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Ambulatory detoxification in alcohol use disorder and opioid use disorder

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Abstract

Ambulatory detoxification in alcohol use disorder and opioid use disorder is an important component in the management of patients experiencing withdrawal symptoms from alcohol or opioids. The goal of withdrawal management is ultimately to provide each patient with comfort and safety. Having the knowledge of the possible signs and symptoms of intoxication and withdrawal assists providers to institute the most appropriate treatment protocol and setting for the patient. Pharmacists play a vital role in choosing appropriate therapeutic management options for common or complex clinical situations involving ambulatory detoxification from alcohol and opioids. Ambulatory detoxification serves as an appealing option to many patients and helps save the limited inpatient resources that many institutions have for those patients with more severe withdrawal presentations.

Keywords: detoxification, alcohol use disorder, opioid use disorder

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Introduction

The 2018 National Survey on Drug Use and Health (NSDUH) estimated that 16.6 million people (or 6.1% of the US population) were heavy users of alcohol in the past month.[1] This same 2018 NSDUH survey estimated that 10.3 million people (or 3.1% of the US population) aged 12 or older misused opioids in the past year.[1] Many of these individuals using alcohol or opioids may require detoxification to prevent withdrawal symptoms when discontinuing use. Detoxification from substances is a set of interventions intended to manage acute intoxication and withdrawal with the goal of reducing the physical harm and adverse effects caused by the abuse of substances.[2] The Center for Substance Abuse Treatment consensus panel that developed "Detoxification and Substance Abuse Treatment: A Treatment Improvement Protocol" (TIP 45) recommends detoxification from alcohol, opioids, and sedative hypnotics be conducted in a hospital setting.[2] This option is often not available due to a lack of available inpatient beds and is typically reserved for the most severe cases of substance withdrawal. For patients who cannot undergo detoxification in a hospital setting, it is recommended that a setting with nursing and medical backup (24 hours, 7 d/wk) be utilized. Utilization of proper assessment/evaluation, stabilization, and fostering the patient's entry into treatment are the essential components of detoxification. Standards on determining the optimal care setting that matches the patient's needs and personal characteristics have been developed by the American Society of Addiction Medicine (ASAM)[3]:

Take Home Points:

1. Knowledge of the signs and symptoms of alcohol and opioid intoxication and withdrawal allows clinicians to effectively manage these situations and determine whether ambulatory detoxification is appropriate.
2. Ambulatory detoxification for mild-to-moderate alcohol withdrawal can be effectively and safely carried out with benzodiazepine and nonbenzodiazepine protocols for patients experiencing adverse effects from cessation of alcohol.
3. Ambulatory detoxification of opioid withdrawal can be safely conducted with methadone, buprenorphine/naloxone, clonidine, guanfacine, and/or lofexidine. The level of support, maintenance medication(s) for opioid use disorder, and treatment programs available to the clinician treating the withdrawal symptoms may influence treatment choices.

1. Level I-D: Ambulatory detoxification without extended onsite monitoring
2. Level II-D: Ambulatory detoxification with extended onsite monitoring
3. Level II.2D: Clinically managed residential detoxification
4. Level III.7D: Medically monitored inpatient detoxification
5. Level IV-D: Medically managed intensive inpatient detoxification

Many patients with mild-to-moderate withdrawal symptoms seeking detoxification can be safely managed on an outpatient/ambulatory basis.[4] Level I-D ambulatory detoxification is an organized outpatient service, which is monitored at predetermined intervals.[2] Level II-D ambulatory detoxification consists of extended onsite monitoring by licensed and credentialed staff.[2] This review focuses on ambulatory detoxification of alcohol and opioids (Levels I-D and II-D).

Considerations in Determining Ambulatory Detoxification

When determining if ambulatory detoxification is the optimal treatment setting, the treatment team must consider both the psychosocial and biomedical characteristics of each patient on a case-by-case basis when they present with substance use issues needing possible detoxification. Practitioners in all settings need to be vigilant of substance abuse and the impact it may have on medical or psychiatric issues. It is imperative that a detailed history and assessment of the patient's current symptoms be completed. A patient may present with mild withdrawal symptoms, which could easily be addressed in an ambulatory care setting, but psychosocial issues, such as homelessness, lack of transportation, risk of violence, or inability to properly follow routine medical instructions, may prevent an ambulatory detoxification from being effectively carried out.[2] Withdrawal symptoms can be highly unpredictable, but a detailed history of previous withdrawal symptoms can inform the clinician's treatment decisions.

Ambulatory Detoxification in Alcohol Use Disorder

Detoxification from alcohol in an ambulatory care setting provides increased access to care for patients who may have barriers to hospitalization, such as lack of insurance, money to pay for an inpatient hospitalization, lack of available inpatient hospital beds to conduct detoxification, or patient preference, and who may, otherwise, go through withdrawal with no assistance at all. Ambulatory detoxification from alcohol also has associated risks, which need to be considered. The unpredictable nature of alcohol withdrawal poses the greatest risk. Severe withdrawal symptoms, such as seizures and delirium, may emerge, are very difficult to adequately manage in an ambulatory setting, and can be life threatening if not properly addressed. Risk mitigation of severe alcohol withdrawal symptoms is best addressed through assessment and identification of those patients at higher risk for these symptoms.

The first step in determining the appropriateness of ambulatory detoxification in alcohol use disorder is recognizing the clinical presentation of alcohol intoxication and withdrawal. The TIP 45 manual has detailed information on blood alcohol levels and corresponding clinical presentation likely to be encountered although tolerance may mask the true level of intoxication in chronic users.[2] (See Table 1.) Obtaining either a blood alcohol level (typically emergency department or hospital settings) or breath alcohol level (outpatient setting if the patient is cooperative) along with clinical observation of both signs of intoxication and withdrawal dictate the course of action for the patient's needs. If the patient is intoxicated, the best practice is to ensure patient safety while monitoring and treating the patient's intoxication symptoms and potential withdrawal. Alcohol clearance/elimination is often 10 to 30 mg percentage per hour, and in ideal circumstances, the patient should be monitored until no longer intoxicated and able to participate in the evaluation. Higher blood alcohol levels typically lead to higher levels of care necessary to safely manage the symptoms of alcohol intoxication.

TABLE 1: Symptoms of alcohol intoxication[a,b]

Blood Alcohol Level (Blood Alcohol Content), mg[c]	Clinical Presentation
20% to 100% (0.02 to 0.1)	Mood and behavioral changes Reduced coordination Impairment of ability to drive a car or operate machinery
101% to 200% (0.101 to 0.2)	Reduced coordination of most activities Speech impairment Trouble walking General impairment of thinking and judgment
201% to 300% (0.201 to 0.3)	Marked impairment of thinking, memory, and coordination Marked reduction in level of alertness Memory blackouts Nausea and vomiting
301% to 400% (0.301 to 0.4)	Worsening of above symptoms with reduction of body temperature and blood pressure Excessive sleepiness Amnesia
401% to 800% (0.401 to 0.8)	Difficulty waking the patient (coma) Serious decreases in pulse, temperature, blood pressure, and rate of breathing Urinary and bowel incontinence Death

[a]Adapted from TIP 45 (Consensus Panelist Robert Malcolm, MD).[2]

[b]Varies greatly with patient alcohol tolerance level (chronic users may show fewer symptoms at higher levels of alcohol).

[c]Blood alcohol content equal to or above 0.08 exceeds the limit to safely operate a motorized vehicle in the United States (except Utah is 0.05).

Symptoms of acute alcohol withdrawal typically presents within 6 to 24 hours after the patient's last drink of alcohol.[2] (See Table 2.) Alcohol withdrawal symptoms should always be considered along with the patient's age, comorbidity status (medical and psychiatric), general health status, and nutritional status as each of these factors may increase the severity of a patient's alcohol withdrawal symptoms and may preclude ambulatory detoxification. If withdrawal symptoms emerge while detectible blood alcohol levels are present, this may be indicative of a more severe course of withdrawal symptoms. The most common scale/instrument utilized to assess acute alcohol withdrawal symptoms is the Clinical Institute Withdrawal Assessment for Alcohol scale-revised (CIWA-Ar).[5] This is a 10-item instrument with a range of 0 to 67 and takes less than 5 minutes to administer by a trained clinician. It examines patient symptoms of nausea and vomiting, tremor, paroxysmal sweats, anxiety, tactile disturbances, auditory disturbances, visual disturbances, headache (fullness in head), agitation, and orientation and clouding of sensorium on a 0 (*no symptoms*) to 7 (*most severe*) scale. With a total score of 10 or less, a patient typically does not need medication to assist with withdrawal symptoms. Programs conducting ambulatory detoxification most often utilize a score of 15 or less (very mild to mild withdrawal symptoms) as their cutoff to safely conduct detoxification on an ambulatory basis. Presence of lifetime history of severe withdrawal symptoms, such as delirium tremens, hallucinations, or seizures, most often lead to exclusion of ambulatory detoxification because individuals with these histories are at a higher risk of having severe symptoms again with subsequent detoxifications. Medical issues, such as melena, hematochezia, or hematemesis, could be potentially life threatening and would require further testing in an inpatient setting.

TABLE 2: Symptoms of alcohol withdrawal

Restlessness, irritability, anxiety, agitation
Anorexia (lack of appetite), nausea, vomiting
Tremor (shakiness), elevated heart rate, increased blood pressure
Insomnia, intense dreaming, nightmares
Poor concentration, impaired memory and judgment
Increased sensitivity to sound, light, and tactile sensations
Hallucinations (auditory, visual, or tactile)
Delusions, usually paranoid or persecutory
Grand mal seizures
Hyperthermia
Delirium with disorientation to time, place, person, and situation; fluctuations in level of consciousness

Case 1: Ambulatory Alcohol Detoxification

A.G. is a 37-year-old patient with a 12-year alcohol use disorder history. A.G. presented to a walk-in mental health clinic accompanied by the patient's spouse requesting alcohol detoxification. A.G. reported drinking 3 beers approximately 7 hours ago. Breath alcohol level read

TABLE 3: Comparison of benzodiazepines used in alcohol withdrawal[7,8]

Benzodiazepine	Peak Onset of Action, Oral, h	Half-Life Parent, h	Half-Life Active Metabolite, h	Oral Equivalent Doses, mg	Dosing Range, mg/d	Advantages of Use
Long-acting						
Chlordiazepoxide	0.5 to 2	24 to 48	14 to 95	25	Max 200 tapered down	Smooth course of treatment, decreased risk of rebound symptoms, less need for gradual tapers
Diazepam	0.25 to 2.5	44 to 48	100	5	Max 40 tapered down	
Intermediate-acting						
Lorazepam	0.5 to 2	12 to 14	. . .	1	Max 8 tapered down	Safer in liver dysfunction and those at high risk of medical issues with sedation (severe lung disease, elderly), lack of drug accumulation/active metabolites
Oxazepam	2 to 3	6 to 11	. . .	15	Max 120 tapered down	

0.00%, and A.G. appeared mildly irritable, mildly to moderately anxious, and restless. Physical exam indicated blood pressure was 138/87 mm Hg, pulse 98 beats/min, temperature of 98.2°F, mild hand tremor with arm extension, sweaty palms and feeling "clammy", sensitivity to light and sound, mild headache, and moderate nausea with no vomiting. A.G. denied any history of or current hallucinations; any melena, hematochezia, hematemesis, disorientation; or signs or symptoms of delirium tremens. A CIWA-Ar was conducted, and A.G.'s total score was 12. A.G. denied assistance with detoxification from alcohol in the past. A.G. reported working full time as a welder and owned own house. A.G.'s spouse reported the drinking had begun to impact their home life. A.G. drank daily, typically 6 to 10 beers a night after work. A.G. reported the longest time of abstinence/sobriety over the last 12 years was about 5 years ago for a period of 2.5 years. The patient noticed the drinking had been affecting work quality and feared it may result in job loss if it continued. There was a history of hypertension and A.G. took lisinopril 10 mg daily for the past 5 years with good control of blood pressure despite continued drinking. A.G. was also prescribed sertraline 50 mg daily for depression for the past 3 years with partial resolution of depressive symptoms. A.G. was interested in doing outpatient groups as A.G. did not feel "I can do it on my own". A.G. reported being able to come in again the next day for an additional follow-up appointment if necessary. Additionally there were reports of cravings and urges for alcohol when the patient got off from work, and these cravings and urges worsened if A.G. did not drink.

Treatment Considerations in Ambulatory Alcohol Detoxification

Benzodiazepines remain the medication of choice for treating alcohol withdrawal.[2] Those benzodiazepines studied (diazepam, chlordiazepoxide, lorazepam, oxazepam) are equally effective and superior to placebo.[6] (See Table 3.[7,8]) A variety of approaches to benzodiazepine administration have been employed depending on the desired treatment setting and resources available. The first method is a loading dose of a benzodiazepine every 1 to 2 hours (intravenous [IV] or oral) until clinically significant improvement is seen (CIWA-Ar reduction to 10 or less) or the patient becomes sedated.[9] This method may be more appropriate for patients at risk for severe withdrawal or those already in severe withdrawal. This detoxification method and the patients experiencing this level of severe symptoms would not be appropriate for ambulatory detoxification.

The second method is symptom-triggered therapy in which patients are typically watched closely in an inpatient setting and, once they reach a given level of symptoms on the CIWA-Ar, are administered a benzodiazepine. An example is administering chlordiazepoxide 50 mg for a CIWA-Ar >9 followed by reassessment of the CIWA-Ar in 1 hour. If the patient's subsequent CIWA-Ar is elevated above 10, then chlordiazepoxide 50 mg is readministered until CIWA-Ar is below 10. The interval and dosage can be adjusted to the clinical situation by the provider.[2] This detoxification method could be used in an ambulatory care setting utilizing direct observation by trained staff, which aligns with ASAM Level II-D standards for care settings.

Gradual, tapering benzodiazepine doses is the third method for patients with stable withdrawal symptoms. With this method, patients are given a predetermined oral benzodiazepine dosing schedule over a 3- to 5-day period, which is gradually tapered down over this time. A wide variety of protocols exist utilizing chlordiazepoxide, diazepam, and lorazepam. An example would be a patient stabilized on chlordiazepoxide 50 mg every 6 hours, then tapered down by 50 mg each subsequent day, and then

TABLE 4: Comparison of anticonvulsants used in alcohol withdrawal[8]

Anticonvulsant	Peak Onset of Action, Oral, h	Half-Life Parent, h	Half-Life Active Metabolite, h	Dosing Range, mg/d	Advantages of Use
Carbamazepine	4 to 5	Variable; initial 25 to 65 (reduces after multiple doses)	34 ± 9	600 to 1200 Tapered down	Most studied with equal or greater efficacy to oxazepam
Divalproex sodium	~4	9 to 16	None	1000 to 1500 Tapered down	Small studies showing reduction of withdrawal symptoms
Gabapentin	2 to 4	5 to 7	None, not metabolized	1200 Tapered down	Equal reduction of withdrawal symptoms versus lorazepam; lower craving, anxiety, and sedation versus lorazepam; good option in liver dysfunction

off by day 5.[2] This is an approach that can be used on an outpatient basis and does not necessitate frequent monitoring. It provides flexibility for patients who cannot make it back to the clinic or hospital. However, this approach may be more likely to result in overdosing or underdosing as compared to the directly observed methods previously discussed. Additionally, this method adds the risk of coadministration of benzodiazepines and alcohol because the patient is supplied multiple days of the benzodiazepine medication and likely has access to alcohol as an outpatient. The provider must use clinical judgment to determine if the patient can safely carry out the protocol as prescribed and understands the importance of not drinking alcohol with benzodiazepines or operating automobiles or machinery while in the taper protocol.

The final method is a single-day dosing protocol. Single daily dosing of diazepam versus multiple daily dosing of chlordiazepoxide has been studied.[10] In this study, both groups were similar in terms of efficacy with withdrawal symptoms as measured by the CIWA-Ar, and neither treatment arm required supplemental medication for withdrawal symptoms. This study[10] was conducted in an inpatient setting, but the authors suggest this method could be useful in community settings if monitoring could be carried out between doses.

Alternative agents for alcohol withdrawal may also be considered. Phenobarbital has previously been used for alcohol detoxification, but risk of accumulation and fatal overdose limits its use to highly supervised settings.[2] If benzodiazepines cannot be used or the provider wants to avoid them, data support the use of carbamazepine,[11] divalproex sodium,[12] and gabapentin.[13] (See Table 4.) Carbamazepine has been the most widely studied of the anticonvulsants in mild-to-moderate alcohol withdrawal. Carbamazepine 800-mg taper was found to be equally as effective as oxazepam 120-mg taper in reducing signs and symptoms on the CIWA-Ar in a 5-day trial[14] and was superior by days 6 and 7 in another 7-day trial.[15] Carbamazepine had further reduction of some drinking behavior indices in postwithdrawal treatment versus lorazepam.[16] Divalproex sodium has not been as well studied but has also been shown to be effective in reducing withdrawal symptoms (CIWA-Ar) in mild-to-moderate alcohol withdrawal compared to placebo at 1500 mg/d and lorazepam.[12,17] Gabapentin had a clinically similar reduction of CIWA-Ar symptoms versus lorazepam over time but had less probability of drinking in the follow-up period and less craving, anxiety, and sedation compared to lorazepam.[13] Advantages of using these anticonvulsant agents are that they are not controlled substances (gabapentin is a class V controlled substance in some states), have lower abuse liability, are less likely to affect motor and cognitive performance, may reduce comorbid psychological symptoms associated with alcohol withdrawal, and do not interact with alcohol. Disadvantages of using anticonvulsants include side effects, worsening of any preexisting hepatic or hematological conditions, and a lack of evidence in severe alcohol withdrawal if these symptoms happen to emerge.

If extreme hypertension, tachycardia, agitation, psychosis/hallucinations, or delirium develop, a patient would no longer meet the criteria for ambulatory detoxification due to medical and psychiatric instability. Agents such as clonidine (alpha adrenergic agonist), beta blockers, or calcium channel blockers may be considered for hypertension and tachycardia.[2] Antipsychotics may be adjunctively used for extreme agitation, psychosis/hallucinations, or delirium with the knowledge that these agents can lower seizure threshold.[2]

In the case of A.G., the provider would need to determine if the patient was appropriate for ambulatory detoxifica-

tion. The overall symptoms fell in the mild-to-moderate range leaning toward ambulatory detoxification. A.G.'s history (never had detoxification, stable mental health/depression, lack of uncontrolled medical issues) and psychosocial characteristics (employed, had stable housing and social supports) made ambulatory detoxification a viable option, especially because inpatient detoxification could be detrimental to A.G.'s current employment. Secondarily, the provider needed to determine if medication would be utilized to assist alcohol withdrawal symptoms. Because the patient's CIWA-Ar is currently a 12, medication-assisted withdrawal management with a benzodiazepine, such as chlordiazepoxide, was appropriate. Due to A.G.'s long history of alcohol use disorder and the unpredictability of withdrawal symptoms, using a gradual taper dose at home would help prevent any further symptom exacerbation and provide a smoother transition off of alcohol. The spouse was also at home and could assist with the taper protocol and help ensure there was no consumption of alcohol with the benzodiazepine. Chlordiazepoxide would be an appropriate option because it is long acting and has active metabolites, which provide easier dosing and a natural self-tapering. Alternatively, use of lorazepam or oxazepam would be preferred if A.G. was elderly or had a compromised liver function.[7,18]

Ambulatory Detoxification in Opioid Use Disorder

Unlike withdrawal from alcohol, opioid withdrawal is rarely medically dangerous.[2] However, opioid withdrawal is very unpleasant. It can produce significant discomfort in a patient in florid withdrawal. Patients often try to avoid these symptoms at all costs, including resuming opioid use or seeking illicit opioids rather than experiencing withdrawal symptoms. Due to the high possibility of opioid relapse, inpatient detoxification allows for close monitoring to help prevent emergence of withdrawal symptoms and successfully initiate medication for the opioid use disorder. Just as with ambulatory alcohol detoxification, ambulatory detoxification of opioids is possible but has its complexities. All opioids produce similar withdrawal signs and symptoms, but differences in severity, time to onset, and duration of withdrawal can be seen depending on the agent used, the duration of use, the daily dose of the opioid, and dosing interval.[2] An illustration of these differences can be seen when comparing heroin and methadone. Withdrawal from heroin begins 8 to 12 hours after last use and subsides within a period of 3 to 5 days, whereas methadone withdrawal begins 36 to 48 hours after last use, peaks within 3 days, and may last a period of 3 weeks or longer.[2] Table 5 provides the signs and symptoms of opioid intoxication and withdrawal.

TABLE 5: Opioid intoxication and withdrawal signs and symptoms[a]

Opioid Intoxication	Opioid Withdrawal
Signs	**Signs**
Bradycardia	Diaphoresis
Head nodding	Hyperreflexia
Hypokinesis	Hypertension
Hypotension	Hyperthermia
Hypothermia	Increased respiratory rate
Miosis	Insomnia
Respiratory depression	Lacrimation
Sedation	Muscle spasms
Slurred speech	Mydriasis
	Piloerection
	Rhinorrhea
	Tachycardia
	Yawning
Symptoms	**Symptoms**
Analgesia	Abdominal cramps
Calmness	Anxiety
Euphoria	Bone and muscle pain
	Diarrhea
	Nausea
	Vomiting

[a]Adapted from TIP 45 (Consensus Panelist Charles Dackis, MD).[2]

Medically supervised detoxification is best guided with an in-depth knowledge of the signs and symptoms of opioid intoxication and withdrawal. Due to the uncomfortable nature of opioid withdrawal (even with mild symptoms), it is recommended to provide withdrawal management with medications.[2] Clinicians need to closely examine patients for intoxication and monitor for emergence of withdrawal symptoms using validated scales, such as the Objective Opiate Withdrawal Scale,[19] Subjective Opiate Withdrawal Scale,[19] or Clinical Opiate Withdrawal Scale (COWS).[20] The COWS is the most commonly used scale and is discussed here in more detail. It examines 11 objective and subjective symptoms, including resting pulse rate, sweating, restlessness, pupil size, bone or joint aches, runny nose or tearing, gastrointestinal upset, tremor, yawning, anxiety or irritability, and gooseflesh skin. Items are rated on an ordinal scale from 0 to 4 or 5, depending on the item. Total scores can range from 0 to 48. A score of 5 to 12 denotes *mild* opioid withdrawal symptoms, 13 to 24 indicates *moderate*, 25 to 36 indicates *moderately severe*, and more than 36 indicates *severe withdrawal*.

Case 2: Ambulatory Opioid Detoxification

J.T. is a 25-year-old patient with a mental health history of posttraumatic stress disorder (PTSD) and major depressive disorder. The patient presented requesting maintenance medications for opioid use disorder. J.T. had been off psychiatric medications, sertraline and hydroxyzine, since the opioid use disorder emerged about 3 years ago. J.T. had been stable on these medications for 4 years. The

patient was provided hydrocodone/acetaminophen for pain from an elbow injury, and the prescription was renewed by the primary care physician while J.T. went through physical therapy over an 8-month period. The hydrocodone "numbed" feelings and lessened anxious and jumpy feelings when others were around, so the patient began to use more than the prescribed doses. After running out of the hydrocodone prescription early a few times and feeling restless, irritable, and achy with gastrointestinal upset, J.T. sought out hydrocodone on the street to cover these times. The patient's physical therapy ended after 6 months, and the primary care physician would no longer prescribe the hydrocodone. J.T. found a street dealer who provided hydrocodone for about 3 months, but the dealer could not get it consistently. The dealer then offered a stronger and cheaper alternative in heroin. J.T. started with insufflation for 3 months and moved on to IV use. For the past 2 years, the patient had been using IV heroin exclusively, and denied use of any other illicit substances. This was the first time J.T. had sought treatment for opioid use disorder. The patient avoided many of the community-based programs due to them being religious-based because J.T. was not particularly religious. Due to the drug use, J.T. was homeless, primarily "couch surfing" with friends and family for the past year. The patient's car was repossessed about 6 months prior, and J.T. had inconsistent and short-lived bartending or server jobs. A COWS was performed with the patient, and a total score of 14 (*moderate withdrawal*) was obtained.

Treatment Considerations in Ambulatory Opioid Detoxification

Opioid detoxification with medications is primarily carried out with one of 5 agents: methadone, buprenorphine/naloxone, clonidine, guanfacine, and lofexidine. Methadone is approved by the Food and Drug Administration for opioid detoxification. It is restricted to licensed methadone programs for opioid detoxification and maintenance treatment.[2] Withdrawal management with methadone is either conducted in an inpatient setting or at an office-based opioid treatment program.[21] Due to its long-acting mu-opioid agonist properties, methadone binds to mu receptors preventing withdrawal symptoms after shorter acting opioids disassociate from mu receptors. Used long term, (maintenance) methadone can reverse the immunologic and endocrinologic defects seen in long-term heroin use.[2] For withdrawal management of short-acting opioids, it is recommended to start with methadone doses between 20 and 30 mg once daily and institute a taper schedule to be completed in 6 to 10 days for patients that do not want to be on long-term methadone maintenance.[21] These patients may be at increased risk of overdose post taper. Optimally, the patient will be stabilized on a dose of methadone during the withdrawal management period and enrolled into a methadone maintenance program that will prevent any opioid withdrawal symptoms along with prevention of cravings or urges.

Buprenorphine/naloxone is also utilized for opioid detoxification.[22-24] It has high affinity for mu-opioid receptors, but it is a partial agonist at the receptor. This partial agonism provides a *ceiling effect* when it comes to overdose potential due to respiratory depression and other subjective measures, such as feeling the drug's effects or euphoria.[25] Buprenorphine/naloxone has similar efficacy to methadone and has superior efficacy to clonidine for opioid withdrawal.[23,26,27] Clinicians must accurately assess patients prior to buprenorphine/naloxone induction as its partial agonist properties may produce a precipitated withdrawal if the patient is not already exhibiting withdrawal symptoms.[21] Usually buprenorphine/naloxone is not started until 12 to 18 hours postdose of a short-acting opioid, such as heroin or oxycodone, and 24 to 48 hours after a long-acting opioid such as methadone.[21] A COWS score of 11 or 12 (mild-to-moderate withdrawal symptoms) is indicative of sufficient withdrawal symptoms to induce with buprenorphine/naloxone.[21] A buprenorphine/naloxone dose of 4 to 16 mg/d of the buprenorphine component is started to suppress withdrawal symptoms and then tapered over 3 to 5 days (or as long as 30 days or more) for withdrawal management.[21] Naloxone is present strictly to prevent abuse via insufflation or injection and has no activity through oral ingestion. Buprenorphine/naloxone prescribers must obtain a Drug Enforcement Administration X-waiver to prescribe the medication, which requires additional training and limits on the number of patients on the panel. This restriction can be a potential barrier to treatment for some patients.

Opioid withdrawal is principally a result of overactivity of the brain's noradrenergic system.[21] Hence, the alpha-2 adrenergic agonists clonidine and guanfacine have been utilized off-label for opioid withdrawal for many years. Clonidine 0.1 mg to 0.3 mg given every 6 to 8 hours with a maximum daily dose of 1.2 mg/d is provided for opioid withdrawal. Clonidine's hypotensive effects often limits its utility. Guanfacine is typically dosed at 3 to 4 mg/d divided 3 times daily. This guanfacine dose is then tapered down over 4 to 7 days. Recently, lofexidine, a central alpha-2 agonist, was approved by the Food and Drug Administration as the first nonopioid treatment for opioid withdrawal.[28] It has been approved for use in the United Kingdom since 1992. It comes in 0.18-mg tablets and patients are given 3 to 4 tablets by mouth every 5 to 6 hours for up to 14 days. The maximum dose is 4 tablets/dose and 16 tablets/d. Lofexidine is to be tapered gradually over 2 to 4 days. These alpha-2 adrenergic agents are often combined with other non-narcotic agents to address specific

withdrawal symptoms, such as benzodiazepines for anxiety, loperamide or bismuth subsalicylate for diarrhea, acetaminophen or nonsteroidal anti-inflammatory drugs for pain or headache, ondansetron for nausea/vomiting, and/or trazodone/hydroxyzine/mirtazapine for insomnia.[21] Overall, these alpha-2 adrenergic agonists would be considered second-line alternatives for patients that do not want to receive an opioid (methadone or buprenorphine); had contraindications to being on methadone or buprenorphine; or had co-occurring alcohol, sedative, or benzodiazepine use disorders that would make coadministration of an opioid dangerous. A comparison of lofexidine versus methadone showed more severe withdrawal symptomatology from days 3 to 7 and on day 10 (last day of treatment) in the lofexidine group. Additionally, the lofexidine group had a higher dropout rate versus the methadone group.[29]

Choosing between the alpha-2 adrenergic agonists depends highly on the symptoms you are trying to treat and the side effects you are trying to avoid while treating opioid withdrawal. Guanfacine and lofexidine are more selective agonists at alpha-2a than alpha-1, alpha-2b, alpha-2C, and imidazoline receptors. This allows guanfacine and lofexidine to retain the sedative/hypnotic properties while causing less hypotension.[30-37] Due to guanfacine and lofexidine having less affinity for alpha-2b and imidazoline receptors, it might be a less effective analgesic agent.[31] Clinical trials suggest a decreased incidence of hypotension and sedation with lofexidine compared with clonidine.[38-41] Unfortunately, to date, we do not have any trials directly comparing guanfacine and lofexidine. Based on comparable primary mechanism of action and the vast current pricing differences in the United States, guanfacine would be favored over lofexidine.

In the case of J.T., it was imperative to examine the patient in a bio-psycho-social-spiritual aspect and take the entire person into account, not solely focusing on the opioid use disorder and opioid withdrawal. Failure to address any medical or psychiatric needs or ignoring J.T.'s current social functioning or spiritual issues (religious beliefs not coinciding with medication-based treatment or being in a religious-based program that does not allow use of medication) may lead to immediate relapse after detoxification and may even put the patient at higher risk of opioid overdose. Ensuring coordinated care addressing each of J.T.'s needs would be optimal. Restarting sertraline and hydroxyzine to address J.T.'s depression and PTSD-associated symptoms would be optimal because some of the opioid use surrounded self-treating these symptoms. The patient's current homelessness, staying in a variety of places, and transportation issues may make daily attendance at a methadone maintenance program difficult. Buprenorphine/naloxone could be an appropriate option to address the current withdrawal symptoms. If J.T. was willing to engage in long-term treatment and an X-waiver provider was on the treatment team, then buprenorphine/naloxone in an office-based opioid treatment setting would be very appropriate and the ideal choice. If J.T. did not want to do maintenance treatment with buprenorphine/naloxone, then guanfacine may be a more appropriate course of detoxification treatment as data suggests patients treated with buprenorphine/naloxone for a short term (1 month) of maintenance treatment and then tapered over 7 or 28 days had high rates of relapse.[42] The treatment team should also ensure the patient's housing situation was addressed by social work and that the major depressive disorder and PTSD were concurrently addressed along with the opioid use disorder.

Conclusion

Ambulatory detoxification for alcohol use disorder and opioid use disorder is a viable treatment option for patients that meet the criteria for it to be safely performed in this treatment setting. Ambulatory detoxification serves as an appealing option to many patients and helps save the limited inpatient resources that many institutions have for those patients with more severe withdrawal presentations.

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