Medications for Alcohol Use Disorder

Jasen Christensen, DO
Associate Professor
Department of Psychiatry and Behavioral Sciences
University of New Mexico School of Medicine

Disclosures

Nothing to disclose

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Identify the FDA-approved and off-label medications for alcohol use disorder.
- Discuss the evidence supporting each medication.
- Apply treatments to appropriate cases.

What is a Standard Drink?

A 12-ounce can of
ordinary BEER

A 5-ounce glass of WINE or
a 2–4-ounce glass of SHERRY

A 1.5-ounce shot of SPIRITS
(whiskey, gin, rum, vodka, etc.)

5% Alcohol

Some beers contain 7% alcohol or more
A pint glass (16 oz) of 7% beer = 1.8 drinks

Screening tools

NIAAA Single Alcohol Screening Question: "How many times in the past year have you had (4 for women, or 5 for men) or more drinks in a day?" A response of *one or more* warrants follow-up

Alcohol Use Disorder Identification Test (AUDIT; 10 items) and **Alcohol Use Disorder Identification Test** (AUDIT-C; 3 items)

QUESTIONS	0	1	2	3	4	5	6	Score
1. How often do you have a drink containing alcohol?	Never	Less than monthly	Monthly	Weekly	2-3 times a week	4-6 times a week	Daily	
2. How many drinks containing alcohol do you have on a typical day you are drinking?	1 drink	2 drinks	3 drinks	4 drinks	5-6 drinks	7-9 drinks	10 or more drinks	
3. How often do you have X (5 for men; 4 for women & men over age 65) or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	2-3 times a week	4-6 times a week	Daily	
							Total	

NIAAA has additional resources for screening tools that may be appropriate for adolescents and people from diverse backgrounds

Medications for AUD

FDA-approved

- Naltrexone (Revia, Depade) - - 1st line tx
- Acamprosate (Campral) - - 1st line tx
- Disulfram (Antabuse)
- Long Acting Injectable Naltrexone (Vivitrol)

Off-label

- Gabapentin (Neurontin)
- Topiramate (Topamax)

Naltrexone Evidence

Cochrane Systematic Review of 50 RTCs (7793 patients)

Reduced risk of heavy drinking to 83% of placebo group

Decreased drinking days by 4%

Rosner S, et al. Opioid antagonists for alcohol dependence.
Cochrane Database Systematic Review, 2010

Naltrexone reduced risk of heavy a drinking day (HR=0.72)

Patients taking Naltrexone fared similarly to those receiving behavioral intervention

Anton R, et al. *Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence, The COMBINE Study: A randomized Controlled Trial* , JAMA 2006; 295(17)

Prescribing **Naltrexone**

- **Patient must be opioid-free for at least 7 days**
- **Naltrexone can be started while patient is still drinking**
- **Prescribe Naltrexone 50mg oral every morning**
- **Some patients benefit from higher dose: 100mg QAM**
- **If AST or ALT >5 x reference max, consider alternatives**
- **Most commonly used anti-craving medication in pregnancy ***

Christensen C. Management of chemical dependence in pregnancy, *Clin Obstet Gynecol* 2008;51 (2): 445

Acamprosate Evidence

Cochrane Systematic Review of 24 RTCs (6915 patients)

Reduced risk of any drinking to 86% of placebo group.

Rosner S, et al. Acamprosate for alcohol dependence.
Cochrane Database Syst Rev. 2010.

Acamprosate showed no significant effect on alcohol use, either alone or in combination with Naltrexone.

Anton R, et al. *Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence, The COMBINE Study: A randomized Controlled Trial* , JAMA 2006; 295(17)

Prescribing **Acamprosate**

- **Start after withdrawal period**
- **But continue treatment even if patient uses alcohol**
- **Dose is 666mg three times per day**
- **Reduce dose to 333mg TID if CrCl is 30-50**
- **Contraindicated if CrCl is less than 30**

Disulfram Evidence

Effective in reducing heavy drinking days, reducing average weekly consumption, increasing # of abstinent days [1]

Trials suggest only effective if taken routinely under supervised conditions [2]

1. Laaksonen E, et al. A randomized, multicentre, open-label, comperative trial of disulfram, naltrexone and acamprosate in the treatment of alcohol dependence. *Alcohol* 2008;43(1):53.

2. Garbutt JC, et al. Pharmacological treatment of alcohol dependence: a systematic review of the evidence. *JAMA* 1999;281(14):1318.

Prescribing **Disulfram**

Dose range 125-500mg daily

Patient MUST be abstinent to start med

Patient must be able to understand that even small amounts of alcohol will cause the reaction (flushing, headache, nausea, vomiting, vertigo, confusion).

For patients who have the goal of maintaining abstinence.

Caution Advised in Hepatic Impairment

Once monthly injectable **Naltrexone**

380mg IM Q4 weeks

Must be opioid free for at least 7 days

Caution advised if CrCl < 50
No adjustment for Child-Pugh Class A or B

Multicenter trial of 315 patients randomly assigned to either LAI Naltrexone or placebo for 3 months

- **73% received all 3 injections**
- **18% abstinence rate (10% for placebo)**
- **Fewer drinking days (p=0.003)**
- **Fewer heavy drinking days (p=0.0045)**

Kranzler H, et al. Naltrexone Depot for Treatment of Alcohol Dependence: A Multicenter, Randomized, Placebo-controlled Clinical Trial. *Alcoholism: Clinical and Experimental Research*. July 2004. 28(7): 1051-1059

Topiramate Evidence

12-week trial, n=150 with alcohol dependence
Topiramate 25-300mg per day vs placebo
- **2.88 fewer drinks per day (p=0.0006)**
- **27.6% fewer heavy drinking days (p=0.0003)**
- **26.2% more days abstinent (p=0.0003)**

Johnson BA, et al. Oral Topiramate for treatment of alcohol dependence: a randomized controlled trial. *Lancet* 2003; 361(9370):1677.

12-week trial, n=155 with alcohol dependence
Topiramate vs Placebo
- **time to first relapse (7.8 vs 5.0 weeks)**
- **weeks of heavy drinking (3.4 vs 5.9)**
- **% abstinent at 4 weeks (67.3 vs 42.6)**
- **% abstinent at 8 weeks (61.5 vs 31.5)**

Baltieri DA, et al. Comparing Topiramate with Naltrexone in treatment of alcohol dependence. *Addiction* 2008; 103(12):2035

12-week trial, n=30 with PTSD and Alcohol Use Disorder
- **Significant reduction in amount of alcohol**
- **Significant reduction in hyperarousal symptoms**

Batki S, et al. Topiramate Treatment of Alcohol Use Disorder in Veterans with PTSD: A Randomized Controlled Pilot Trial. *Alcoholism: Clinical and Experimental Research* 2014;38(8)

Prescribing **Topiramate**

Start 25mg BID, increase to 50mg BID after a week.

Consider advancing to 100mg BID

Can be started while patient is still drinking.

Cognitive and concentration problems more likely at doses >200mg daily.

Induces metabolism of oral contraceptives at doses > 200mg daily.

Teratogenic (craniofacial defects, hypospadias).

Contraindicated if history of Calcium Phosphate renal stones.

Warn about and monitor for side effects:

Paresthesias (50%) **Taste Perversion (23%)**

Decreased Appetite (20%) **Decreased Concentration (15%)**

Gabapentin

Double blind, placebo-controlled RTC (n=150) [1]
Dose: 600mg TID
Abstinence rate 4.1% placebo, 11% gabapentin (p=0.04)
No serious drug-related events.

150 patients with dependence for 6 weeks [2]
Randomized to Naltrexone + Gabapentin vs Naltrexone alone
Combination had longer delay to heavy drinking
Fewer heavy drinking days

1. Mason, BJ. Gabapentin treatment for alcohol dependence: a randomized clinical trial. *JAMA* Internal Med. 2014, 174(1):70

2. Anton R, et al. Gabapentin Combined with Naltrexone for the Treatment of Alcohol Dependence *American Journal of Psychiatry* 2011;168(7):709-717

Thank you for what you do!

Q&A