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Problem Drinking Part 3 - Office Based Management of Alcohol Withdrawal and Prescribing Medications for Alcohol Dependence

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Scope

This guideline provides practitioners with practical information on how to conduct office based management of withdrawal and medication management for adults aged ≥19 years with alcohol dependence.*

The following are outlined in this guideline:

- Office based management of alcohol withdrawal
- Prescribing medications for alcohol dependence

Diagnostic Code

303: Alcohol dependence syndrome

305: Non dependent use of drugs

Family physicians with a supportive, nonjudgmental, yet assertive attitude can be a great asset in confronting and treating patients with alcohol and other substance abuse problems. With the right attitude and the right tools, primary care physicians can manage most patients through the withdrawal phase of their illness and be a powerful influence in their ongoing struggle for recovery. [1]

Section 1 - Office Based Management of Alcohol Withdrawal

Contraindications to Outpatient Withdrawal Management

- History of withdrawal seizure or withdrawal delirium.
- Multiple failed attempts at outpatient withdrawal.
- Unstable associated medical conditions: Coronary Artery Disease (CAD), Insulin-Dependent Diabetes Mellitus (IDDM).
- Unstable psychiatric disorders: psychosis, suicidal ideation, cognitive deficits, delusions or hallucinations.
- Additional sedative dependence syndromes (e.g., benzodiazepines, gamma-hydroxy butyric acid, barbituates and opiates).
- Signs of liver compromise (e.g., jaundice, ascites).
- Failure to respond to medications after 24-48 hours.
- Pregnancy.
- Advanced withdrawal state (e.g., delerium, hallucinations, temperature > 38.5 °).
- Lack of a safe, stable, substance-free setting and care giver to dispense medications.

Benzodiazepines are considered the treatment of choice for the management of alcohol withdrawal symptoms. Benzodiazepines reduce the signs and symptoms of alcohol withdrawal, incidence of delirium, and seizures. Based on indirect comparisons there is currently no strong evidence that particular benzodiazepines are more effective than others and selection should be made on an individual basis.[2,3] Alprazolam and triazolam are not recommended.

* *Significant portions of this guideline were adapted from the National Institute on Alcohol Abuse and Alcoholism (NIAAA), "Helping Patients Who Drink Too Much", A Clinicians' Guide, Updated 2005 Edition, and should be fully acknowledged for developing this useful clinical tool. A full copy of their guideline and reference materials can be found on NIAAA's website at http://pubs.niaaa.nih.gov*

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Diazepam (Valium®) is recommended because of its efficacy profile, wide therapeutic window and "self tapering" effect due to its long half life. Other benzodiazepines can be considered such as: clonazepam, lorazepam and oxazepam. In the case of intolerance to benzodiazepines, physicians may wish to consider using a different class of medications (e.g., anticonvulsants). It is recommended that physicians with less experience with diazepam follow the rigid schedule. Physicians with experience using diazepam for alcohol withdrawal can consider front loading. Three medication protocols are provided (see Table 1).

When Conducting Outpatient Withdrawal, do the following:

- Start on a Monday or Tuesday unless weekend coverage is available.
- See the patient daily for the first three to four days and be available for phone contact.
- Have the patient brought to the office by a reliable family member or caregiver.
- Prescribe thiamine (Vitamin B_1) 100 mg daily for five days.
- Encourage fluids with electrolytes, mild foods and minimal exercise.
- Avoid natural remedies, caffeine or any activity that increases sweating (e.g., hot baths, showers and saunas/sweat lodges).
- Assess vital signs, withdrawal symptoms, hydration, emotional status, orientation, general physical condition and sleep at each visit.
- Encourage patient to call local (including health authority/municipal) Alcohol and Drug or Employee Assistance Programs and attend Alcoholics Anonymous (AA) meeting on day 3.
- Monitor for relapse, explore cause, and correct if possible. If unable to address cause, refer to inpatient detox.

Table 1: Treating Alcohol Withdrawal with Diazepam (Valium) [1, 2]

Schedule	Day 1	Day 2	Day 3	Day 4
Rigid	10 mg four times daily	10 mg three times daily	10 mg twice daily	10 mg at bedtime
Flexible	10 mg every 4 to 6 hours as needed based on symptoms *	10 mg every 6 to 8 hours as needed	10 mg every 12 hours as needed	10 mg at bedtime as needed
Front loading **	20 mg every 2 to 4 hours until sedation is achieved; then 10 mg every 4 to 6 hours as needed. Max 60 mg/day	10 mg every 4 to 6 hours as needed. Max 40 mg/day	10 mg every 4 to 6 hours as needed. Max 40 mg/day	None

* *Pulse rate >100 per minute, diastolic BP > 90 mm Hg or signs of withdrawal.*

** *Frequently, very little additional medication is necessary after initial loading.*

Note: Benzodiazepines should be discontinued after withdrawal symptoms resolved (5-7 days).

Section 2: Prescribing Medications for Alcohol Dependence

Three Medications Are Currently Available:

Naltrexone: Blocks euphoria associated with alcohol use. CONTRAINDICATED in patients taking opiates.

Acamprosate: Reduces chronic withdrawal symptoms.

Disulfiram: Adversive agent, causes nausea, vomiting, dysphoria with alcohol use and requires abstinence and counselling before initiation. Disulfiram should be used with caution.

Why Should Medicications be Considered for Treating an Alcohol Use Disorder?

Consider pharmacotherapy for all patients with alcohol dependency. Patients who fail to respond to psychosocial approaches and/or addiction counselling are particularly strong candidates. The above medications can be used immediately following withdrawal or any time thereafter; however, these medications should be used in conjunction with addiction counselling and other psychosocial supports.

Must Patients Agree to Abstain?

No matter which alcohol dependence medication is used, patients who have a goal of abstinence, or who can abstain even for a few days prior to starting the medication, are likely to have better outcomes. Still, it is best to determine individual goals with each patient. Some patients may not be willing to endorse abstinence as a goal, especially at first. However, abstinence remains the optimal outcome.

A patient's willingness to abstain has important implications for the choice of medication. For example, a study of oral naltrexone demonstrated a modest reduction in the risk of heavy drinking in people with mild dependence who chose to cut down rather than abstain.[4] Acamprosate is approved for use in patients who are abstinent at the start of treatment. Total abstinence is needed with disulfiram. Disulfiram is contraindicated in patients who continue to drink, because a disulfiram-alcohol reaction occurs with any alcohol intake.

Which of the Medications Should be Prescribed?

(see *Appendix A: Prescription Medication Table for Alcohol Dependence*)

Which medication to use will depend on clinical judgment and patient preference. Each has a different mechanism of action. Some patients may respond better to one type of medication than another.

NALTREXONE

Naltrexone works by blocking the euphoria associated with alcohol use. Its use is CONTRAINDICATED in patients taking opiates. Oral naltrexone is associated with lower percentage drinking days, fewer drinks per drinking day, and longer times to relapse.[5,6] It is most effective in patients with strong cravings. Efficacy beyond 12 weeks has not been established. Although it is especially helpful for curbing consumption in patients who have drinking "slips" it may also be considered in patients who are motivated, have intense cravings and are not using or going to be using opioids. It appears to be less effective in maintenance of abstinence as meta-analyses have shown variable results. Monitoring of liver enzymes may be required.

ACAMPROSATE

Acamprosate works by reducing chronic withdrawal symptoms. Acamprosate increases the proportion of dependent drinkers who maintain abstinence for several weeks to months, a result demonstrated in multiple European studies and confirmed by a meta-analysis of 17 clinical trials.[7] However, this has not been demonstrated in patients who have NOT undergone detoxification and NOT achieved alcohol abstinence prior to beginning treatment. Acamprosate should be initiated as soon as possible after detoxification and the recommended duration of treatment is one year. There is currently insufficient evidence to suggest that acamprosate has a therapeutic advantage over naltrexone.

DISULFIRAM

Disulfiram is an adversive agent that causes nausea, vomiting, and dysphoria with alcohol use. Abstinence and counselling are required before initiation of treatment with disulfiram. Data on the effectiveness of disulfiram in alcohol use disorders is mixed. Disulfiram has been shown to have modest effects on maintaining abstinence from alcohol, particularly if it is administered under supervision. It is most effective when given in a monitored fashion, such as in a clinic or by a spouse. Thus the utility and effectiveness of disulfiram may be considered limited because compliance is generally poor when patients are given it to take at their own discretion.[8,9] Disulfiram may be considered for those patients that can achieve initial abstinence, are committed to maintaining abstinence, can understand the consequences of drinking alcohol while on disulfiram, and can receive adequate ongoing supervision. It may also be used episodically for high-risk situations, such as social occasions where alcohol is present. Daily uninterrupted disulfiram therapy should be continued until full patient recovery, which may require months to years.

How Long Should Medications be Maintained?

The risk for relapse to alcohol dependence is very high in the first 6 to 12 months after initiating abstinence and gradually diminishes over several years. Therefore, a minimum initial period of 6 months of pharmacotherapy is recommended. Although an optimal treatment duration has not been established, treatment can continue for one to two years if the patient responds to medication during this time when the risk of relapse is highest. After patients discontinue medications, they may need to be followed more closely and have pharmacotherapy reinstated if relapse occurs.

If One Medication Does Not Work, Should Another Be Prescribed?

If there is no response to the first medication selected, you may wish to consider a second. This sequential approach appears to be common clinical practice, but currently there are no published studies examining its effectiveness. There is not enough evidence to recommend a specific ordering of medications.

Is There Any Benefit to Combining Medications?

There is no evidence that combining any of the medications to treat alcohol dependence improves outcomes over using any one medication alone.

Should Patients Receiving Medications Also Receive Specialized Alcohol Counselling or a Referral to Mutual Support Groups?

Offering the full range of effective treatments will maximize patient choice and outcomes, since no single approach is universally successful or appealing to patients. Medications for alcohol dependence, professional counselling, and mutual support groups are part of a comprehensive approach. These approaches share the same goal while addressing different aspects of alcohol dependence: neurobiological, psychological, and social. The medications are not prone to abuse, so they do not pose a conflict with other support strategies that emphasize abstinence. Using medications to treat patients does not interfere with counselling or other abstinence based programs such as AA.

Almost all studies of medications for alcohol dependence have included some type of counselling, and it is recommended that all patients taking these medications receive at least brief medical counselling. In a recent large trial, the combination of oral naltrexone and brief medical counselling sessions delivered by a nurse or physician was effective without additional behavioral treatment by a specialist.[10] Patients were also encouraged to attend mutual support groups to increase social encouragement for abstinence.

Rationale

Outpatient alcohol withdrawal is safe and cost effective for the vast majority of problem drinkers.[11-14] Only about 20 per cent of problem drinkers require a hospital based or inpatient setting for alcohol detoxification.[1] Patients are treated earlier in the course of their disease in an office based setting which prevents further complications, and reduces the need for hospitalization. Withdrawal as an outpatient is more effective in reaching certain populations that may not use inpatient detox, such as women, children, youth, older adults, psychiatric populations, human immunodeficiency virus (HIV) affected, and people with other disabilities.

Resources

References

1 Bayard M, Mcintyre J, Hill KR, et al. Alcohol withdrawal syndrome. Am Fam Physician. 2004 Mar 15;69(6):1443-1450.
2 Myrick H, Anton RF. Treatment of alcohol withdrawal. Alcohol Health Res World. 1998;22(1):38-43.
3 Amato L, Ninozzi S, Vecchi S, et al. Benzodiazepines for alcohol withdrawal. Cochrane Database of Systematic Reviews. 2010, Issue 3.
4 Kranzler HR, Armeli S, Tennen H, et al. Targeted naltrexone for early problem drinkers. J Clin Psychopharmacol. 23(3):294-304, 2003.
5 Bouza C, Angeles M, Munoz A, et al. Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: A systematic review. Addiction. 2004;99(7):811-828.
6 Srisurapanont M, Jarusuraisin N. Naltrexone for the treatment of alcoholism: A meta-analysis of randomized controlled trials. Int J Neuropsychopharmacol. 2005;8(2):267-280.
7 Mann K, Lehert P, Morgan MY. The efficacy of acamprosate in the maintenance of abstinence in alcohol-dependent individuals: Results of a metaanalysis. Alcohol Clin Exp Res. 2004;28(1):51-63.
8 Fuller RK, Gordis E. Does disulfiram have a role in alcoholism treatment today? Addiction. 2004;99(1):21-24.
9 Allen JP, Litten RZ. Techniques to enhance compliance with disulfiram. Alcohol Clin Exp Res. 1992;16(6):1035-1041.
10 Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioural interventions for alcohol dependence: The COMBINE study: A randomized controlled trial. JAMA. 2006;295(17):2003-17.
11 Prater CD, Miller KE, Zylstra RG. Outpatient detoxification of the addicted or alcoholic patient. Am Fam Physician. 1999;60:1175-83.

12 Hayashida M, Alterman AI, McLellan AT, et al. Comparative effectiveness and costs of inpatient and outpatient detoxification of patients with mild-to-moderate alcohol withdrawal syndrome. N Engl J Med. 1989;320:358-65.
13 Hayashida M, Alterman A, McLellan T, et al. Is inpatient medical alcohol detoxification justified: results of randomized, controlled study. NIDA Res Monogr. 1988;81:19-25.
14 Stockwell T, Bolt L, Milner I, et al. Home detoxification from alcohol: its safety and efficacy in comparison with inpatient care. Alcohol Alcohol. 1991;26:645-50.
15 Kranzler HR, Gage A. Acamprosate efficacy in alcohol-dependent patients: Summary of results from three pivotal trials. Am J Addict. 2008 Jan-Feb;17(1):70-6.
16 Sass H, Soyka M, Mann K, et al. Relapse prevention by acamprosate: Results from a placebo-controlled study on alcohol dependence. Arch Gen Psychiatry. 1996 Aug;53(8):673-80.
17 U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Alcohol Abuse and Alcoholism. Helping patients who drink too much: A clinician's guide. 2005.

Appendices

Appendix A: Prescription Medication Table for Alcohol Dependence

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Appendix A: Prescription Medication Table for Alcohol Dependence [a]

Generic Name Brand/Trade Name	Adult Oral Dose	Mechanism of Action	Cautions/ Contraindications [b]	Therapeutic Considerations (including side effects and drug interactions) [b]	PharmaCare Coverage	Annual Cost (cost per tablet/capsule)
Naltrexone [c] **(ReVia®)** *(Approved indication: treatment of alcohol dependence to support abstinence and decrease relapse risk)*	50 mg once daily (start at 25 mg once daily to minimize side effects)	Blocks the action of endorphins when alcohol is consumed.	Must be opioid free for 7 to 10 days before initiating and must stop for 7 days if opioid therapy required. Liver failure, current or anticipated opioid use, hypersensitivity.	Some side effects include: nausea, vomiting, headache, fatigue, somnolence, hepatotoxicity. Drug interactions: opioids, medications that can also contribute to hepatocellular injury (i.e. NSAIDS)	Limited coverage[d]	Annual cost = $1952.50 (50 mg tablet = $5.30)
Acamprosate **(Campral®)** *(Approved indication: maintenance of abstinence from alcohol in patients who are abstinent at treatment initiation)*	666 mg three times daily 333 mg three times daily if mild to moderate renal impairment	Restores the imbalance of neuronal excitation and inhibition caused by chronic alcohol use.	Severe renal impairment, pregnancy, hypersensitivity.	Some side effects include: diarrhea, nausea, headache, depression. Suicidal ideation (rare) Can be used in patients with liver disease Drug interactions: naltrexone	Limited coverage[d]	Annual cost = $1817.70 (333 mg tablet = $0.80)
Compounded disulfiram **(Antabuse® no longer available)** *(Approved indication: deterrent to alcohol use/abuse)*	Maintenance: 250 mg once daily Range: 125 to 500 mg once daily	Blocks alcohol metabolism causing an aversive reaction to alcohol when it is consumed. Reaction: flushing, nausea, vomiting, headaches, palpitations, hypotension.	Total abstinence is needed. Do not give to intoxicated individuals or within 36 hours of alcohol consumption. Cardiac disease, cerebrovascular disease, renal/ hepatic failure, pregnancy, psychiatric disorders, alcohol consumption, hypersensitivity.	DO NOT ADMINISTER WITHOUT PATIENT'S KNOWLEDGE. Alcohol reaction can occur up to two weeks after last dose and symptoms (severe) can include: hepatoxicity, peripheral neuropathy, respiratory depression, psychotic reactions, optic neuritis. Some common side effects include: drowsiness, metallic taste, impotence, headache. Drug interactions: alcohol containing medications, metronidazole, warfarin, diazepam, amitriptyline. phenytoin.	Regular Benefit	Annual cost = $146 (125 mg capsule = $0.30) (250 mg capsule = $0.40) (500 mg capsule = $0.80)

a. All treatments should be part of a comprehensive treatment program that includes psychosocial support.
b. This is not an exhaustive list. For complete details please refer to the drug monographs.
c. Naltrexone injectable extended release (Vivitol®) is not available in Canada at time of publication.
d. PharmaCare coverage will only be provided for a patient who meets the Limited Coverage criteria, and whose prescription is written by a prescriber who has entered into a Collaborative Prescribing Agreement.

Note: Please check with Health Canada for product monographs and for advisories, warnings and recalls at: www.hc-sc.gc.ca

Pricing is approximate as per PharmaNet 2010/06/24 and does not include dispensing fee.

The information in this chart was drawn primarily from package inserts and references 15, 16 and 17.
And also: Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals. Toronto, Ontario; 2010.
Micromedex Healthcare Series Website.
Accessed June 20, 2010.

PharmaCare Coverage Definitions

G: generic(s) are available.
regular coverage: also known as regular benefit; does not require Special Authority; patients may receive full coverage*
partial coverage: Some types of regular benefits are only partially covered* because they are included in the Low Cost Alternative (LCA) program or Reference Drug Program (RDP) as follows:
LCA: When multiple medications contain the same active ingredient (usually generic products), patients receive full coverage* for the drug with the lowest average PharmaCare claimed price. The remaining products get partial coverage.
RDP: When a number of products contain different active ingredients but are in the same therapeutic class, patients receive full coverage* for the drug that is medically effective and the most cost-effective. This drug is designated as the Reference Drug. The remaining products get partial coverage.
Special Authority: requires Special Authority for coverage. Patients may receive full or partial coverage* depending on LCA or RDP status. These drugs are not normally regarded as first-line therapies or there are drugs for which a more cost-effective alternative exists.
no coverage: does not fit any of the above categories;
*coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See www.health.gov.bc.ca/pharmacare/ for further information.