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Concurrent opioid and alcohol withdrawal management

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Abstract

Concurrent alcohol and opioid withdrawal syndrome is a common and challenging clinical scenario with little published evidence or guidance to inform pharmacotherapy strategies. Concurrent use of benzodiazepines and opioid agonists, which are considered first-line agents for management of each withdrawal syndrome independently, is controversial and often avoided in clinical practice. Strategies to provide effective, simultaneous medication treatment of alcohol and opioid withdrawal while optimizing patient safety are demonstrated through 3 patient cases.

Keywords: alcohol withdrawal, opioid withdrawal, benzodiazepines, medications for opioid use disorder, medications for alcohol use disorder

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Introduction

Principles for the treatment of alcohol or opioid withdrawal independently are well-established in clinical practice guidelines and primary literature; however, there is often uncertainty among clinicians about how to manage these withdrawal syndromes when they co-occur. Goals for the management of concurrent alcohol and opioid withdrawal should include prevention of potentially life-threatening alcohol withdrawal complications, relief from distressing opioid withdrawal symptoms, and transition to substance use disorder treatment. This should include timely initiation of medications for opioid use disorder (MOUD) and alcohol use disorder (MAUD).[1–5] With increasing rates of alcohol- and opioid-related mortality, it is essential to provide safe and effective withdrawal management and increase utilization of evidence-based treatments for both alcohol (AUD) and opioid use disorders (OUD).[6,7]

Opioid withdrawal management alone (ie, detoxification) without ongoing MOUD treatment is not recommended.[1,3–5] One common barrier to initiating evidence-based MOUD is the presence of co-occurring AUD. One study found that patients with OUD and co-occurring AUD were 25% less likely to receive medications for OUD.[8] In clinical practice, this barrier can be confounded in the setting of concurrent alcohol and opioid withdrawal in which alcohol withdrawal treatment is often prioritized over OUD-related needs. Of the 2.8 million Americans diagnosed with OUD, past estimates for co-occurring AUD range from approximately 26% to 38%.[9,10] More recently, the onset of the COVID-19 pandemic has been linked to a significant increase in unhealthy alcohol use and associated consequences, including increased emergency department (ED) presentation for withdrawal management and alcohol-related mortality.[6] This could further increase the estimated incidence of co-occurring OUD, AUD, and withdrawal treatment episodes. Key principles to optimize safety and efficacy of pharmacotherapy for concurrent alcohol and opioid withdrawal are reviewed through 3 hypothetical patient cases that are representative of real-world scenarios.

Take Home Points:

1. Relief from uncomfortable and distressing opioid withdrawal symptoms should be prioritized along with prevention of potentially life-threatening complications of alcohol withdrawal to ensure patient safety and comfort, prevent patient-directed discharge, and facilitate initiation of medications for opioid use disorder and alcohol use disorder.
2. Individualized, scheduled pharmacotherapy regimens may be preferred due to lack of clinical trials evaluating efficacy of symptom-triggered protocols and complexities affecting validity of symptom severity scales in this population.
3. First-line treatments for alcohol and opioid withdrawal, including benzodiazepines and opioid agonists, can be utilized simultaneously in controlled, inpatient settings with close monitoring. Alpha-2 agonists should not be used as monotherapy in the absence of evidence-based pharmacotherapy for alcohol withdrawal due to the potential to mask alcohol withdrawal.
4. Strategies to minimize the risk of negative outcomes associated with respiratory depression with the combination of benzodiazepines and opioid agonists include conservative initial dosing of opioid agonists, cautious but effective dose titration, and utilization of "hold" parameters on inpatient medication order sets.

Case 1: Create a Measurement-Based Care Monitoring Plan to Support Individualized Treatment of Concurrent Opioid and Alcohol Withdrawal

A 41-year-old with AUD and OUD presented to the ED and was admitted for alcohol and opioid withdrawal syndrome. Recent substance use history includes 12 (12-ounce) beers and 100 mg oxycodone daily from nonprescription sources with last reported period of abstinence from alcohol or opioids more than 1 year ago. The patient reported at least 1 past episode of alcohol withdrawal and no history of seizures or delirium tremens (ie, complicated withdrawal). The last reported use of alcohol and opioids occurred approximately 2 hours prior to ED presentation. Pertinent vitals and laboratory results at presentation include BP = 140/92 mmHg, pulse = 121 bpm, T = 98.9°F, blood alcohol level = 210 mg/dl, urine drug screen positive for opioids and oxycodone; AST = 278 IU/L, ALT = 156 IU/L, alkaline phosphatase = 240 IU/L; basic metabolic panel and complete blood count within normal limits. Upon admission, facility inpatient symptom-triggered protocols for alcohol and opioid withdrawal were ordered, including Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar) and Clinical Opioid Withdrawal Scale (COWS) monitoring every 4 hours along with medication orders for lorazepam 2 mg every 4 hours PRN CIWA-Ar > 8 and buprenorphine/naloxone 2 mg/0.5 mg every 4 hours PRN COWS > 10.[11,12] Approximately 12 hours after admission, CIWA-Ar and COWS scores were 13 and 11, respectively, indicating moderate alcohol and mild opioid withdrawal severity. The patient was given lorazepam 2 mg and buprenorphine/naloxone 2 mg/0.5 mg per symptom-triggered protocols. The primary team subsequently initiated an individualized, scheduled pharmacotherapy regimen of lorazepam 2 mg 4 times daily with plans to taper by 50% daily over 3 days and buprenorphine/naloxone 2 mg/0.5 mg 3 times daily with plans to increase as indicated for opioid withdrawal symptoms. CIWA-Ar and COWS monitoring were continued every 4 hours to guide dose adjustments to the scheduled medication regimen or determine need for additional PRN doses until symptoms resolved. The patient discharged to residential substance use disorder treatment with a plan to continue buprenorphine/naloxone 8 mg/2 mg twice a day and acamprosate 666 mg 3 times per day.

TABLE 1: Risk factors for complicated alcohol withdrawal or complications of withdrawal[2]

Increase risk:
History of alcohol withdrawal delirium or alcohol withdrawal seizure
Numerous prior withdrawal episodes in the patient's lifetime
Comorbid medical or surgical illness (especially traumatic brain injury)
Increased age (>65)
Long duration of heavy and regular alcohol consumption
Seizure(s) during the current withdrawal episode
Marked autonomic hyperactivity on presentation
Physiological dependence on GABAergic agents such as benzodiazepines or barbiturates
May increase risk:
Concomitant use of other addictive substances
Positive blood alcohol concentration in the presence of signs and symptoms of withdrawal
Signs or symptoms of a cooccurring psychiatric disorder are active and reflect a moderate level of severity.

There is consensus among guidelines that inpatient management is recommended for patients at risk for withdrawal from alcohol along with other substances, including opioids.[1,2,4,5] In general, clinicians should prioritize substance withdrawal treatments based on the patient's potential for physical dependence and severity of withdrawal symptoms for each substance. If the patient is at risk for alcohol withdrawal, this would be prioritized due to the potential for life-threatening complications, such as seizures or delirium tremens. A pharmacotherapy plan for opioid withdrawal should be established concurrently or shortly thereafter to prevent or relieve distressing withdrawal symptoms and decrease risk for patient-directed discharge, also known as "against medical advice" discharge. Treatment guidelines recommend stabilizing OUD with opioid agonists such as buprenorphine or methadone while simultaneously treating alcohol withdrawal.[1,2] Opioid "detoxification"

TABLE 2: Classification of withdrawal severity[a]

Alcohol Withdrawal Severity[2]	Opioid Withdrawal Severity[12]
CIWA-Ar <10 = mild	COWS < 13 = mild
CIWA-Ar 10-18 = moderate	COWS 13-24 = moderate
CIWA-Ar ≥ 19 = severe	COWS 25-36 = moderate severe
CIWA-Ar ≥ 19 = complicated in presence of seizure or signs of delirium	COWS >36 = severe

[a]CIWA-Ar and COWS are used as examples herein; validated scales and score ranges indicating mild, moderate, and severe withdrawal severity vary widely in the literature and practice. Withdrawal severity should ultimately be determined by the clinician's judgment.

can then be considered after completion of alcohol withdrawal by tapering the opioid agonist to discontinuation; however, this should be reserved only for those who decline continuation of MOUD.[1,2,4]

Risk for developing severe or complicated alcohol withdrawal should be determined by using patient-specific factors (Table 1) and a validated withdrawal risk assessment scale, such as the Prediction of Alcohol Withdrawal Severity Scale.[2,13] Validated scales to assess current withdrawal severity are strongly recommended for comprehensive monitoring of alcohol and opioid withdrawal.[1,2,5] Whereas several validated scales are utilized in clinical practice, CIWA-Ar and COWS are among the most widely utilized (Table 2).[1–3,11,12] Of note, the Brief Alcohol Withdrawal scale may show promise for accurate assessment of alcohol withdrawal severity in this population as approximately 30% of patients in the validation study received concurrent opioid withdrawal treatment.[14]

For alcohol withdrawal, symptom-triggered benzodiazepine regimens are preferred across guidelines as they reduce treatment duration and total benzodiazepine dose exposure without increasing risk for seizures or delirium.[2,4,5] However, their use in patients at risk for withdrawal from multiple substances should be approached with caution due to a lack of studies establishing safety and efficacy in this population. Treatment guidelines recommend scheduled regimens for those considered "high risk" for alcohol withdrawal and note that concurrent withdrawal to another substance may increase risk for complicated alcohol withdrawal.[1,2,4] In general, CIWA-Ar symptom-triggered protocols were studied in lower risk populations and excluded patients with history of complicated withdrawal or potential opioid dependence.[15–20] Guidelines also recommend scheduled versus symptom-triggered regimens in those for whom it would be difficult to obtain an accurate withdrawal severity score.[1,2] The accuracy of most withdrawal severity scales in patients at risk for alcohol and opioid withdrawal cannot be determined as patients using multiple substances are typically excluded from validation studies to optimize internal validity.[11,12,21] Presence of both alcohol and opioid withdrawal symptoms could falsely elevate either withdrawal score due to overlapping symptoms, including elevated pulse, anxiety, irritability, restlessness, sweating, tremor, nausea, and vomiting. This could lead to overmedication or administration of medication earlier than indicated if using a symptom-triggered protocol. For example, patients with a falsely elevated CIWA-Ar score may receive more PRN benzodiazepine doses than needed, increasing risk for adverse effects, whereas patients with a falsely elevated COWS score may receive PRN buprenorphine earlier than truly indicated, increasing risk for precipitated opioid withdrawal.

Withdrawal severity scales can be useful to determine when to begin a scheduled regimen for either withdrawal syndrome and the need for dose adjustments throughout the treatment course. This approach may lower the risk for precipitated withdrawal in those initiating buprenorphine by delaying the first dose until symptoms are approaching moderate opioid withdrawal severity.[3] The American Society of Addiction Medicine (ASAM) recommends that, for patients with mild alcohol withdrawal (ie, CIWA-Ar < 10) and minimal risk for severe withdrawal, the decision to initiate medication is based on the clinician's judgment.[2] Therefore, in patients at high risk for opioid withdrawal but low risk for alcohol withdrawal due to factors such as intermittent or lower level alcohol use, opioid agonists to stabilize OUD can be initiated along with ongoing CIWA-Ar monitoring as a precaution to identify the need to initiate alcohol withdrawal pharmacotherapy. One important caveat is to ensure alpha-2 agonists are not initiated as monotherapy for opioid withdrawal prior to initiation of first-line pharmacotherapy for alcohol withdrawal due to the potential for alpha-2 agonists to mask alcohol withdrawal syndrome.[1,2] Presence of symptoms identified via withdrawal symptom scales that are more unique to alcohol withdrawal (ie, elevated blood pressure, headache, auditory/visual/tactile disturbances, clouding of sensorium) or opioid withdrawal (ie, diarrhea, bone/joint aches, dilated pupils, runny nose or tearing eyes, increased yawning, gooseflesh skin) may be particularly helpful for tailoring dosing or duration of individualized medication plans.

Case 2: Design a Pharmacotherapy Regimen for Managing Alcohol and Opioid Withdrawal Concurrently

A 54-year-old patient with chronic pain, migraines, OUD, and AUD was admitted to the inpatient medical unit for acute pancreatitis. Alcohol use history includes up to 1 fifth liquor daily, last use 12 hours prior to admission, last sustained period of abstinence 6 months prior to admission, multiple past alcohol withdrawal–related admissions, and no history of complicated withdrawal. Recent opioid use history includes heroin daily by insufflation for 6 months with last use approximately 24 hours prior to admission. Pertinent vitals and laboratory results at the time of admission included BP = 168/105 mmHg, pulse = 99 bpm, T = 99.0°F, blood alcohol level =140

mg/d, urine drug screen positive for opioids and fentanyl, WBC = 15,100 cells/μL, glucose = 312 mg/dl; basic metabolic panel and complete blood count otherwise within normal limits. Facility monitoring protocols for alcohol and opioid withdrawal were ordered, including CIWA-Ar and COWS scale every 4 hours. Approximately 4 hours after admission, CIWA-Ar and COWS scores were 19 and 8, respectively, indicating severe alcohol and mild opioid withdrawal severity. On day 1 of admission, diazepam 20 mg 4 times a day was initiated with a plan to taper by 50% daily to discontinuation over 4 days. Diazepam 10 mg Q4hours PRN CIWA-Ar > 8 was ordered for symptoms not adequately treated by the scheduled regimen. Preferences for substance use disorder treatment, including MOUD, were discussed with the patient on day 1 to inform the withdrawal treatment strategy. Methadone was initiated at 10 mg daily on day 1 and gradually titrated to 30 mg daily by day 7 to prevent opioid withdrawal and facilitate continuation of the patient's preferred MOUD upon discharge.[22,23] Discharge medication on day 7 included topiramate 25 mg twice a day for AUD with a warm hand-off to a local opioid treatment program for ongoing methadone treatment.

Although guidance on specific strategies for managing alcohol and opioid withdrawal concurrently is lacking, medication principals for managing each withdrawal syndrome independently can be combined to provide effective, simultaneous treatment. Benzodiazepines remain first-line treatment for alcohol withdrawal syndrome and should be initiated prophylactically in those at risk for severe or complicated withdrawal or in the presence of moderate or severe withdrawal (ie, CIWA-Ar ≥ 10).[1,2] The patient in case 2 appropriately received diazepam for treatment of alcohol withdrawal after presentation of severe withdrawal symptoms as evidenced by CIWA-Ar = 19. Other patient-specific factors indicating high risk for withdrawal or complications of withdrawal that supported initiation of a scheduled benzodiazepine regimen included a sustained period of heavy alcohol use, evidence of autonomic hyperactivity upon presentation, and use of multiple substances.[2]

Opioid agonists (ie, methadone, buprenorphine) should be considered first-line treatment for opioid withdrawal over alpha-2-agonists (ie, clonidine, lofexidine) given superiority for opioid withdrawal severity, withdrawal treatment retention, and completion.[3,5] Outcomes from 2 retrospective studies evaluating patient characteristics associated with patient-directed discharge reinforce this recommendation in those with concurrent alcohol and opioid withdrawal.[24,25] Whereas 100% of patients with alcohol withdrawal who received clonidine for concurrent opioid withdrawal experienced patient-directed discharge in the initial review, patients who received buprenorphine or methadone for opioid withdrawal were no more likely to experience patient-directed discharge than those without opioid withdrawal in the latter.[24,25] ASAM Clinical Practice Guidelines on Alcohol Withdrawal Management explicitly state that, in those with concurrent alcohol withdrawal and OUD, OUD should be stabilized with an opioid agonist while simultaneously treating alcohol withdrawal. Alpha-2 agonists are appropriate alternatives in patients who decline opioid agonists, have contraindications, or state preference for ER naltrexone for MOUD.[2] Uncertainty about the legality of inpatient methadone and buprenorphine prescribing has been a common barrier to optimizing their utilization for opioid withdrawal. The use of methadone in case 2 for the patient admitted for acute pancreatitis is in compliance with federal regulations permitting inpatient administration to prevent opioid withdrawal while receiving treatment for an acute medical condition.[22,23] Although the same federal regulation has also historically permitted inpatient administration of buprenorphine for patients admitted for acute medical illness, removal of the X-waiver eliminates yet another potential source of uncertainty among clinicians to increase patient access to evidenced-based care in this setting.[22,26]

Although practice guidelines acknowledge that those at risk for concurrent alcohol and opioid withdrawal may receive benzodiazepines along with opioid agonists in controlled inpatient settings, the controversy of coprescribing is a common barrier to administering these two first-line treatments simultaneously in clinical practice.[2] Following a 2016 FDA safety communication, a boxed warning was added to labels for prescription opioids for pain or cough and benzodiazepines to emphasize the associated risk for respiratory depression.[27] Highlighted data demonstrate increased rates of ED presentation and overdose deaths related to both prescription and nonprescription use of this combination.[28,29] Since that time, several guidelines and deprescribing initiatives nationwide have aimed to minimize coprescribing of opioids and benzodiazepines.[30–32] As a result, many clinicians are justifiably inclined to avoid this combination regardless of the opioid-related indication. In 2017, the FDA released a follow-up statement clarifying that opioid agonists for the treatment of OUD should not be withheld in those using benzodiazepines or other central nervous system (CNS) suppressants.[33] The safety announcement again acknowledged the risk of respiratory depression; however, it concluded that the risk of untreated OUD is likely greater.[33–35] This should reassure clinicians that the benefit of short-term coadministration in a controlled, inpatient setting for those at risk for concurrent alcohol and opioid withdrawal outweighs the risk of withholding first-line pharmacotherapy.

When coprescribing benzodiazepines and opioid agonists, several strategies can be considered to minimize the risk for negative outcomes associated with respiratory depression. Buprenorphine is theoretically less likely to induce respiratory depression given its ceiling effect compared with methadone.[36] This may give preference to buprenorphine over methadone in patients receiving concurrent treatment for

alcohol withdrawal syndrome with CNS depressants; however, in the author's opinion, the patient's preference and access to ongoing MOUD treatment options should be weighed significantly in this decision. A retrospective case-control cohort compared the incidence of admission for any acute alcohol-related event in patients with OUD on days with versus days without medication for OUD. Treatment with buprenorphine (43% reduction; odds ratio [OR], 0.57; 95% confidence interval [CI], 0.52-0.61), methadone (66% reduction; [OR], 0.34; 95% CI, 0.26-0.45), and naltrexone ER (37% reduction; OR, 0.63; 95% CI, 0.52-0.76) were all associated with decreased odds of any acute alcohol-related event versus nontreatment days. Notably, the reduction in acute alcohol-related events was numerically greater in patients receiving methadone compared with other MOUD agents in this study.[37] The potential long-term benefit for methadone on overall OUD-related outcomes as demonstrated in this cohort may outweigh the short-term increased risk for respiratory depression in an inpatient setting with close monitoring.

Although therapeutic doses of recommended agents for alcohol withdrawal should always be used to ensure optimal efficacy for preventing seizures and delirium tremens, the clinician may consider use of more conservative initial opioid agonist dosing. In case 2, a therapeutic diazepam starting dose of 20 mg 4 times a day was utilized along with a conservative initial methadone dose of 10 mg daily as opposed to the standard initial dose of up to 30 mg daily for patients with opioid tolerance.[2,3,36] Lower methadone starting doses such as 10 to 20 mg daily may be considered in the presence of risk factors for respiratory depression, such as concurrent CNS depressants, impaired respiratory function, or moderate-to-severe hepatic impairment. Presence of multiple risk factors may lead to use of an even lower 5 mg starting dose or selection of an alternative opioid withdrawal agent.[36] Lower initial doses of buprenorphine 2 mg or less can be considered in patients receiving other CNS depressants compared with standard starting doses up to 4 mg.[3,36] Because sublingual buprenorphine products FDA-approved for OUD are typically unavailable in dosing increments less than 2 mg in an inpatient setting due to the need for "tablet splitting," off-label products, such as buprenorphine buccal films or transdermal patch, could be used to obtain lower initial dosing options equivalent to approximately 0.5 to 1 mg of SL buprenorphine.[39] After assessing initial tolerance to the combination of either opioid agonist and CNS depressants, the opioid agonist should be titrated accordingly to relieve withdrawal symptoms. Hold parameters such as "hold for respiratory rate <12 or excessive sedation" can be added to inpatient medication orders to further minimize this risk.

Alternatives to benzodiazepines for alcohol withdrawal include phenobarbital, carbamazepine, and gabapentin.[2] Available evidence suggests a similar incidence of respiratory depression as evidenced by the need for intubation or mechanical ventilation between phenobarbital and benzodiazepines in the management of alcohol withdrawal.[40] One retrospective study evaluating medication management of concurrent alcohol and opioid withdrawal showed no occurrence of clinically significant respiratory depression in patients receiving buprenorphine and either lorazepam or phenobarbital.[41] Of note, phenobarbital use is recommended only by experienced clinicians due to its narrow therapeutic index and long half-life, which make it challenging to dose correctly.[2] Carbamazepine or gabapentin can be considered as alternatives to minimize the risk for respiratory depression when opioid agonists are indicated. These agents are appropriate for patients experiencing mild-to-moderate alcohol withdrawal and who are also at minimal risk for severe withdrawal.[2] Clinicians should be mindful that phenobarbital and carbamazepine, strong CYP3A4 inducers, have the potential to decrease serum concentrations and efficacy of both buprenorphine and methadone (cyp 3A4 substrates).[42–45]

Case 3: Select MOUD and MAUD With the Goal of Continuation After Resolution of Withdrawal

A 36-year-old with OUD, AUD, and major depressive disorder was admitted to an acute psychiatric unit for suicidal ideation and substance withdrawal. Recent alcohol use history included intermittent binge use up to 1 pint liquor per day approximately 2 days per week. Last use was more than 48 hours prior to admission with periods of abstinence up to 5 days in recent months. The patient denied history of complicated alcohol withdrawal or past admissions for alcohol withdrawal. Recent opioid use history included daily intravenous heroin use, no identified period of abstinence in the past 12 months, and last use approximately 24 hours prior to admission. Vitals upon admission included BP = 123/86 mmHg, pulse = 95 bpm, T = 98.6°F, weight = 77 kg. Pertinent labs included BAL < 10 mg/dl, urine drug screen positive for opioids and negative for all other substances, hepatitis C screening positive, HIV screening negative, CBC within normal limits, and CMP significant for AST = 88 IU/L, ALT = 105 IU/L, Tbili = 1.6 mmol/L. Upon admission, facility monitoring protocols for alcohol and opioid withdrawal were ordered, including CIWA-Ar and COWS scale every 4 hours. Upon admission, CIWA-Ar and COWS scores were equal to 6 and 17, respectively, indicating mild alcohol and moderate opioid withdrawal severity. On day 1, the treatment team provided thorough patient education on guideline recommendations to initiate MOUD prior to discharge and risks and benefits of each agent. The patient shared a strong preference for ER naltrexone over opioid agonists for MOUD. Gabapentin 600 mg every 6 hours was initiated based on the presence of mild alcohol withdrawal and minimal risk for developing severe withdrawal given the pattern of intermittent binge alcohol use with recent identified periods of abstinence.[2] Clonidine 0.1 mg every 6 hours was initiated for

opioid withdrawal with a plan to continue for approximately 7 days until initiation of ER naltrexone. The following comfort medications were available as needed for opioid withdrawal symptoms: ondansetron 4 mg q8h PRN nausea, hydroxyzine 50 mg Q6h PRN anxiety or insomnia, dicyclomine 20 mg Q6H PRN stomach cramps, loperamide 2-4 mg Q6H PRN diarrhea, and methocarbamol 500 mg Q6H PRN muscle spasms. CIWA-Ar scores remained less than 8, and COWS scores gradually decreased throughout the admission. On day 8, COWS = 2 (1 = restlessness, 1 = pulse rate), and a naltrexone 50 mg oral test dose was given with no significant increase in opioid withdrawal symptoms as evidenced by COWS = 3 (1 = restlessness, 1 = pulse rate, 1 = anxiety) 2 hours after naltrexone administration. ER naltrexone 380 mg injection was administered the same day prior to discharge with a plan for substance use disorder intensive outpatient treatment based on the patient's preferences. Gabapentin 600 mg 3 times a day was continued off-label for medication treatment of AUD.[5,46,48]

Clinicians should prioritize prompt initiation of pharmacotherapy to prevent potentially life-threatening alcohol withdrawal while also being mindful that opioid withdrawal management alone (ie, detoxification) is not recommend without ongoing maintenance treatment in those with concurrent OUD. SAMHSA's Treatment Improvement Protocol for substance withdrawal advocates that "a successful detoxification process can be measured, in part, by whether an individual who is substance dependent enters, remains in, and is compliant with. . .a substance use disorder treatment program."[1 (p xv)] Medications for OUD, including buprenorphine, methadone, and ER naltrexone, with access to psychosocial interventions, are the standard for OUD care.[3,36] Based on clinical experience, it is essential to discuss MOUD preferences with patients early in an opioid-withdrawal treatment course. Patient preference for either buprenorphine or methadone for OUD should prompt initiation early in the admission with the goal of stabilizing OUD and preventing opioid withdrawal.[2] Conversely, patient preference for ER naltrexone warrants consideration of an alpha-2 agonist for opioid withdrawal as administration of an opioid agonist during the admission could delay ER naltrexone initiation up to 14 days after last exposure. This would most likely rule out the potential to initiate ER naltrexone prior to discharge based on hospital length-of-stay limitations. Patient education to guide shared decision making should include the strong recommendation for MOUD, benefits for reducing opioid use and opioid-related mortality, specific nuances related to formulations, treatment settings, and risks of individual agents.[36] Whereas ER naltrexone can be considered for those with comorbid OUD and AUD, there is no evidence to suggest it is superior to opioid agonists for opioid or alcohol-related outcomes in this population.[37,38] Instead of withholding opioid agonists in patients with AUD, a higher level of care than what is offered in a standard outpatient setting, such as intensive outpatient treatment, residential treatment, or an opioid treatment program may be considered.[3,5,36] However, a patient's lack of access or interest in a higher level of care should not prohibit ongoing opioid agonist treatment.[3] Because patients with concurrent OUD and AUD are at higher risk for negative outcomes, including return to substance use, all-cause mortality, fatal overdose, and liver-related deaths, than patients with either disorder alone, it is the author's opinion that efforts should be made to offer any treatments that could potentially improve outcomes, including MAUD.[49] With the exception of naltrexone, patient preference for MAUD does not directly affect development of a concurrent opioid and alcohol withdrawal treatment plan and, therefore, can be discussed later in the treatment admission. There is no compelling evidence to support preference of any particular MAUD agent in patients with concurrent OUD.

Conclusion

Concurrent management of alcohol and opioid withdrawal presents a challenging clinical scenario, and the simultaneous use of first-line treatments, including benzodiazepines and opioid agonists is controversial. Although clinicians should approach concurrent prescribing of these agents with care, the benefit of effectively managing both alcohol and opioid withdrawal likely outweighs the risk in a controlled, inpatient setting. Strategies to minimize the risk for respiratory depression with this combination include conservative initial dosing of opioid agonists, cautious but effective dose titration, and hold parameters on inpatient medication order sets. Scheduled medication regimens may be preferred based on the lack of evidence for symptom-triggered protocols and complexities affecting symptom scale validity in patients using multiple substances. Although additional studies are needed, first-line alcohol and opioid withdrawal pharmacotherapy strategies can be used concurrently to achieve all important treatment goals, including prevention of life-threatening alcohol withdrawal symptoms, relief from distressing opioid withdrawal symptoms, prevention of patient-directed discharge, and access to MOUD and MAUD to improve long-term substance use disorder–related outcomes, including decreased risk for return to alcohol or opioid use, hospital readmission, and overdose mortality.

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