Pharmacologic treatment of alcohol use disorder

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Clinical question

Which Health Canada–approved pharmacologic treatments are effective for alcohol use disorder (AUD)?

Bottom line

Both acamprosate and naltrexone show benefit for alcohol abstinence compared with placebo. For every 12 patients treated with acamprosate, and every 20 patients treated with naltrexone, 1 fewer patient returns to drinking compared with placebo after 12 to 52 weeks. For harm reduction, naltrexone can reduce return to heavy drinking for 1 of every 13 patients.

Evidence

Results are statistically significant unless noted.

- In a systematic review of RCTs of 12- to 52-week treatments, most included supportive therapy and required detoxification. Results versus placebo were as follows[1]:
  -Return to any drinking:
  —For acamprosate (16 RCTs, N=4847), the most common dose was 666 mg 3 times per day. The rate was 76% versus 83% for placebo (number needed to treat [NNT] of 12).
  —For 50 mg of oral naltrexone daily (16 RCTs, N=2347), the rate was 63% versus 68% with placebo (NNT=20).
  —There was no difference with injectable naltrexone (2 RCTs, N=939) or disulfiram (2 RCTs, N=492).
  -Return to heavy drinking:
  —For 50 mg of oral naltrexone daily (19 RCTs, N=2875), the rate was 46% versus 54% with placebo (NNT=13).
  —There was no difference with acamprosate (7 RCTs, N=2496).
- Earlier systematic reviews of acamprosate[2] and naltrexone[3] reported similar results.
- Evidence is insufficient or finds no benefit for acamprosate or naltrexone on mortality[1,4,5] or quality of life.[1]
- The most common adverse effects for naltrexone[3,5] were nausea (26% vs 16% for placebo, number needed to harm [NNH] of 10) and sleepiness (21% vs 16% for placebo, NNH=20). For acamprosate,[4] the incidence of diarrhea (16% vs 10% for placebo, NNH=17) decreases after the first 4 weeks of treatment.

Context

- Guidelines suggest that first-line pharmacotherapy include acamprosate for abstinence or naltrexone for reduced drinking or abstinence, and give practical prescribing tips.[6]
- Limited evidence has evaluated as-needed naltrexone. It might reduce alcohol consumption when used as cravings arise or before expected drinking.[7]
- Supportive interventions, including brief interventions in primary care, might benefit 1 in 10 individuals with excessive alcohol intake.[8]
- If patients do not respond to approved medications, a trial of alternative medications (eg, topiramate, gabapentin) might be reasonable.[6]

Implementation

In Canada, alcohol use is linked to about 8% of all deaths.[6] Hospitalizations for AUD have increased over time, as has the number of patients presenting to primary care for alcohol-attributable diseases.[9] Only limited numbers of individuals with AUD are offered treatment.[6] The existence of multiple medications with evidence of benefit provides options for shared, informed decision making with patients. While abstinence is a laudable goal, reductions in return to heavy drinking or reduced heavy drinking days are also associated with improved outcomes.[10]

Ms Finley is a medical student, **Dr Rumley** is a second-year family medicine resident, and **Dr Korownyk** is a family physician and Associate Professor in the Department of Family Medicine, all at the University of Alberta in Edmonton.

Competing interests
None declared

References

1. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. *JAMA* 2014;311(18):1889-900.
2. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. *Cochrane Database Syst Rev* 2010;(9):CD004332.
3. Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2010;(12):CD001867.
4. Rosenthal RN, Gage A, Perhach JL, Goodman AM. Acamprosate: safety and tolerability in the treatment of alcohol dependence. *J Addict Med* 2008;2(1):40-50.
5. Bolton M, Hodkinson A, Boda S, Mould A, Panagioti M, Rhodes S, et al. Serious adverse events reported in placebo randomized controlled trials of oral naltrexone: a systematic review and meta-analysis. *BMC Med* 2019;17:10.
6. British Columbia Centre on Substance Use, BC Ministry of Health, BC Ministry of Mental Health and Addictions. *Provincial guideline for the clinical management of high-risk drinking and alcohol use disorder.* Vancouver, BC: British Columbia Centre on Substance Use; 2019.
7. Heinälä P, Alho H, Kiianmaa K, Lönngvist J, Kuoppasalmi K, Sinclair JD. Targeted use of naltrexone without prior detoxification in the treatment of alcohol dependence: a factorial double-blind, placebo-controlled trial. *J Clin Psychopharmacol* 2001;21(3):287-92.
8 Salvalaggio G, Korownyk C. *Getting patients to drink less—are words mightier than drink?* Tools for Practice #134. Edmonton, AB: Alberta College of Family Physicians; 2015.
9. Slaunwhite AK, Macdonald S. Primary health care utilization for alcohol-attributed diseases in British Columbia Canada 2001-2011. *BMC Fam Pract* 2015;16:34.
10. Witkiewitz K, Roos CR, Pearson MR, Hallgren KA, Maisto SA, Kirouac M, et al. How much is too much? Patterns of drinking during alcohol treatment and associations with post-treatment outcomes across three alcohol clinical trials. *J Stud Alcohol Drugs* 2017;78(1):59-69.

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