

High dose buprenorphine induction precipitating non-cardiogenic pulmonary edema requiring intubation



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Background & Introduction

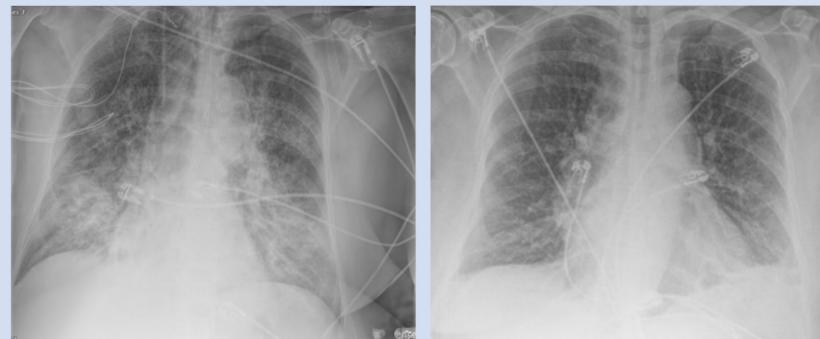
- In the era of high-potency synthetic opioids, there is growing interest in the high-dose buprenorphine initiation (HDBI) protocol [1,2].
- HDBI utilizes buprenorphine's increased mu-opioid receptor activation at high doses (beyond 8mg sublingual) to provide relief of withdrawal symptoms. However, data supporting the safety and efficacy of HDBI remains limited.
- Here, we present a case where a HDBI protocol precipitated withdrawal and culminated in severe respiratory distress requiring intubation.

Case Description

- JJ is a 52yo caregiver with mild COPD admitted for a fever to 105F in the context of injection fentanyl use.
 - severe opioid use disorder (OUD): previously on buprenorphine and methadone, 10g intranasal and injection use daily
 - moderate benzodiazepine use disorder: 4-5mg non-prescribed clonazepam daily
- JJ's goals: achieve recovery through a transition to buprenorphine and return home quickly to care for her partner.
- Medications for OUD history:
 - Buprenorphine: assisted 3 years of remission
 - Methadone: inflexibility of dosing previously interfered with caregiving capacity
- Indications for HDBI with short-acting agonist bridge:
 - strong preference for an expedited transition to buprenorphine
 - strong fear of precipitated withdrawal from traditional and low-dose buprenorphine induction protocols based on prior experiences
 - explicit avoidance of methadone for withdrawal management, with worries about self-directed discharge if temporarily feeling well enough on methadone
- We held a PARQ (Procedure, Alternative, Risk, Question) conference and pursued a high-dose buprenorphine induction with JJ's informed consent.

KEY FINDINGS

- Consider the diagnosis of non-cardiogenic pulmonary edema, along with early initiation of diuretic therapy and positive pressure ventilation, for management of respiratory distress in an opioid overdose or withdrawal.
- Shared decision-making is key when considering novel buprenorphine induction protocols.



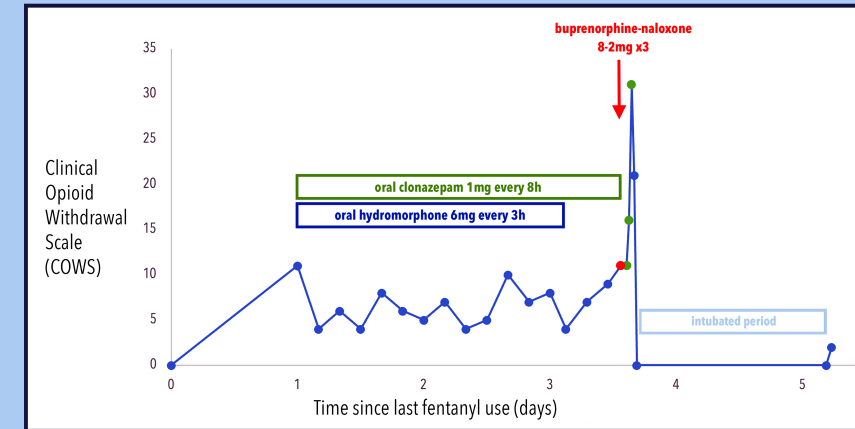
Chest radiography revealed new pulmonary edema.



References:

- Herring, A. A. et al (2021). High-dose buprenorphine induction in the emergency department for treatment of opioid use disorder. JAMA Network Open, 4(7), e2117128. doi:10.1001/jamanetworkopen.2021.17128
- Weimer, M. B. et al (2023). ASAM clinical considerations: Buprenorphine treatment of opioid use disorder for individuals using high-potency synthetic opioids. Journal of Addiction Medicine. doi:10.1097/ADM.0000000000001202
- Winkhofer, S. et al (2014). Post-mortem whole body computed tomography of opioid (heroin and methadone) fatalities: frequent findings and comparison to autopsy. European Radiology, 24(6), 1276-1282. doi:10.1007/s00330-014-3128-7
- Faikas, A. et al (2020). Pulmonary complications of opioid overdose treated with naloxone. Annals of Emergency Medicine, 75(1), 39-48. doi:10.1016/j.annemergmed.2019.04.006
- Sporer, K. A. et al (2001). Heroin-related noncardiogenic pulmonary edema. Chest, 120(5), 1628-1632. doi:10.1378/chest.120.5.1628

Timeline of High Dose Buprenorphine Induction



Case Follow Up

- Buprenorphine, repeat attempt: low-dose protocol with belbuca 225mcg every 8 hours. After 24h, she shared significant anxiety associated with buprenorphine uptitration and decided to pursue methadone.
- Methadone: 80mg (day 1), 100mg (day 2), 100mg (day 3, discharge)

Discussion

- This case highlights a rare, adverse reaction of HDBI. Pulmonary edema has been associated with a majority of fatal opioid overdoses [3]. Non-cardiogenic pulmonary edema has been associated with heroin and naloxone, each with incompletely defined pathophysiology [4,5].
- Pathophysiology: Naloxone is proposed to trigger an adrenergic crisis, increasing pulmonary vasculature permeability; this mechanism might be presumed of HDBI-associated precipitated withdrawal.
- DDx: While more specific imaging such as a cardiac MRI is needed to definitively exclude a HFpEF diagnosis, echocardiography did not reveal a cardiac cause of fulminant pulmonary edema.