Clinical Guideline Highlights for the Hospitalist: 2020 American Society of Addiction Medicine Clinical Practice Guideline on Alcohol Withdrawal Management

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GUIDELINE TITLE: The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management

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TARGET POPULATION: Adults hospitalized with alcohol withdrawal syndrome of any severity

Alcohol is the most common substance implicated in hospitalizations for substance use disorders,[1] and as a result, hospitalists commonly diagnose and manage alcohol withdrawal syndrome (AWS) in the inpatient medical setting. The 2020 guidelines of the American Society of Addiction Medicine (ASAM) provide updated recommendations for the diagnosis, monitoring, and treatment of patients hospitalized with AWS, which we have condensed to emphasize key changes from the last update[2] and clarify ongoing areas of uncertainty.

KEY RECOMMENDATIONS FOR THE HOSPITALIST

Diagnosis

Recommendation 1. All inpatients who have used alcohol recently or regularly should be risk-stratified for AWS, regardless of whether or not they have suggestive symptoms (recommendations I.3, I.4, I.5, II.10). The Alcohol Use Disorders Identification Test-(Piccinelli) Consumption (AUDIT-PC) identifies patients at risk for AWS, and the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) identifies those at risk for severe or complicated AWS, which includes seizures and alcohol withdrawal delirium (formerly delirium tremens). The guideline emphasizes use of these tools rather than simply initiating Clinical Institute Withdrawal Assessment for Alcohol, revised (CIWA-Ar) monitoring on all such patients to diagnose AWS, as CIWA-Ar was developed for monitoring response to treatment, not diagnosis (recommendation I.6).

Treating Mild/Moderate or Uncomplicated AWS

Recommendation 2. Because of their proven track record of reducing the incidence of seizure and alcohol withdrawal delirium, benzodiazepines remain the recommended first-line therapy (recommendations V.13, V.16). Symptom-triggered administration of benzodiazepines (via CIWA-Ar) is recommended over fixed-dose administration because the former is associated with shorter length of stay and lower cumulative benzodiazepine administration[3,4] (recommendation V.23). Patients with mild AWS who are at low risk for severe or complicated withdrawal should be monitored for up to 36 hours for the development of worsening symptoms (recommendation V.1). For patients with high CIWA-Ar scores or who are at increased risk for severe or complicated AWS, frequent administration of moderate to high doses of a long-acting benzodiazepine early in AWS treatment (a practice called frontloading) is recommended to quickly control symptoms and prevent clinical worsening. This approach has been shown to reduce the incidence of seizures and alcohol withdrawal delirium (recommendations V.14, V.19, V.24).

Carbamazepine or gabapentin may be used in mild or moderate AWS if benzodiazepines are contraindicated; however, neither agent is recommended as first-line therapy because a clear reduction in seizure and withdrawal delirium has not been established (recommendation V.16). Alpha-2 agonists (eg, clonidine, dexmedetomidine) may be used to treat persistent autonomic hyperactivity or anxiety when these are not adequately controlled by benzodiazepines alone (recommendation V.36).

Treating Severe or Complicated AWS

Recommendation 3. The guideline defines severe AWS as withdrawal with severe signs and symptoms, and complicated AWS as withdrawal accompanied by seizures or delirium (Appendix Table[5]). The development of complications warrants prompt treatment. Patients who experience seizure should receive a fast-acting benzodiazepine (eg, intravenous [IV] diazepam or lorazepam) (recommendation VI.4). Patients with withdrawal delirium should receive a benzodiazepine (preferably parenterally) dosed to achieve light sedation. Clinicians should be prepared for the possibility that large doses may be required and to monitor patients for oversedation and respiratory depression (recommendations VI.13, VI.17). Antipsychotics may be used as adjuncts when withdrawal delirium or other symptoms, such as hallucinosis, are not adequately controlled

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by benzodiazepines alone, but should not be used as monotherapy (recommendation VI.20). The guideline emphasizes that alpha-2 agonists should not be used to treat withdrawal delirium (recommendation VI.21), but they may be used as adjuncts for resistant alcohol withdrawal in the intensive care unit (ICU) (recommendations VI.27, VI.29). Phenobarbital is an acceptable alternative to benzodiazepines for severe withdrawal (recommendation V.17); however, the guideline recommends that clinicians should be experienced in its use.

Treating Wernicke Encephalopathy

Recommendation 4. Thiamine should be administered to prevent Wernicke encephalopathy (WE), with parenteral formulations recommended in patients with malnutrition, severe/complicated withdrawal, or requiring ICU-level care (recommendations V.7, V.8). In particular, all patients admitted to an ICU for AWS should receive thiamine, as diagnosis of WE is often difficult in this population. Although there is no consensus on the required dose of thiamine to treat WE, 100 mg IV or intramuscularly (IM) daily for 3 to 5 days is commonly administered (recommendation V.7). Because of a lack of evidence of harm, thiamine may be given before, after, or concurrently with glucose or dextrose (recommendation V.7). The guideline does not make a specific recommendation regarding how to risk-stratify patients for WE.

Treating Underlying Alcohol Use Disorder

Recommendation 5. Hospitalization for AWS is an important opportunity to engage patients in treatment for alcohol use disorder (AUD), including pharmacotherapy and connection with outpatient providers (recommendation V.12). The guideline emphasizes that treatment for AUD should be initiated concomitantly with AWS management whenever possible but does not make recommendations regarding specific pharmacotherapies.

CRITIQUE

This guideline was authored by a committee of emergency medicine physicians, psychiatrists, and internists using the Department of Veterans Affairs/Department of Defense guidelines and the RAND/UCLA appropriateness method to combine the scientific literature with expert opinion. The result is a series of recommendations for physicians, physician assistants, nurse practitioners, and pharmacists that are not rated by strength; an assessment of the quality of the supporting evidence is available in an appendix. Four of the nine guideline committee members reported significant financial relationships with industry and other entities relevant to these guidelines.

Despite concern about oversedation from phenobarbital raised in small case series,[6] observational studies comparing phenobarbital with benzodiazepines suggest phenobarbital has similar efficacy for treating AWS and that oversedation is rare.[7-9] Large randomized controlled trials in this area are lacking; however, at least one small randomized controlled trial[10] among patients with AWS presenting to emergency departments supports the safety and efficacy of phenobarbital when used in combination with benzodiazepines. Given the growing body of evidence supporting the safety of phenobarbital, we believe a stronger recommendation for use in patients presenting with alcohol withdrawal delirium or treatment-resistant alcohol withdrawal is warranted. The guidelines also suggest that only "experienced clinicians" use phenobarbital for AWS, which may suppress appropriate use. Nationally, phenobarbital use for AWS remains low.[11]

Finally, although the guideline recommends initiation of treatment for AUD, specific recommendations for pharmacotherapy are not provided. Three medications currently have approval from the US Food and Drug Administration for treatment of AUD: acamprosate, naltrexone, and disulfiram. Large randomized controlled trials support the safety and efficacy of acamprosate and naltrexone, with or without counselling, in the treatment of AUD,[12] and disulfiram may be appropriate for selected highly motivated patients. We believe more specific recommendations to assist in choosing among these options would be useful.

AREAS IN NEED OF FUTURE STUDY

More data are needed on the safety and efficacy of phenobarbital in patients with AWS, as well as comparative effectiveness against benzodiazepines. Recruitment is ongoing for a single clinical trial comparing the effect of phenobarbital and lorazepam on length of stay among patients in the ICU with AWS (NCT04156464); to date, no randomized trials of phenobarbital have been conducted in medical inpatients with AWS. In addition, gaps in the literature exist regarding benzodiazepine selection, and head-to-head comparisons of symptom-triggered usage of different benzodiazepines are lacking.

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