate preoperative recommendations for this patient regarding her oral naltrexone regimen?***

# Case #3, continued

- *How long does she need to be off the naltrexone before it's cleared out of her system?*
- *Oral naltrexone  $\frac{1}{2}$ -life= 14 hours. Current recommendations are to discontinue naltrexone use 72 hours before elective surgery to allow 5 half-lives to pass, resulting in elimination of nearly 98% of the drug.*
- *Injectable intramuscular naltrexone  $\frac{1}{2}$ -life=5 days, resulting in a 25 day time period for a 98% elimination of the drug.*

- \*Discontinuation of the naltrexone results in a vulnerable time for relapse (and potentially overdose) for a previously opiate dependent patient, so, close observation and care is prudent.\*

***If the surgery is elective and your patient is on IM naltrexone therapy, consider transitioning to oral therapy with discontinuation 3 days preoperatively.***

- *There is no one accepted guideline as to when to discontinue naltrexone therapy, but one must weigh the risk of relapse versus the risk of continuing therapy.*

# References

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# PCSS-MAT Mentoring Program

- PCSS-MAT Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.
- PCSS-MAT Mentors comprise a national network of trained providers with expertise in **medication-assisted treatment, addictions and clinical education.**
- Our 3-tiered mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.
- The mentoring program is available, at no cost to providers.

**For more information on requesting or becoming a mentor visit:**

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For More Information: [www.pcssmat.org](http://www.pcssmat.org)



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