Buprenorphine for Naltrexone-XR-Precipitated Opioid Withdrawal Syndrome

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INTRODUCTION

- Naltrexone is a μ-opioid antagonist which is FDA-approved to treat alcohol use disorder (AUD) and opioid use disorder (OUD)
- It can precipitate opioid withdrawal syndrome (OWS) in patients with opioid dependence if administered too soon after a full opioid agonist
- Optimal treatment of naltrexone-XR-precipitated OWS is not well-established
- Some case reports suggest buprenorphine can improve symptoms in cases of naltrexone- or naloxone-precipitated OWS; data is more limited naltrexone-XR-precipitated OWS as well as tolerance maintained by a long-acting full opioid agonist such as methadone
- This case describes a patient who was maintained on methadone for OUD and was given injectable naltrexone-XR for AUD. He was treated with buprenorphine with notable improvement in symptoms.

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CASE

- A 61-year-old male with a PMH of COPD, DM2, depression, tobacco use disorder, OUD (three bags daily, no IV use), and AUD presented to the ED for 1 day of chills and rhinorrhea
- He went to his PCP 1 day ago, where he received naltrexone-XR for AUD. ~1 hour later, he developed subjective fever, chills, rhinorrhea, and diarrhea. He had taken methadone 100mg that morning.
- Initial ED vital signs: BP 137/84, T 99.7 F, HR 112, RR 22, O2 sat 100% on RA
- He was offered buprenorphine, but he declined. He was instead given methadone 30mg PO, hydromorphone 6mg IV, ondansetron 4mg IV, loperamide 4mg PO, oxycodone IR 30mg PO, oxycodone ER 60mg PO, hydromorphone 10mg IV, diazepam 10mg IV, and 1L of LR. He was admitted for further care.
- Addiction medicine was consulted on day 2. He had persistent signs of OWS, though he was overall improved from initial presentation. He was started buprenorphine-naloxone 8-2mg SL three times daily.
- He felt significantly improved on day 3. He was amenable to continuing buprenorphine-naloxone for at least 1 month. His long-term plan was to return to methadone treatment.
- On day 4, he was discharged in good condition with no symptoms of opioid withdrawal. He filled a buprenorphine-naloxone prescription at discharge.

CONCLUSION

- Naltrexone is a full competitive antagonist of the μ-opioid receptor with a high binding affinity, allowing it to displace full agonists already occupying the μ-opioid receptors and to outcompete additional full agonists administered
- In this case, naltrexone displaced methadone molecules occupying the μ-opioid receptors, causing sudden and severe onset of OWS
- The patient had incomplete relief of symptoms with subsequent doses of methadone, oxycodone, and hydromorphone
- Buprenorphine is a partial μ-opioid agonist with a very high binding affinity. It can displace both full antagonists and agonists at the μ-opioid receptor.
- OWS symptoms were completely resolved after administration of buprenorphine-naloxone in this case. The pharmacologic properties of buprenorphine make it a good option for managing naltrexone-XR-precipitated OWS.

Opioid	Ki (Binding Affinity)
Buprenorphine	0.22
Naltrexone	0.29
Hydromorphone	0.37
Methadone	3.38
Oxycodone	25.87