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- 78 Substance use disorders among older adults: A review of randomized controlled pharmacotherapy trials
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Substance use disorders among older adults: A review of randomized controlled pharmacotherapy trials

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Abstract

Substance use disorders (SUDs) are a growing problem among older adults. Acamprosate, disulfiram, and naltrexone are United States Food and Drug Administration (referred to as FDA) approved for the treatment of alcohol use disorder, and buprenorphine is approved for the treatment of opiate use disorder among adults. However, the data on the use of these medications for the treatment of SUDs among older adults are unclear from randomized controlled trials (referred to as RCTs). A review of the literature indicates that there are only two RCTs that evaluated the use of pharmacologic agents for SUDs among older adults (≥ 50 years). One trial evaluated the use of naltrexone when compared to placebo for the treatment of alcohol use disorder among individuals, 50-70 years in age. The other trial evaluated the use of naltrexone or placebo as adjuncts with sertraline in the treatment of alcohol use disorder among individuals older than 55 years in age. Both trials indicated that the use of naltrexone reduced the rates of relapse among older adults with alcohol use disorder. However, we did not identify any RCTs that studied the use of buprenorphine, acamprosate, or disulfiram for SUDs among older adults. Based on available evidence, it would be safe to conclude that limited data indicate some efficacy for naltrexone in the treatment of alcohol use disorder among older adults. However, data from controlled trials on the use of other medications that are FDA approved for the

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treatment of SUDs among younger adults are nonexistent among older adults with SUDs.

Key words: Older adults; Substance use; Naltrexone; Acamprosate; Disulfiram; Buprenorphine

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Core tip: Substance use disorder is a growing problem among the older adult population. Unfortunately, there is very limited controlled research data on pharmacotherapy to help with this situation. Our review indicates benefits for naltrexone in the treatment of alcohol use disorder, but we were not able to find data regarding pharmacotherapy for any other substance use disorder among older adults. This review is our attempt to draw attention towards the topic of substance use disorder treatment among older adults and to encourage further research in this field.

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INTRODUCTION

The number of adults over the age of 65 years who are expected to need substance use treatment is projected to increase from 1.7 million in 2001 to nearly 4.4 million by 2020^[1]. Substance use disorders (SUDs) among older adults are often unidentified and under- or mis-diagnosed^[2]. In this population, substance use causes greater harm due to the underlying physiological changes inherently related to aging, the presence of chronic medical illness, and due to drug-medication interactions^[2]. Prolonged exposure to illicit substances can also have negative physiological and psychological effects that are especially relevant in older adults^[2]. These include delirium, memory loss or cognitive impairment, suicide, falls and consequential fractures, and exacerbation of underlying medical comorbidities^[2]. The goals of rehabilitation for SUDs for older adults are comparable to any other age group: to encourage, sustain motivation, and prevent relapse^[3].

There are several pharmacologic treatments available for SUDs that have been approved by the FDA for adults^[4,5]. The FDA has approved naltrexone, acamprosate, and disulfiram for the treatment of alcohol use disorder, whereas buprenorphine is approved for the treatment of opioid use disorder^[4,5]. Naltrexone, an opioid-receptor antagonist, reduces cravings associated with heavy alcohol use and is thought to prevent the rate of relapse in individuals with alcohol use disorder. Acamprosate is a glutamate modulator agonist that acts in the putamen and is thought to decrease the physical and psychological discomfort that is associated with acute withdrawal from alcohol. Disulfiram is an inhibitor of the enzyme acetaldehyde dehydrogenases that is involved in alcohol metabolism and causes unpleasant physical symptoms when it interacts with alcohol^[4]. Buprenorphine is a partial agonist at the mu opioid receptor and can be used in the treatment of opioid use disorder^[5].

The aim of this editorial is to review the literature on published randomized control trials (RCTs) that evaluated the efficacy and tolerability of the four treatment modalities (acamprosate, disulfiram, naltrexone, and buprenorphine) for the treatment of SUDs among older adults (defined as individuals greater than 50 years in age).

EVIDENCE FROM RCTs

A review of literature only found two trials that evaluated the use of pharmacologic agents for SUDs among older adults from RCTs (Table 1)^[7,8]. Although both the studies used placebo as the comparator to naltrexone for alcohol use disorder among older adults, one study assessed the efficacy of treatment of depression with the

concurrent SUD^[8]. Both studies were assessed as being of good quality based on the Centre for Evidence-Based Medicine criteria (Table 2). The details of the two studies are described in Table 3. We did not find any RCTs that investigated the use of acamprosate, disulfiram, or buprenorphine for the treatment of SUDs among individuals ≥ 50 years in age.

DISCUSSION

Available data from RCTs on the use of pharmacotherapy, *i.e.* buprenorphine, acamprosate, or disulfiram, for SUDs among older adults are currently non-existent. The only two trials that we found in the literature evaluated the efficacy of naltrexone in reducing the rates of alcohol relapse among older adults when compared to placebo.

In the first included study, naltrexone was found to be effective in reducing the rates of relapse among a group of older male veterans^[7]. However, it was not effective in reducing craving for alcohol or in reducing reported measures of depression and anxiety. In the second study, naltrexone did not enhance the treatment responsiveness either for depression or for alcohol consumption when combined with sertraline and individualized psychosocial support^[8]. There was a significant correlation between alcohol relapse during the trial and poor response to depression treatment, but the study did not distinguish between relapse in alcohol use with no improvement in depression versus worsening of depression. The favorable outcome in drinking behavior was similar to the results of using naltrexone alone from previous studies, and the addition of antidepressants or individualized psychosocial support did not demonstrate additional efficacy.

The major limitation for both studies was the small sample sizes; and in the case of one of the studies, a limitation was that the majority of the participants were men^[8]. These aspects limit the ability to extrapolate and apply any resulting conclusions to the general population or even specifically to all older adults. There is a need for further research that overcomes these limitations, assesses concurrent variables like gender, and addresses the need for larger sample sizes and generalized applicability.

In general, very few treatment options have been studied for SUDs in older adults. Among these interventions, naltrexone appears to be the most widely used for the treatment of alcohol use disorder and is the most studied. In contrast, disulfiram is less commonly used due to the risk of cardiovascular side effects, medication interactions, and exacerbation of underlying medical conditions or mood disorders in this population^[9]. Of note, studies analyzing other pharmacological treatments such as acamprosate, disulfiram, and buprenorphine are lacking among older adults^[10].

Several prior studies have assessed the use of non-pharmacological interventions, such as cognitive-based therapy for substance use in older adults^[10]. However, there is limited data on the effectiveness of combining these therapies with pharmacological interventions. This highlights the need for further research on both the efficacy and safety of a variety of pharmacological interventions for SUDs in older adults and on the combination of pharmacotherapy with other skill-based therapies.

CONCLUSION

This review indicates that there is a scarcity of evidence for the use of pharmacotherapy for the treatment of SUDs among older adults. There are only two controlled studies available in this population, and these studies indicate that naltrexone may show some benefit in the treatment of alcohol use disorder among older adults. However, the studies had a limited number of participants and predominantly included men, which further restricts the generalizability of the results. The need to investigate further the effectiveness of different pharmacotherapeutic modalities for the management of SUDs among older adults is, therefore, essential.

Table 1 Summary of included studies

Study	Number of participants	Age in yr	Setting	Comparators	Duration in wk
Oslin <i>et al</i> ^[7] , 1997	44	50-70	Veterans affairs	Naltrexone <i>vs</i> placebo	12
Oslin <i>et al</i> ^[8] , 2005	74	≥ 55	Outpatient	Naltrexone + sertraline <i>vs</i> placebo + sertraline	12

Table 2 Quality of included studies

Study	Randomization	Similar groups initially?	Equal treatment?	Analyzed groups in which they were randomized	Objective/ "blind" treatments?	Overall quality of study
Oslin <i>et al</i> ^[7]	Yes	Yes	Yes	Yes	Yes	Good
Oslin <i>et al</i> ^[8]	Yes	Yes	Yes	Yes	Yes	Good

Table 3 Results summary from included studies

Name of study	Outcomes	Tolerability	Limitations
Oslin <i>et al</i> ^[7]	(1) Those who drank alcohol was 1.9% of days for the naltrexone group <i>vs</i> 6.5% of days in the placebo group, $P = 0.275$; (2) The relapse rates were 25% in all clinical subjects; 14.3% in the naltrexone group <i>vs</i> 34.8% in the placebo group, $P = 0.117$; (3) Those who sampled alcohol and relapsed: 3 of 6 in the naltrexone group <i>vs</i> 8 of 8 in the placebo group, $P = 0.024$; (4) There were no differences in the abstinence rates between the two groups, $P = 0.659$; (5) There were no differences in prolonging abstinence between the two groups, $P = 0.532$	(1) Most common side effects were sleep disturbances and anxiety; (2) For naltrexone, the common side effects were depression, sedation, and constipation; (3) For placebo, the common side effects were memory lapse, asthma attack, "fleeting thoughts", and frequent urination; (4) None of the subjects dropped out of study due to medication effects	(1) There were a small number of subjects; (2) The method of assessment was self-report
Oslin <i>et al</i> ^[8]	(1) Those who relapsed on alcohol use was 35.1% in the naltrexone group <i>vs</i> 32.4% in placebo group, OR: 1.25, $P = 0.690$; (2) Those who were abstinent from alcohol use was 43.2% in the naltrexone group <i>vs</i> 54.1% in the placebo group, OR: 1.34, $P = 0.575$; (3) Those individuals in whom the depression had remitted was 51.4% in the naltrexone group <i>vs</i> 54.1% in the depression group, OR: 1.40, $P = 0.537$; (4) Overall improvement was noted in 40.5% of individuals in the naltrexone group <i>vs</i> 43.2% in the depression group, OR: 1.40, $P = 0.537$	(1) Common adverse events noted during treatment included; 58.1% headache, 51.4% anxiety, 41.9% nausea, 39.2% decreased sexual functioning, 24.3% vomiting; (2) The occurrence of adverse effects was not different between the two groups; (3) The symptoms were not related to the completion of the trial or to the adherence with the medication	(1) There were a small number of veterans and were mainly male; (2) The method of assessment was self-report; (3) The outcomes measured were dually dependent on depression remission and the lack of relapse on alcohol

OR: Odds ratio.

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