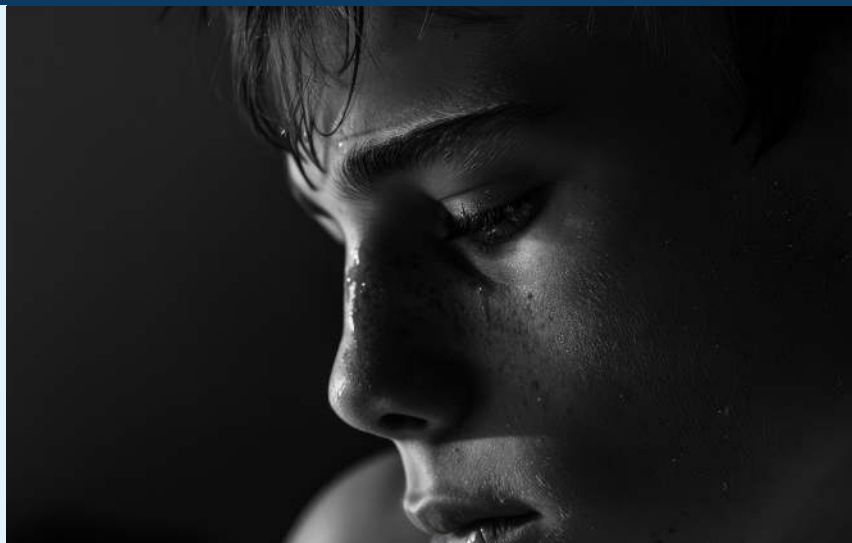


Defining Precipitated Withdrawal

Precipitated withdrawal is characterized by the rapid onset of opioid withdrawal symptoms immediately following administration or ingestion of a partial opioid agonist or opioid antagonist in opioid dependent individuals. These symptoms can include myalgia, nausea, vomiting, diarrhea, abdominal cramps, yawning, agitation, restlessness, rhinorrhea/lacrimation, piloerection and mydriasis. This is seen when MOUD transition with partial agonist or antagonist is initiated too soon after last opioid use and is considered an adverse outcome for buprenorphine induction.

The adulteration of the drug supply with fentanyl has made it increasingly challenging to initiate buprenorphine therapy due to its unique pharmacological properties. Fentanyl is a highly potent synthetic opioid that binds strongly to the opioid receptors. When transitioning to buprenorphine, which is a partial opioid agonist with a higher affinity for receptors, it displaces fentanyl from the receptors. This displacement triggers sudden and severe withdrawal symptoms. Additionally, because fentanyl is fat-soluble, it is stored in fatty tissues and can be released slowly over time, making it difficult to predict when a person is in the appropriate stage of withdrawal to safely administer buprenorphine.

Additionally, when transitioning from methadone to buprenorphine products there is also a higher likelihood of a patient experiencing precipitated withdrawal symptoms due to methadone being a full opioid agonist. Likewise, patients should be advised to be abstinent from all full or partial opioid agonists for 7-10 days prior to starting naltrexone.



How to Avoid Precipitated Withdrawal

The Clinical Opiate Withdrawal Scale (COWS) is a validated tool for assessing opioid withdrawal severity. Prior to instituting this assessment tool, the patient must be physically dependent on opioids and determined to be in opioid withdrawal. It is essential to delay the initiation of buprenorphine until the patient reaches a moderate (13-24) to severe (25 or higher) withdrawal score on the COWS.

It may be helpful to complete the COWS assessment with the patient at the practice to assess withdrawal and use as a baseline for the patient to gauge the severity of their symptoms they may experience as time passes.

Initiation of buprenorphine should be delayed for at least **24 hours from last use of fentanyl and 36-48 hours from last use of methadone** to reduce the risk of precipitated withdrawal. Patients should be counseled not to take their first dose of buprenorphine until they are in moderate to severe withdrawal and the symptoms are no longer tolerable.

Precipitated withdrawal can also happen when initiating naltrexone for Opioid Use Disorder (OUD), which is why the patient should be completely abstinent from any opioids or MOUD for a minimum of 7 days.

Treating Precipitated Withdrawal

Once it has been identified that a patient is experiencing precipitated withdrawal, there are three ways to treat them:

1. Aggressively increasing the dosage of buprenorphine

- Repeated 4-8mg doses of buprenorphine every 15-30 minutes
- Clonidine 0.1 mg every 8 hours (caution regarding hypotension)
- Antiemetics for nausea
- NSAIDs to treat joint and muscle pain

2. Abandoning buprenorphine treatment and reverting to treatment with full opioid agonists (treating with opioids)

3. Reassurance and symptomatic medication

(not advised due to minimal effectiveness and risk of overdose)

REFERENCES

- Martin, S. A., Chiodo, L. M., Bosse, J. D., & Wilson, A. (2021). The next stage of buprenorphine care for opioid use disorder. *PubMed Central (PMC)*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8248003/>
- Casadonte, P. (2021). *Guidance for buprenorphine induction*. PCSS. <https://pcssnow.org/wp-content/uploads/2021/12/PCSS-GuidanceBuprenorphineInduction.Casadonte.pdf>
- Rastegar, D. A. (2020, December 28). *Fentanyl and norfentanyl detected in urine for 7 or more days after regular use*. Alcohol, Other Drugs, and Health: Current Evidence. <https://www.bu.edu/aodhealth/2020/12/28/fentanyl-and-norfentanyl-detected-in-urine-for-7-or-more-days-after-regular-use/>