

Background

- Naltrexone is an opioid antagonist approved for opioid-use disorder and alcohol-use disorder (AUD).¹
- Naltrexone is prescribed either as a daily oral medication or as a monthly long-acting injectable.²
- Long-acting injectable naltrexone was developed to improve adherence to the medication as the therapeutic plasma concentration is maintained for 4 weeks.³
- The consensus on management of IM naltrexone for AUD in the perioperative period is to defer elective surgery until twenty-eight days after administration of intramuscular naltrexone.⁴
- Cessation of naltrexone may not always be feasible for emergent or time-sensitive surgeries.
- Upon literature review, there were no reports on the perioperative management of patients who were within three weeks long-acting naltrexone dosing.

Purpose

This case report demonstrates the challenges of perioperative analgesic management for a patient who underwent major abdominal surgery within the therapeutic window of his long-acting injectable naltrexone. It also highlights sufentanil's ability to potentially displace naltrexone at the μ -opioid receptor as a rescue therapy that bridged the patient until a definitive regional technique could be performed.

Case Report

- Patient is a 50-year-old male with a past medical history of recurrent pancreatitis, type 1 diabetes mellitus, hypertension, GERD, and AUD.
- He is in recovery for AUD, maintained on naltrexone therapy via intramuscular (IM) microsphere long-acting injectable (LAI) of 380 mg every 4 weeks.
- Patient was scheduled for an elective distal pancreatectomy and splenectomy for recurrent episodes of pancreatitis.
- The patient was seen 2 weeks prior to surgery by perioperative optimization via telehealth at which time continuation of naltrexone was recommended in the perioperative period, and he received his scheduled dose of long-active IM naltrexone on the day prior to surgery.
- This case occurred in a large academic center located in Philadelphia, Pennsylvania.
- Patient informed consent obtained.

Perioperative Patient Management

Intra-op

Medication	Total dose
Midazolam	2 mg IV
Fentanyl	700 mcg IV
Hydromorphone	4 mg IV

Post Anesthesia Care Unit

Medication	Total dose
Hydromorphone	0.5mg q5min (3 mg IV)
Ketamine	25 mg/hr (0.32 mg/kg/hr) IV
Lidocaine	2 mg/min (1.56 mg/kg/hr) IV
Gabapentin	300mg every 8 hours PO
Acetaminophen	1000mg every 6 hours IV



Pain remains 10/10 with severe functional limitations

Post-Op Day 1

Medication	Total Dose
Sufentanil	10 mcg IV



Pain improved to 5/10 with improvement in function and ability to tolerate nursing care

Medication	Total dose
Sufentanil	10 mcg IV
Bilateral Ropivacaine 0.2% (perineural)	8 ml/hr



Pain further improved to 2/10

Discussion & Conclusion

- In the setting of opioid receptor antagonism, fentanyl (700 mcg) and hydromorphone (7 mg) showed negligible clinical effect.
- Implementation of multimodal analgesia included ketamine infusion, lidocaine infusion, intravenous acetaminophen and oral gabapentin also did not provide satisfactory analgesia.
- Bilateral erector spinae plane (ESP) catheters were deemed to be an appropriate regional technique; however, it was felt the patient would not be able to tolerate positioning for catheter placement due to the severity of the patient's pain.
- Sufentanil was trialed as a rescue therapy because of its high binding affinity to the μ -opioid receptor as demonstrated by Volpe et al. (Table 1).⁵
- Patient reported subjective improvement in pain score after initial dosing with sufentanil and ability to tolerate positioning for ESP catheters
- Based on the improvement in analgesia, sufentanil may displace naltrexone from the opioid receptor at modest doses.
- This case study shows that sufentanil is a reasonable opioid for rescue administration in patients under therapeutic μ -opioid receptor blockade with naltrexone.
- While Volpe did not include antagonists in his comparison of opioid binding affinities, sufentanil has the highest binding affinity as would be the best candidate to compete with the binding of an antagonist.
- Further investigation including the comparative binding of agonists and antagonists is warranted.

Medication	μ -Opioid Receptor Equilibrium Dissociation Constant (K_i)
Tramadol	12,486
Fentanyl	1.346
Hydromorphone	0.3654
Buprenorphine	0.2157
Sufentanil	0.1382

Table 1: A selection of the calculated equilibrium dissociation constants of various opioid medications with the μ -opioid receptor, published by Volpe et al.⁵

References

- Center for Substance Abuse Treatment. Incorporating Alcohol Pharmacotherapies Into Medical Practice. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2009. (Treatment Improvement Protocol (TIP) Series, No. 49.) Chapter 4—Oral Naltrexone. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK64042/>
- Singh D, Saadabadi A. Naltrexone. [Updated 2023 May 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534811/>
- Center for Substance Abuse Treatment. Incorporating Alcohol Pharmacotherapies Into Medical Practice. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2009. (Treatment Improvement Protocol (TIP) Series, No. 49.) Chapter 5—Extended-Release Injectable Naltrexone. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK64031/>
- Goel A, Kapoor B, Wu M, et al. Perioperative Naltrexone Management: A Scoping Review by the Perioperative Pain and Addiction Interdisciplinary Network. *Anesthesiology*. 2024;141(2):388-399. doi:10.1097/ALN.0000000000005040
- Volpe DA, McMahon Tobin GA, Mellon RD, et al. Uniform assessment and ranking of opioid μ receptor binding constants for selected opioid drugs. *Regul Toxicol Pharmacol*. 2011;59(3):385-390. doi:10.1016/j.yrtph.2010.12.007