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Baclofen for Alcohol Use Disorder: A Cochrane Review Summary With Commentary

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Key Points

- Alcohol use disorder (AUD) affects approximately 5% of adults globally, with only about 1% receiving medication-assisted treatment, despite evidence of effectiveness.
- A Cochrane Review found moderate-certainty evidence that baclofen probably reduces relapse risk and increases abstinent days, particularly among patients who have completed detoxification.
- An RTI–University of North Carolina Evidence-based Practice Center review found low certainty of evidence for baclofen in reducing return to any drinking.
- Treatment decisions should consider medication effectiveness, ease of use, side effects, and patient preferences, with stronger evidence supporting Food and Drug Administration–approved medications like naltrexone and acamprosate compared with off-label options like baclofen.
- Future research should prioritize direct comparisons between medications, studies in primary care settings, and investigation of treatment effectiveness in diverse populations.

Background

This paper summarizes the published Cochrane Review, "Baclofen for Alcohol Use Disorder," by R. Agabio, R. Saulle, S. Rösner, and S. Minozzi[1,*]

Alcohol use disorder (AUD) affects millions globally, contributing significantly to physical, psychological, and social burdens. Current treatments, including psychosocial and pharmacological approaches, often have limited efficacy. Baclofen is being explored as a potential pharmacotherapy for AUD, particularly in patients resistant to existing treatments or at high risk of relapse. This Cochrane Review examines the evidence for the effectiveness and safety of baclofen in reducing alcohol consumption and promoting abstinence in individuals with AUD. Baclofen is a gamma-aminobutyric acid type B (GABA-B) receptor agonist. GABA-B receptors interact with biological pathways involved in AUD. The agonist's mechanism of action is unclear, but the primary mechanism of action for AUD may be the reduction of the reinforcing

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properties of alcohol by suppressing alcohol-stimulated dopamine release in the mesolimbic dopamine system.[2]

Unhealthy alcohol use is the third leading preventable cause of death in the United States, accounting for more than 140,000 deaths annually.[3] Data from the 2020 National Survey on Drug Use and Health suggest that more than 28.3 million Americans 12 years of age or older met *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition,[4] criteria for AUD in the past year.[5,6] Only 0.9% of Americans who reported an AUD in the past year received any medication-assisted AUD treatment, with 1% prescribed an approved medication as part of treatment, despite evidence of effectiveness for some pharmacotherapies.[7]

Methods

The Cochrane Review evaluated baclofen to achieve abstinence or to reduce alcohol consumption in people with AUD and included 17 randomized controlled trials (RCTs) with 1,818 participants. Participants were adults diagnosed with AUD and treated in outpatient settings.[1] Baclofen was compared with placebo, naltrexone, or acamprosate, with dosages ranging from 30 mg to 300 mg daily and treatment durations lasting 12 weeks or longer. Primary outcomes assessed included relapse, frequency of use including mean number or percentage of days abstinent and heavy drinking days, amount of use, adverse events, and dropouts from treatment, and secondary outcomes assessed included cravings, anxiety, and depression. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system was used to evaluate the certainty of evidence, and results were stratified by dose, treatment duration, and detoxification status.

Search Methodology

The Cochrane Review authors searched for studies of baclofen interventions in AUD in November 2021. Systematic searches were conducted in multiple databases, including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, PsycINFO, Web of Science, and CINAHL. Clinical trial registries and reference lists of relevant publications were also examined. No restrictions were placed on language, year, or publication status. Eligible studies were RCTs of at least 12 weeks in duration that compared baclofen with placebo or active controls in individuals with AUD.

Main Results

The review included 17 RCTs with a total of 1,818 participants with a diagnosis of AUD according to the *Statistical Manual of Mental Disorders*, 4th edition,[8] or International Classification of Diseases, 10th edition, criteria. Most studies were conducted in the United States (n = 5), with additional studies in Australia (n = 2), France (n = 2), Italy (n = 2), India (n = 2), Germany (n = 1), Israel (n = 1), Russia (n = 1), and the Netherlands (n = 1). Participants were primarily male (70%), with an average age of 46.5 years. Baclofen was studied at various doses (30 mg to 300 mg daily), and treatment durations ranged from 12 weeks to over a year. Psychosocial treatments were integrated in 16 studies to accompany pharmacotherapy.

Across the included studies, 12 focused on participants with a diagnosis of AUD who had completed detoxification, while 5 included mixed populations of participants who had completed detoxification and those who had not. Participants who completed detoxification included those who were abstinent from alcohol at least 3 days before treatment and participants who were not detoxified include those who were still drinking at the beginning of treatment. Fifteen RCTs compared baclofen with placebo, two RCTs compared baclofen with acamprosate, and two RCTs compared baclofen with naltrexone. Key findings are detailed in the following section.

Comparison 1: Baclofen Compared With Placebo

Primary Outcomes

Relapse: Return to Any Drinking at End of Treatment. Twelve studies with 1,057 participants showed that baclofen likely reduces the risk of relapse compared with placebo (risk ratio [RR]: 0.87; 95% confidence interval [CI]: 0.77 to 0.99; moderate-certainty evidence). Certainty in this finding was downgraded to moderate due to inconsistency.

Frequency of Use: Percentage of Days Abstinent. Sixteen comparisons from 12 studies with 1,273 participants showed that baclofen increased the percentage of abstinent days compared with placebo (mean difference [MD]: 9.07%; 95% CI: 3.30 to 14.85; high certainty evidence).

Heavy Drinking Days. Thirteen studies with 840 participants showed that baclofen had little to no impact on the number of heavy drinking days compared with placebo (standardized mean difference [SMD]: -0.18; 95% CI: -0.48 to 0.11). The certainty of evidence was downgraded to moderate due to inconsistency.

Drinks per Drinking Day. Baclofen likely does not reduce the number of drinks per drinking day (MD: -0.45; 95% CI: -1.20 to 0.30; 9 studies, 392 participants). Certainty of evidence was downgraded to moderate due to high risk of attrition and reporting bias.

Adverse Events and Dropouts

Baclofen does not significantly increase the likelihood of experiencing at least one adverse event compared with placebo (RR: 1.05; 95% CI: 0.99–1.11; 10 studies, 738 participants).

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Certainty of evidence was high. Common adverse effects include fatigue, dizziness, and muscle spasms.

Baclofen did not significantly affect dropout rates (RR: 0.88; 95% CI: 0.74 to 1.03; 17 studies, 1,563 participants; high-certainty evidence). Dropout rates due to adverse events were higher but not statistically significant (RR: 1.39; 95% CI: 0.89–2.18; 16 studies, 1,499 participants; high-certainty evidence).

Subgroup Results

When possible, review authors examined results by subgroups, including detoxification status, dose variability, and study duration:

Detoxification Status. Baclofen's effects were more pronounced among participants who completed detoxification. For relapse, individuals who were detoxified showed a pooled effect of RR: 0.87 (95% CI: 0.77 to 0.99), with moderate-certainty evidence supporting reduced relapse rates compared with placebo. In contrast, participants who were not detoxified did not demonstrate a significant reduction in relapse rates. Similarly, the increase in abstinent days was significant in participants who were detoxified (MD: 9.07%; 95% CI: 3.30 to 14.85; high-certainty evidence), while no significant improvement in abstinent days was observed for individuals who were not detoxified.

Dose Variability. Studies grouped by baclofen dose showed that lower doses (<100 mg/day) had no significant effect on heavy drinking days (SMD: -0.18; 95% CI: -0.48 to 0.11), while higher doses (>100 mg/day) were associated with marginal reductions. However, evidence for higher doses was less certain due to limited sample sizes in the subgroup analysis.

Study Duration. Longer-duration studies (>12 weeks) showed more consistent reductions in relapse rates compared with shorter studies. High-certainty evidence indicated that prolonged baclofen treatment increases abstinent days and reduces adverse events. Shorter studies produced inconsistent results, potentially reflecting insufficient treatment durations to achieve maximum efficacy.

These subgroup analyses indicated that the effect of baclofen varied based on detoxification status, dose, and treatment duration, with the strongest effects observed in participants who were detoxified, had higher doses, and participated in studies lasting over 12 weeks.

Secondary Outcomes

Craving. Baclofen had little to no impact on reducing alcohol craving (SMD: -0.16; 95% CI: -0.37 to 0.04; 17 studies, 1,275 participants). Certainty of evidence was downgraded to moderate due to high heterogeneity.

Anxiety and Depression. No significant differences were found between baclofen and placebo in terms of anxiety (MD: -0.01; 95% CI: -0.14 to 0.11; 15 studies, 1,123 participants) or depression (SMD: 0.07; 95% CI: -0.12 to 0.27; 11 studies, 1,029 participants). Certainty of evidence was downgraded to moderate due to imprecision and variability in baseline anxiety levels among participants and high heterogeneity, respectively.

Comparison 2: Baclofen Compared With Other Medications

Primary Outcomes

Baclofen Versus Acamprosate

Relapse: Return to Any Drinking. One study (60 participants) showed no significant difference between baclofen and acamprosate in relapse rates (RR: 1.25; 95% CI: 0.71 to 2.20). The certainty of evidence was very low due to high risk of bias and imprecision.

Adverse Events and Dropouts. Baclofen had fewer reported adverse events compared with acamprosate (RR: 0.63; 95% CI: 0.23 to 1.69; very low-certainty evidence). The dropout rate was lower for baclofen, but evidence remains uncertain (RR: 0.56; 95% CI: 0.21 to 1.46; very low-certainty evidence). Dropout rates due to adverse events were also lower but were not statistically significant (RR: 0.33; 95% CI: 0.01 to 7.87). The certainty of evidence was very low due to high risk of bias and imprecision.

Baclofen Versus Naltrexone

Relapse: Return to Any Drinking. One study (60 participants) showed baclofen may increase the risk of relapse compared with naltrexone (RR: 2.50; 95% CI: 1.12 to 5.56). The certainty of evidence was very low due to high risk of bias and imprecision.

Adverse Events and Dropouts. Baclofen was associated with fewer adverse events than naltrexone (RR: 0.35; 95% CI: 0.15 to 0.80; 2 studies, 80 participants; very low-certainty evidence). There were no significant differences between baclofen and naltrexone in dropout rates, but evidence remains uncertain (RR: 1.00; 95% CI: 0.32 to 3.10; very low-certainty evidence). The certainty of evidence was very low due to high risk of bias and imprecision.

Subgroup Results

The subgroup analyses for baclofen compared with acamprosate and naltrexone were more limited due to the smaller number of studies and inconsistencies in reporting.

Detoxification Status. Among participants who completed detoxification, one study (n = 60) showed no significant difference in relapse rates between baclofen and acamprosate (RR: 1.25; 95% CI: 0.71 to 2.20). In comparison with naltrexone, participants who were detoxified treated with

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baclofen had a higher risk of relapse (RR: 2.50; 95% CI: 1.12 to 5.56; very low-certainty evidence).

Dose Variability and Study Duration. Evidence for dose effects and study duration in comparison between baclofen and other medications was limited. The available studies did not consistently report outcomes stratified by dose or duration, making it difficult to assess whether these factors influenced the comparative effects of baclofen, acamprosate, or naltrexone.

Secondary Outcomes

Craving. There were no significant differences between baclofen and naltrexone in terms of craving (MD: 2.08; 95% CI: -3.71 to 7.87; 1 study, 60 participants). There were also no significant differences between baclofen and acamprosate in terms of craving (MD: 5.80; 95% CI: -11.84 to 23.44).

Cochrane Review Authors' Conclusions

The authors of the Cochrane Review concluded that baclofen likely reduces the risk of relapse to any drinking and increases the percentage of abstinent days, without increasing adverse events or study dropout. Evidence was strongest among participants who were detoxified. The authors did not find evidence that baclofen reduced the number of heavy drinking days or the number of drinks per drinking day.

The authors note that baclofen increased the percentage of abstinent days by 9% compared with placebo. This translates to almost three additional abstinent days per month for participants treated with baclofen compared with participants who received placebo. However, findings from this review suggest baclofen does not have an effect in other important measures of alcohol consumption like heavy drinking days and drinks per drinking day compared with placebo. Baclofen may help patients with AUD maintain abstinence but may be of limited benefit for other alcohol consumption outcomes.

We conducted a dual appraisal of the quality of the systematic review using AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews) and concluded that we had high confidence in the Cochrane Review.

Original Commentary

Commentary: Implications of the Cochrane Evidence for Policy and Practice

Conclusions from the Cochrane Review suggest there is moderate certainty of evidence that baclofen reduces the risk of return to any drinking for patients with AUD. The RTI International and University of North Carolina Evidence-based Practice Center (RTI-UNC EPC) recently completed a systematic review on pharmacotherapy, including baclofen, for AUD in outpatient settings.[9] This review concluded there was low certainty of evidence that baclofen reduced return to any drinking for patients with AUD. The Cochrane Review focused specifically on baclofen and included 17 RCTs. The RTI review included 13 RCTs on baclofen and excluded 4 of the RCTs included in the Cochrane Review due to narrower inclusion criteria regarding eligible study designs and outcomes. The difference in the certainty of evidence ratings was likely the result of inclusion of different studies and possible differences in the methodologies for grading evidence. Both reviews found baclofen had limited impacts on other alcohol consumption outcomes and limited safety concerns, although common adverse events included fatigue and dizziness.

The RTI review included pharmacotherapies in addition to baclofen and found moderate-certainty evidence for acamprosate and naltrexone, which are Food and Drug Administration (FDA) approved for the treatment of AUD.[9,10] Oral naltrexone had moderate-certainty evidence for reducing return to any drinking, return to heavy drinking, percent drinking days, and percent heavy drinking days at the once-daily 50 mg oral dose. The number needed to treat to prevent one person from returning to any drinking was 18, and the number needed to treat to prevent one person from returning to heavy drinking was 11. There was moderate certainty evidence that acamprosate significantly reduced return to any drinking and drinking days. The number needed to treat for preventing one person from returning to any drinking for acamprosate was 11.[9] Acamprosate is generally taken as multiple pills, 3 times daily, which may reduce ease of use and impact patient preferences. Notably, studies included in this review generally also included counseling co-interventions in all study groups.[9]

In addition to the RTI-UNC EPC review, researchers at RTI contributed to a systematic review and network meta-analysis of both pharmacologic and psychotherapy trials for individuals with co-occurring AUD or other drug use disorders and posttraumatic stress disorder (PTSD).[11] This review did not include any studies of baclofen. It concluded that pharmacotherapy with and without trauma-focused psychotherapies were more effective in reducing alcohol use severity than placebo. This review also found trauma-focused interventions targeting both PTSD and AUD were more effective at reducing PTSD symptoms than integrated non–trauma-focused psychotherapy, AUD-focused psychotherapy, and other control psychotherapies.[11]

In addition to systematic review–related research, RTI is also advancing research related to the development of new AUD treatments. As the operations core for the Pharmacotherapies for Alcohol and Substance Use Disorder Alliance (PASA),

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RTI collaborates with investigators and provides centralized oversight of research studies. The overarching goal of PASA is to advance pharmacological treatments for alcohol and substance use disorders, especially for patients with comorbid PTSD. PASA aims to fund studies to test new chemical entities and repurpose existing medications in preclinical and nonclinical models of AUD and substance use disorder with comorbid PTSD and other disorders; clinical trials of safety and doses for potential efficacy in subjects with AUD; and multisite clinical trials of efficacy and safety.[12]

Commentary: Implications for Research

Significant research gaps in AUD treatment persist, particularly in head-to-head comparisons between medications. Most studies compare single medications to placebo rather than to other active treatments, making it difficult to determine optimal medication choices for different patient populations. Studies in primary care settings remain particularly scarce. Although medication efficacy does not depend on setting, there may be meaningful differences with regard to population, availability of concomitant therapies, and provider knowledge. Given the increasing numbers of patients with AUD, it is likely that primary care providers will be essential to any treatment strategy. Evidence from the National Survey on Drug Use and Health indicates that alcohol screening in primary care has increased, but important disparities exist with Black and Asian American patients being less likely to be screened than white patients.[13] Understanding best approaches to using pharmacotherapy for treatment in primary care is an area worthy of additional investigation.

Despite evidence supporting multiple pharmacotherapy options for AUD, treatment rates remain strikingly low, with less than 1% of patients receiving medication-assisted treatment.[7] Health care systems and policymakers should address barriers to treatment access, including improving insurance coverage, reducing stigma, and increasing provider education about available treatment options.

Future research should prioritize direct comparisons between medications, studies in primary care settings, and investigation of treatment effectiveness in diverse populations. Research into predictors of treatment response could help match patients with optimal medications. Additionally, studies examining real-world implementation and cost-effectiveness could inform efforts to expand treatment access.

Conclusions

While evidence supports multiple medication options for AUD treatment, including baclofen, a larger body of higher-certainty evidence exists for FDA-approved medications like naltrexone and acamprosate. Treatment decisions should consider individual patient factors, medication characteristics, and setting-specific considerations. Expanding access to evidence-based treatments remains a critical public health priority.

Data Availability Statement

In this publication, we do not report on, analyze, or generate any data.

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