University of Iowa Hospitals and Clinics

P & T News

Published by the Pharmacy and Therapeutics Subcommittee **of the University Hospital Advisory Committee and the Department of Pharmaceutical Care**

Volume 29 Number 6 April/May 2009

INSIDE INDEX

Treatment of Alcohol Withdrawal

James J. Amos, MD
Jill Fowler, PharmD
Joe Mac, PharmD

Alcohol abuse or dependence occurs in approximately 20% of hospitalized patients in some settings, and in about 40% of emergency room patients.[1,2] Alcohol withdrawal symptoms are usually minor, though in some patients they may be severe and potentially fatal.[1] Serious complications of alcohol withdrawal include seizures and alcohol withdrawal delirium, commonly called delirium tremens. Seizures usually occur within 6 to 48 hours of cessation of drinking, and patients with a history of alcohol withdrawal seizures are at increased risk.[3] Alcohol withdrawal delirium develops in approximately 5% of untreated patients and is characterized by a disturbance in consciousness with a change in cognition or perceptual disturbances. It typically does not develop until 2 to 3 days after cessation of drinking.[1] To meet diagnostic criteria for alcohol withdrawal, a patient must have two or more of the following after cessation of (or reduction in) heavy, prolonged alcohol use: autonomic hyperactivity, increased hand tremor, insomnia, nausea and vomiting, transient hallucinations or illusions, psychomotor agitation, anxiety, and grand mal seizures.[4] Pharmacologic treatment is often required to manage troublesome and potentially dangerous symptoms of alcohol withdrawal.

Benzodiazepines

Benzodiazepines are considered to be the treatment of choice for alcohol withdrawal symptoms and for prevention of complications (seizures and alcohol withdrawal delirium). By facilitating the action of the inhibitory neurotransmitter GABA, benzodiazepines suppress the CNS excitation that occurs following cessation of chronic alcohol use. Several randomized, double-blind, placebo controlled trials, as well as years of clinical experience, have established the efficacy of benzodiazepines in reducing signs and symptoms of alcohol withdrawal. In addition, meta-analysis of prospective studies showed that benzodiazepines significantly reduce the incidence of both seizures and alcohol withdrawal delirium.[5]

All the benzodiazepines appear to be equally efficacious in treating the symptoms of alcohol withdrawal; therefore, there is no consensus as to the best agent to prescribe. The long-acting agents, such as chlordiazepoxide and diazepam, generally allow for a smoother course of withdrawal and may provide superior efficacy in prevention of seizures and delirium. The use of intermediate-acting agents, such as lorazepam and oxazepam, may provide additional safety in those patients with severe liver disease or the elderly.[2,5]

Several prospective studies have shown that symptom-triggered administration of benzodiazepines can reduce the overall amount of benzodiazepines needed to treat alcohol withdrawal, helping to minimize medication side effects and possibly reducing the length of hospital stay.[5-8] Most published studies evaluating symptom-triggered benzodiazepine dosing have based doses on Clinical Institute Withdrawal Assessment Scale for Alcohol (CIWA-Ar) scores. Nurses at UIHC currently assess alcohol withdrawal symptoms using a different scale, which evaluates temperature, pulse, diastolic blood pressure, sweating, tremor, nausea/vomiting, agitation, orientation, and insomnia. Success of symptom-triggered dosing strategies is dependent on adequate education and training of staff. In cases where this training has not been provided, use of fixed doses of benzodiazepines may be a safer alternative.[5]

Examples of fixed-schedule benzodiazepine regimens utilized at UIHC:

Chlordiazepoxide 50 mg PO q 4 hours for 6 doses then,
Chlordiazepoxide 50 mg PO q 6 hours for 4 doses then,
Chlordiazepoxide 25 mg PO q 4 hours for 6 doses

- or –

Lorazepam 2 mg PO q 4 hours for 6 doses then,
Lorazepam 2 mg PO q 6 hours for 4 doses then,
Lorazepam 1mg PO q 4 hours for 6 doses then,
Lorazepam 1mg PO q 6 hours for 4 doses

The above medication regimens would be initiated when the patient presents with symptoms of withdrawal and meets the threshold of severity based on the structured assessment scale noted previously. The degree of withdrawal severity varies in individual patients, and the dosage of medications may need to be adjusted to adequately control withdrawal symptoms. The scheduled benzodiazepine dose should be held for ataxia, slurred speech, over-sedation, sleeping, or nystagmus. In patients with histories of seizures associated with alcohol withdrawal, it is reasonable to initiate the benzodiazepine regimen prior to emergence of symptoms in order to prevent recurrence of seizures.[5]

Potential Adjunctive Agents

Alternative agents are not recommended as monotherapy due to the lack of evidence to support their use as the primary agent for the management of alcohol withdrawal syndrome. **Beta-blockers** and **clonidine** have been used to help reduce the severity of withdrawal symptoms, but they do not protect against seizures and could potentiate delirium.[5] Additionally, these agents can mask the symptoms of alcohol withdrawal, leading to inappropriate delays in benzodiazepine therapy. **Carbamazepine** has evidence to support its effectiveness in treating symptoms of alcohol withdrawal without delirium; however, there is no evidence to support its use in alcohol withdrawal delirium.[1,2,5] Neuroleptic agents, such as **haloperidol**, are commonly used to manage agitation in patients with alcohol withdrawal delirium. However, caution should be used since these agents may lower the seizure threshold and have been associated with a longer duration of delirium and increased mortality.[1,2] While antihypertensives, anticonvulsants, and neuroleptic agents may have some utility for managing certain symptoms of alcohol withdrawal, all symptoms and complications of alcohol withdrawal can generally be treated with benzodiazepine monotherapy, thereby avoiding the potential adverse effects and drug interactions that may come from prescribing additional agents.

Ethyl Alcohol

Intake of ethyl alcohol (ethanol) reduces the symptoms of alcohol withdrawal, and some practitioners have used intravenous or oral administration of ethyl alcohol for this purpose. The evidence to support this practice is limited and based primarily on uncontrolled studies and case series. A recent randomized, open-label study comparing intravenous ethanol to oral diazepam for management of alcohol withdrawal in trauma patients found no advantage of ethanol over diazepam in terms of efficacy for controlling symptoms or prevention of over-sedation.[9] Intravenous alcohol administration requires monitoring of blood alcohol levels to prevent toxicity, and there is a risk of tissue damage at the injection site.[5] Use of oral ethyl alcohol (in the form of alcoholic beverages) may overcome these complications, though this practice may be viewed as condoning the continued use of alcohol in patients who suffer from alcohol dependence.[10] The dose of oral ethyl alcohol may be difficult to titrate appropriately as it has a short half-life and patients often under-report their regular consumption of alcohol. Additionally, ethyl alcohol is associated with numerous adverse effects, including well-known gastrointestinal, hepatic, hematological, and neurologic toxicities.[1,5] For these reasons, **experts do not recommend the use of ethyl alcohol for treatment of alcohol withdrawal.**[1,2,5]

Vitamin Deficiencies

Patients with alcohol dependence may be malnourished and are often thiamine deficient, putting them at high risk for Wernicke's encephalopathy and subsequent Wernicke-Korsakoff syndrome. The administration of thiamine before any source of glucose is recommended to prevent precipitation of Wernicke's encephalopathy.[1,2] The current practice at UIHC is to give a one-time 100 mg IM/IV dose of **thiamine**, followed by 100 mg orally for at least 5 days. Daily **folic acid** 1 mg orally and a daily **multivitamin** are also recommended.

Summary

Benzodiazepines are considered the drugs of choice for the management of alcohol withdrawal. Some medications, including haloperidol, may have an adjunctive role in managing alcohol withdrawal symptoms. However, due to toxicity concerns, **use of intravenous or oral ethyl alcohol (ethanol) is not recommended in this setting.** Both symptom-triggered and fixed-dose benzodiazepine regimens have been shown to be effective for suppressing the symptoms and avoiding the complications of alcohol withdrawal. Vitamin supplementation is also indicated in malnourished alcoholic patients to avoid complications from deficiencies, particularly Wernicke's encephalopathy.

References

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Written by: James J. Amos, MD, Clinical Associate Professor, Department of Psychiatry; Jill Fowler, PharmD, Clinical Pharmacy Specialist, Department of Pharmaceutical Care; and Joe Mac, PharmD, Clinical Pharmacist, Department of Pharmaceutical Care

PHARMACY AND THERAPEUTICS SUBCOMMITTEE ACTIONS

DRUGS ADDED TO STOCK

BASILIXIMAB (SIMULECT® - NOVARTIS) INJECTION
Indicated for the prophylaxis of acute organ rejection in patients receiving renal transplantation.
Cost: $1716 per 20 mg vial.

GADOXETATE (EOVIST® - BAYER) INJECTION
Indicated for use in MRI of the liver.
Cost: $126 per 10 ml vial.

HISTRELIN ACETATE (SUPPRELIN®-LA - INDEVUS) IMPLANT
Indicated for the treatment of central precocious puberty.
Cost: $14,068 per implant.

LACOSAMIDE (VIMPAT® - UCB PHARMA) TABLETS
Indicated for adjunctive therapy of partial onset seizures.
Note: Restricted to prescribing for patients with seizure disorders.
Cost: $3.45 per 50 mg tablet; $5.38 per 100 mg tablet; $6.01 per 150 mg tablet; $6.26 per 200 mg tablet.

MULTIVITAMINS AND MINERALS (STROVITE® FORTE - EVERETT) ORAL LIQUID
Indicated as a nutritional supplement for physiologically stressful conditions.
Cost: $31.38 per 483 ml bottle.

ROMIPLOSTIM (NPLATE® - AMGEN) INJECTION
Indicated for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenic purpura who have not adequately responded to corticosteroids, immunoglobulin, or splenectomy.
Note: Restricted to prescribing by attending physicians from Hematology/ Oncology.
Cost: $1032 per 250 mcg vial; $2063 per 500 mcg vial.

SODIUM BICARBONATE AND SODIUM CHLORIDE POWDER FOR MOUTHWASH (EXTEMPORANEOUSLY COMPOUNDED)
Indicated for use as a mouthwash to treat and prevent mucositis symptoms.
Cost: $18 per 120 gm bottle.

SODIUM HYALURONATE (SYNVISC®-ONE - GENZYME) INJECTION
Indicated for the treatment of knee pain associated with osteoporosis who have failed to respond adequately to conservative nonpharmacologic therapy and simple analgesics.
Cost: $684 per dose.

TREPROSTINIL (REMODULIN® - UNITED THERAPEUTICS) INJECTION
Indicated for the treatment of pulmonary arterial hypertension in patients with NYHA class II-IV symptoms.
Note: Restricted to use by the Pulmonary Hypertension Program.
Cost: $1345 per 20 mg vial.

ADDITIONAL ACTIONS

FENOFIBRATE 67 MG and 200 MG MICRONIZED CAPSULES
All fenofibrate and fenofibric acid product orders will be therapeutically substituted to the 67 mg and 200 mg generic fenofibrate capsules.

SODIUM AND POTASSIUM PHOSPHATE TABLETS
K-Phos Neutral® tablets were added to stock. Each tablet contains 250 mg (8mM) phosphorous, 45 mg (1.1 mEq) potassium, and 298 (13 mEq) sodium.

DRUGS DELETED FROM STOCK

CHLORAL HYDRATE 500 mg SUPPOSITORIES
Discontinued by the manufacturer.

DRUGS DELETED FROM STOCK (Cont'd)

FENOFIBRATE (TRICOR®) TABLETS
Replaced with generic fenofibrate capsules.

LANSOPRAZOLE (PREVACID®) CAPSULES and ORAL SUSPENSION
Replaced with omeprazole.

METAPROTERENOL (ALUPENT®) INHALATION SOLUTION
Discontinued by the manufacturer. Albuterol inhalation solution is available.

METRONIDAZOLE VAGINAL SUPPOSITORIES
Discontinued by the manufacturer. Metronidazole 0.75% vaginal gel (Metrogel® - Vaginal) is available.

NEDOCROMIL ORAL INHALER
Discontinued by the manufacturer. Cromolyn oral inhaler is available.

NEPAFENAC OPHTHALMIC SOLUTION (NEVANAC®)
Discontinued due to low use. Ketorolac ophthalmic solution is available.

PHENYLEPHRINE 0.5% NASAL SOLUTION
Discontinued due to low use. A 1% solution is available.

PREDNISONE 4 mg/ml ORAL SUSPENSION
Discontinued by the manufacturer; prednisolone 3 mg/ml solution (Orapred®) is available.

PROGESTERONE 50 and 200 mg SUPPOSITORIES
Discontinued by the manufacturer. Progesterone 100 mg vaginal inserts are available.

PROCAINAMIDE EXTENDED-RELEASE TABLETS
Note: Discontinued by all manufacturers. Other antiarrhythmics are available.

PROGESTERONE INTRAUTERINE DEVICE (PROGESTASERT®)
Discontinued by the manufacturer. Levonorgesterol (Mirena®) intrauterine device is available.

PSEUDOEPHEDRINE 10 mg with BROMPHENIRAMINE 12 mg EXTENDED-RELEASE CAPSULES
Pseudoephedrine 120 mg and chlorpheniramine 8 mg extended-release capsules are available.

PSEUDOEPHEDRINE 60 mg with CHLORPHENIRAMINE 4 mg EXTENDED-RELEASE CAPSULES
Pseudoephedrine 120 mg and chlorpheniramine 8 mg extended-release capsules are available.

RIMANTADINE (FLUMADINE®) ORAL SOLUTION
Discontinued by the manufacturer. Rimantadine oral capsules are available.

SPECIAL MOUTHWASH
Discontinued by the manufacturer.

TRETINOIN 0.05% TOPICAL LOTION
Discontinued by the manufacturer.

TRIAMCINOLONE (NASACORT AQ®) NASAL SPRAY
Replaced with budesonide (Rhinocort Aqua®) nasal spray.

UREA 40% TOPICAL OINTMENT
Discontinued by the manufacturer.

WRIGHT'S BUFFER SOLUTION
Discontinued by the manufacturer.