Managing procedural pain in a patient taking naltrexone

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Mr. M, age 55, presents to his primary care physician (PCP) with hematochezia. Mr. M states that for the past week, he has noticed blood upon wiping after a bowel movement and is worried that he might have cancer.

Mr. M has a 10-year history of opioid use disorder as diagnosed by his psychiatrist. He is presently maintained on long-acting injectable naltrexone, 380 mg IM every 4 weeks, and has not used opioids for the past 1.5 years. Mr. M is also taking simvastatin, 40 mg, for dyslipidemia, lisinopril, 5 mg, for hypertension, and cetirizine, 5 mg as needed, for seasonal allergies.

A standard workup including a physical examination and laboratory tests are performed. Mr. M's PCP would like for him to undergo a colonoscopy to investigate the etiology of the bleeding. In consultation with both the PCP and psychiatrist, the gastroenterologist determines that the colonoscopy can be performed within 48 hours with no changes to Mr. M's medication regimen. The gastroenterologist utilizes a nonopioid, ketorolac, 30 mg IV, for pain management during the procedure. Diverticula were identified in the lower gastrointestinal tract and are treated endoscopically. Mr. M is successfully withdrawn from sedation with no adverse events or pain and continues to be in opioid remission.

Naltrexone competitively antagonizes opioid receptors with the highest affinity for the μ-opioid receptor. It is approved for treatment of alcohol and opioid dependence following opioid detoxification.[1] Its competitive inhibition at the μ-opioid receptor results in the inhibition of exogenous opioid effects. The medication is available as an orally administered tablet as well as a long-acting injection administered intramuscularly (***Table 1***,[1] ***page 47***). The long-acting injection can be useful in patients who have difficulty with adherence, because good adherence to naltrexone is required to maximize efficacy.

Due to its ability to block opioid analgesic effects, naltrexone presents a unique challenge for patients taking it who need to undergo procedures that require pain control. Pharmacologic regimens used during

Practice Points

- **Patients with opioid use disorder, and especially those receiving naltrexone, represent a unique challenge for pain control** during and after elective procedures.
- Strategies for procedural analgesia in naltrexone-treated patients include **briefly stopping the medication or using a nonopioid analgesic regimen**.
- **The use of a nonopioid analgesic agent can provide an alternative for patients receiving naltrexone**; however, multidisciplinary consultation is key for providing a regimen that is safe and effective.

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Table 1

Formulations of naltrexone

Brand	Generic	Release	Formulation	Available doses	Tmax	Half life
ReVia	Naltrexone	IR	Tablet	50 mg	1 hour	Parent: 4 hours Metabolite: 14 hours
Vivitrol	Naltrexone	ER	Powder for suspension	380 mg	First peak: 2 hours after injection Second peak: 2 to 3 days after injection	5 to 10 days

Source: Reference 1

IR: immediate release; ER: extended release; Tmax: time to peak concentration

Table 2

Nonopioid options for managing procedural pain

Nonopioid	Notes
Ketamine	Noncompetitive NMDA receptor antagonist produces analgesia. Contraindicated for use in patients with uncontrolled hypertension. Can cause neuropsychiatric effects (eg, hallucinations)
Dexmedetomidine	Selective alpha-2 agonist that produces analgesic, sedative, and anxiolytic effects. Does not cause respiratory depression. May cause bradycardia and hypotension due to sympatholytic effects
Ketorolac	Acetic acid that nonselectively inhibits cyclooxygenase, anti-inflammatory. Inhibits platelet activity and can worsen renal function. Several contraindications. Avoid in patients with renal dysfunction. IV formulation is available
Ibuprofen	Propionic acid that nonselectively inhibits cyclooxygenase, anti-inflammatory. Inhibits platelet activity and can worsen renal function. Several contraindications. IV formulation is available
Acetaminophen	Does not have antiplatelet or gastrointestinal toxicity concerns seen with NSAIDs, but hepatotoxicity is a concern. IV formulation is available

Source: References 2-5

NMDA: *N*-methyl-D-aspartate; NSAIDs: nonsteroidal anti-inflammatory drugs

procedures often contain a sedative agent, such as propofol, and an opioid for analgesia. Alternative strategies are needed for patients taking naltrexone who require an opioid analgesic agent for procedures such as colonoscopies.

One strategy could be to withhold naltrexone before the procedure to ensure that the medication will not compete with the opioid agent to relieve pain. This strategy depends on the urgency of the procedure, the formulation of naltrexone being used, and patient-specific factors that may increase the risk for adverse events. For a non-urgent, elective procedure, it may be acceptable to hold oral naltrexone approximately 72 hours before the procedure. However, this is likely not a favorable approach for patients who may be at high risk for relapse or for patients who are receiving the long-acting formulation. Additionally, the use of an opioid agent intra- or post-operatively for pain may increase the risk of relapse. The use of opioids for such procedures may also be more difficult in a patient with a history of opioid abuse or dependence because he or she may have developed tolerance to opioids. Conversely, if a patient has been treated with

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Related Resources

- American Society of Anesthesiologists. Standards guidelines and related resources. https://www.asahq.org/quality-and-practice-management/standards-guidelines-and-related-resources-search.
- American Society of Addiction Medicine. Clinical resources. https://www.asam.org/resources/guidelines-and-consensus-documents.

Drug Brand Names

Acetaminophen • Tylenol
Cetirizine • Zyrtec
Dexmedetomidine • Precedex
Ibuprofen • Caldolor (IV), Motrin (oral)
Ketamine • Ketalar
Ketorolac • Toradol
Lisinopril • Prinivil, Zestril
Naltrexone • ReVia, Vivitrol
Propofol • Diprivan
Simvastatin • Juvisync, Simcor

Clinical Point

Nonopioid regimens might include ketamine, dexmedetomidine, an NSAID, or acetaminophen

naltrexone for an extended period, a lack of tolerance may increase the risk of respiratory depression with opioid administration due to upregulation of the opioid receptor.[2]

Nonopioid analgesic agents

For a patient receiving naltrexone who needs to undergo a procedure, a multidisciplinary consultation between the patient's psychiatrist and other clinicians is key for providing a regimen that is safe and effective. A nonopioid analgesic agent may be considered to avoid the problematic interactions possible in these patients (***Table 2***,[3-5] ***page 47***). Nonopioid regimens can be utilized alone or in combination, and may include the following[3-5]:

Ketamine is a non-competitive antagonist at the *N*-methyl-D-aspartate receptor that can provide sedation and analgesia with a rapid onset and short duration of action. However, analgesics should still be used for patients undergoing procedures that might cause visceral pain. Ketamine is contraindicated for patients with uncontrolled hypertension.

Dexmedetomidine is an alpha-2 agonist that can provide sedative and analgesic effects. It can cause procedural hypotension and bradycardia, so caution is advised in patients with cardiac disease and hepatic and/or renal insufficiencies.

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or ketorolac, inhibit cyclooxygenase enzymes and can be considered in analgesic regimens. However, for most surgical procedures, the increased risk of bleeding due to platelet inhibition is a concern.

Acetaminophen. Although its full mechanism of action has not been discovered, acetaminophen may also act on the cyclooxygenase pathway to produce analgesia. Compared with the oral formulation, IV acetaminophen is more expensive but may offer certain advantages, including faster plasma peak levels and lower production of acetaminophen's toxic metabolite, N-acetyl-p-benzoquinone imine. Nonetheless, hepatotoxicity and overdose remain a concern.

The use of nonopioid analgesics during elective procedures that require pain control will allow continued use of an opioid antagonist such as naltrexone, while minimizing the risk for withdrawal or relapse. Their use must be evaluated on a case-by-case basis to ensure maximum safety and efficacy for each patient from both a medical and psychiatric standpoint. Overall, with the proper expertise and consultation, nonopioid pain regimens represent a reasonable alternative to opiates for patients who take naltrexone.

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