Cochrane for Clinicians

Putting Evidence into Practice

Effectiveness of Acamprosate in the Treatment of Alcohol Dependence

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Dr. Cayley presents a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://www.cochrane.org/reviews/en/ab004332.html.

EB CME

This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 537.

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Clinical Scenario

A patient who successfully completed inpatient treatment for alcohol dependence is concerned about relapse and requests advice on measures that can help maintain abstinence from alcohol use.

Clinical Question

Is acamprosate (Campral) effective for maintaining abstinence from alcohol use?

Evidence-Based Answer

When used in conjunction with detoxification and psychosocial interventions for treating alcohol dependence, acamprosate can reduce the risk of any return to drinking and improve cumulative abstinence rates.[1] (Strength of Recommendation = A, based on consistent, good-quality patient-oriented evidence)

Practice Pointers

Alcohol abuse is a major health risk worldwide, causing approximately 3 percent of deaths globally and contributing significantly to the risks of stroke, ischemic heart disease, hypertension, diabetes mellitus, and liver cancer, as well as motor vehicle collisions, drownings, and homicides.[2] Although treatment of alcoholism is complex and studies of treatment effectiveness are challenging, a previous Cochrane review found that brief interventions can reduce weekly alcohol consumption, emergency department visits, and alcohol-related injuries in outpatient settings.[3] Other evidence has shown that disulfiram (Antabuse) may reduce total days of drinking without improving overall abstinence,[4] and naltrexone (Revia) is effective for reducing overall alcohol use.[5]

Acamprosate is a synthetic glutamate receptor agonist that has been prescribed in Europe for more than 20 years and was approved by the U.S. Food and Drug Administration in 2004. Although its mechanism of action remains unclear, it has been suggested that acamprosate may act to reduce processes related to alcohol withdrawal, as well as reduce the rewarding effects of alcohol intake.[1]

This Cochrane review evaluated the effectiveness and tolerability of acamprosate for helping patients dependent on alcohol to maintain abstinence. In all 24 of the included trials, acamprosate was prescribed for at least four weeks in addition to psychosocial interventions, which varied across studies. All trials except for one were in adult populations, and all trials except for one included pretreatment alcohol detoxification. The majority of patients included in the trials met diagnostic criteria for alcohol dependence. The typical acamprosate dosage was four to six tablets (333 mg each) per day.

Among patients taking acamprosate in the 24 trials, risk of return to any drinking was 86 percent that of patients treated with placebo (i.e., 14 percent less risk in treatment group compared with placebo). Based on statistical weighting of trials, the authors calculated a number needed to treat of 9 to prevent one additional patient from returning to drinking. Patients treated with acamprosate also maintained cumulative abstinence (i.e., total days without alcohol use, whether or not the patient had periodic return to drinking) for 11 percent longer than patients taking placebo. The only adverse effect of acamprosate that reached statistical significance compared with placebo was diarrhea (the authors calculated a

Cochrane Abstract

Background: Alcohol dependence is among the main health risk factors in most developed and developing countries. Therapeutic success of psychosocial programs for relapse prevention is moderate, but could potentially be increased by an adjuvant treatment with the glutamate antagonist acamprosate.

Objectives: To determine the effectiveness and tolerability of acamprosate in comparison with placebo and other pharmacologic agents.

Search Strategy: The authors searched the Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE, and CINAHL in January 2009. They also asked manufacturers and researchers about any unpublished trials.

Selection Criteria: All double-blind, randomized controlled trials that compare the effects of acamprosate with placebo or active control on drinking-related outcomes.

Data Collection and Analysis: Two authors independently extracted data. Trial quality was assessed by one author and cross-checked by a second author. Individual patient data meta-analyses were used to verify the primary effectiveness outcomes.

Main Results: Twenty-four randomized controlled trials with 6,915 participants fulfilled inclusion criteria and were considered in the review. Compared with placebo, acamprosate was shown to significantly reduce the risk of any drinking (risk ratio [RR] = 0.86; 95% confidence interval [CI], 0.81 to 0.91; number needed to treat [NNT] = 9.09; 95% CI, 6.66 to 14.28) and significantly increase the cumulative abstinence duration (mean difference = 10.94 days; 95% CI, 5.08 to 16.81), whereas secondary outcomes (e.g., γ-glutamyltransferase level, heavy drinking) did not reach statistical significance. Diarrhea was the only adverse effect that was more frequently reported for acamprosate treatment than placebo (risk difference = 0.11; 95% CI, 0.09 to 0.13; NNT = 9.09; 95% CI, 7.69 to 11.11). Effects of industry-sponsored trials (RR = 0.88; 95% CI, 0.80 to 0.97) did not significantly differ from those of nonprofit-funded trials (RR = 0.88; 95% CI, 0.81 to 0.96). In addition, the linear regression test did not indicate a significant risk of publication bias ($P = .861$).

Authors' Conclusions: Acamprosate appears to be an effective and safe treatment strategy for supporting continuous abstinence after detoxification in alcohol-dependent patients. Although the sizes of treatment effects appear to be rather moderate in their magnitude, they should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.

weighted number needed to harm of 9), but this adverse effect did not affect adherence to treatment. Overall trial dropout because of adverse effects or any other cause was actually greater in patients taking placebo.

Three of the studies also compared acamprosate versus naltrexone; two studies compared combination treatment of acamprosate and naltrexone versus placebo; and two studies compared combination treatment of acamprosate and naltrexone versus acamprosate alone. None of these comparisons demonstrated statistically significant treatment benefits among interventions. However, these comparisons showed that acamprosate carried a higher risk of diarrhea, and that the combination of acamprosate and naltrexone led to a markedly higher rate of withdrawal because of adverse events compared with placebo or acamprosate alone.

Ten trials reported posttreatment follow-up. They found that treatment effects for return to drinking and for cumulative abstinence remained statistically significant three to 12 months after study conclusion, indicating that benefits of acamprosate may persist beyond the treatment period.

Although treatment of alcohol abuse is complicated and can be associated with high relapse rates, use of acamprosate in addition to psychosocial interventions for patients who have already been detoxified is associated with reduced return to drinking and increased cumulative abstinence during treatment and for up to one year afterward.

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Cochrane Briefs

Stage-Based Interventions for Smoking Cessation

Clinical Question

Should interventions for helping patients stop smoking be tailored to their stage of readiness to quit?

Evidence-Based Answer

Although providing stage-based smoking cessation interventions for those trying to quit appears to be more effective than not intervening at all, the evidence does not support tailoring interventions to a patient's perceived motivational stage of change. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

Tobacco use is the cause of more than 400,000 deaths in the United States each year.[1] Studies show that interventional counseling by primary care physicians has a modest but measurable impact on cessation rates.[2] Some advocate tailoring motivational counseling to a patient's perceived readiness to quit. One stage-based model of behavioral analysis suggests that smokers begin in the precontemplation stage, from which they progress through the stages of contemplation, preparation, action, and finally to maintenance as they quit smoking.

The authors of this Cochrane Review searched for studies evaluating the effectiveness of stage-based intervention strategies compared with non–stage-based interventions or usual care. Trials that did not include a minimum of six months' follow-up after start of treatment were excluded, as were those in which assessment of patients' stage of change did not alter the intervention. Forty-one trials met inclusion criteria. Four trials involving 3,255 patients directly compared stage-based with non–stage-based interventions. Of these, two trials compared the use of these strategies in self-help materials and two compared these strategies during individual counseling. For stage-based versus standard self-help materials, the combined relative risk (RR) was 0.93 (95% confidence interval [CI], 0.62 to 1.39). For stage-based versus counseling, the RR was 1.0 (95% CI, 0.82 to 1.22). Thus, there was no clear difference between patient outcomes when the intervention was determined by stage of change.

In the remainder of trials, which compared stage-based interventions with usual care or no intervention in a variety of settings (e.g., telephone, lay, or physician interviewing; computer games), there was a small but clear benefit to the intervention. For example, in six trials comparing stage-based self-help versus usual care or assessment, the RR was 1.32 (95% CI, 1.01 to 1.59). In 13 trials comparing individual counseling with any control, the RR was 1.24 (95% CI, 1.08 to 1.42).

These data support the use of interventional counseling to help patients stop smoking. Smoking cessation counseling strategies should be used regardless of the patient's perceived readiness to quit.

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