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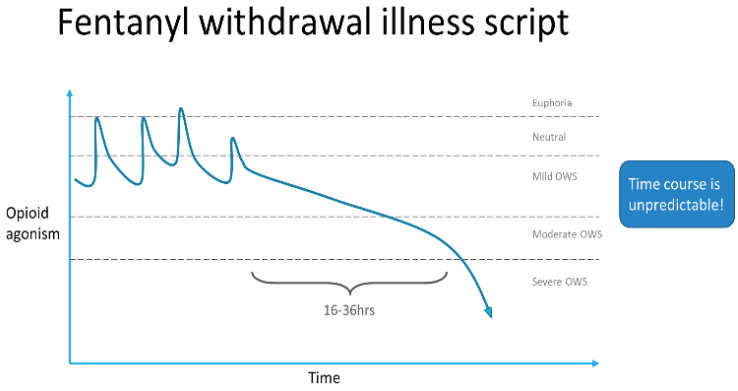
Treating Opioid Withdrawal In the Fentanyl Era: Inpatient Fundamentals

Context[1,2]: Fentanyl is 50X stronger than heroin, stigma is common, patients with SUD are 15-20X more likely to direct their own discharge, and in hospital medication for OUD lowers this risk



Current: Partner around shared goals, assess substance history, use of other substances: stimulant, nicotine, alcohol

Cutting Edge: COWS used to measure opioid withdrawl, but does not include cravings, which is often the most bothersome symptom and may lead to in-hospital substance use and patient directed discharge. Don't forget that newer drugs like xylazine (alpha-2 agonist, adulterant) – refractory agitation and anxiety, ulcerated wounds

Overview of Withdrawal[1,2]

Context: underestimation of opioid requirements in setting of fentanyl use disorder; physical/psychological trauma; Very high COWS: benzos/alcohol withdrawal or acute medical illness (sepsis)

Current: Recognize and assess for medical illness, concurrent withdrawal from other substances, self-treatment of opioid withdrawal (in-hospital use)

Cutting edge: Fentanyl is lipophilic, builds up in adipose tissue, causing a depot effect. Withdrawal kinetics similar to a long-acting opioid, such as methadone. Caution with traditional buprenorphine initiation for this reason.

How do you treat Fentanyl Withdrawal?

Day 1	• Methadone 20-30mg • 5-10mg of methadone q4 prn opioid withdrawal or cravings	40 mg maximum dose on day 1
Day 2	• Methadone total day 1 dose • 5-10mg of methadone q4 prn opioid withdrawal or cravings	50 mg maximum dose on day 2
Day 3	• Methadone total day 2 dose • 5-10mg of methadone q4 prn opioid withdrawal or cravings	60 mg maximum dose on day 3
Day 4 and beyond	Uptitrate until patient reaches 60mg or stop at a lower dose based on patient symptoms.	After 60, wait 3-5 days until methadone reaches steady state
Almost all patients need additional prn opioids		

Context: Non-Opioid Adjuncts, Methadone, Buprenorphine, Short Acting Opioid Agonists.

Current: Non-Opioid Adjuncts: clonidine, hydroxyzine, ondansetron, loperamide, APAP, NSAIDs, trazodone – not enough alone. Underlying pathophysiology of opioid withdrawal means opioids necessary unless the patient does not want them

Methadone[3]: start 20-30 mg daily in setting of fentanyl use disorder, add 5-10 mg prn q4h for withdrawal or cravings, monitor for dose stacking, drawback: delayed time to effect and achieving therapeutic dose, at 60 mg wait 3-5 days until steady state, give additional prn opioids, taper short acting opioids once cravings/withdrawal improved (methadone doses ~60-100mg)

Buprenorphine[4,5]: microinduction preferred, standard high dose (macro dose) may need higher COWS, withdrawal may start at 48-72h due to fentanyl's long half-life. For microinduction: cross titrate with full agonists, but stop/taper them once > 8 mg bup in 24 hour period

Short-acting opioids [6,7]: rapidly treat withdrawal and pain, relieves suffering but can't be used for OUD/withdrawal outside hospital, if appropriate restart with lower doses and titrate up: IV hydromorphone 2 mg q2h, PO oxycodone 20 mg q3h; consider this if severe pain and high tolerance

Cutting Edge: For fentanyl use, titrate methadone as quickly as you can based on your institution
Treat Xylazine withdrawal with clonidine, tizanidine, dexmetomidine.
Consider low-dose buprenorphine ("micro-dose") titration in the hospital, patients will be more comfortable but requires overlap with full agonists, especially if acute pain.

References: 1, Martin, M et al.. Jof Addiction Medicine 2023, 2 Englander H, et al. J Hosp Med. 2020, 3. Buresh M et al. JSAT 2022. 4 Ghosh, S et al Can J Addiction Medicine 2019, 5 Klaire, S et al. Am J on Addictions 2019, 6Thakrar AP, JAMA IM 2022. 7 Kleinman RA, Ann Intern Med 2021.