

Original Article

Medication adherence and therapeutic outcomes of disulfiram in patients with alcohol use disorder: A prospective observational study

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ABSTRACT

Objectives: Alcohol use disorder (AUD) is a chronic relapsing condition, and while disulfiram remains an effective deterrent therapy, its success is largely dependent on adherence. Evidence suggests that better adherence is directly linked to improved treatment outcomes. This article, derived from a larger thesis, focuses on two parameters – adherence assessed by the medication adherence rating scale (MARS) and therapeutic outcomes measured using the AUDs identification test (AUDIT) – to evaluate the clinical effectiveness of disulfiram in AUD.

Materials and Methods: The present prospective observational study was carried out over a period of 1 year in the Psychiatry Outpatient Department at King George's Medical University, Lucknow. Ninety-one patients aged 18–60 years, diagnosed with AUD as per DSM-5 criteria and prescribed disulfiram 250 mg daily and were enrolled after informed consent. Adherence was assessed using the MARS, and therapeutic outcomes were evaluated using the AUDIT at baseline, 4 weeks and 8 weeks. Statistical analysis included the Wilcoxon signed-rank test and Pearson correlation, with $P < 0.05$ considered statistically significant.

Results: At 4 weeks, the mean MARS score was 3.57 ± 0.85 , which increased significantly to 5.55 ± 1.18 at 8 weeks ($P < 0.001$). Mean AUDIT scores showed a progressive decline from 28.18 ± 4.49 at baseline to 25.19 ± 4.52 at 4 weeks and 22.80 ± 4.70 at 8 weeks, with all reductions significant ($P < 0.001$). Correlation analysis revealed no significant association between adherence and AUDIT scores at 8 weeks ($r = -0.083$, $P = 0.436$).

Conclusion: Disulfiram therapy significantly improved medication adherence and reduced alcohol use severity in patients with AUD. However, adherence and therapeutic outcomes did not show a direct correlation at 8 weeks, indicating that additional psychosocial support may be essential to sustain recovery.

Keywords: Alcohol use disorder, Alcohol use disorders identification test, Disulfiram, Medication adherence, Medication Adherence Rating Scale, Therapeutic outcomes

INTRODUCTION

Alcohol use disorder (AUD) is widely recognised as a chronic, relapsing condition with neurobiological underpinnings that go far beyond issues of personal choice. The disorder is characterised by impaired control over alcohol intake and maladaptive patterns of use that persist despite serious adverse health and social consequences. Advances in neurocircuitry research have demonstrated that addiction involves dysfunction in reward, motivation and inhibitory control

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networks, with dopamine, glutamate and γ -aminobutyric acid systems playing central roles in perpetuating compulsive alcohol use.^[1] Such neurobiological alterations contribute to tolerance, withdrawal, craving and the high likelihood of relapse that define the clinical course of AUD.

The global health burden of alcohol use remains immense. Harmful alcohol consumption is responsible for an estimated 3.3 million deaths annually, representing nearly 6% of all global mortality.^[2] Its impact extends across more than 200 disease conditions, including hepatic cirrhosis, pancreatitis, cardiovascular disease, hypertension, stroke and several malignancies. Psychiatric morbidity is closely linked with alcohol misuse, with strong associations observed between alcohol dependence and depression, anxiety disorders and cognitive dysfunction.^[3] Beyond morbidity and mortality, the societal costs of alcohol misuse are staggering, encompassing reduced productivity, workplace accidents, road traffic injuries, interpersonal violence and strain on healthcare and legal systems.^[2]

India is experiencing a worrying rise in alcohol use, with changing social norms, rapid urbanisation and economic transitions contributing to shifting consumption patterns. According to the National Family Health Survey-4, nearly one-third of Indian men and a small but significant proportion of women report alcohol use, although true prevalence may be higher due to underreporting and stigma.^[4] Regional variations exist, with some states reporting particularly high rates of hazardous drinking. A surge in binge drinking among young adults has also been noted, heightening the risks of road traffic accidents, interpersonal violence and progression to dependence.^[5] The public health implications are substantial, given the intersection of alcohol misuse with domestic abuse, workplace inefficiency and financial distress at the household level. Despite regulatory efforts such as taxation policies, restrictions on advertising and prohibition in certain states, alcohol dependence continues to rise, necessitating robust treatment approaches.^[5]

Pharmacotherapy has long played an essential role in managing AUD, complementing psychosocial interventions. A range of medications has been approved for the management of alcohol dependence, among which naltrexone, acamprosate and disulfiram are commonly used.^[6] Naltrexone, an opioid receptor antagonist, reduces cravings by attenuating reward pathways; acamprosate stabilises glutamatergic transmission, reducing protracted withdrawal symptoms. Disulfiram, however, is unique in its reliance on aversive conditioning. By irreversibly inhibiting aldehyde dehydrogenase, it prevents the metabolism of acetaldehyde during alcohol consumption, producing an unpleasant reaction marked by flushing, nausea, vomiting, tachycardia and hypotension.^[6] This negative reinforcement discourages drinking and supports abstinence.

However, the effectiveness of disulfiram is largely determined by the degree of patient compliance with the prescribed regimen. Unlike naltrexone or acamprosate, which exert their effects pharmacodynamically irrespective of patient intent, disulfiram requires a conscious commitment not to consume alcohol. Adherence rates in naturalistic settings are often suboptimal due to fear of adverse reactions, ambivalence about abstinence or psychosocial pressures.^[6] Clinical evidence has consistently shown that adherence improves markedly when disulfiram is taken under supervision. In a randomised multicentre trial, supervised disulfiram was associated with significantly better abstinence and reduced drinking days compared with acamprosate and naltrexone.^[7] Long-term follow-up studies have demonstrated that deterrent medications such as disulfiram, when combined with structured outpatient monitoring, are associated with higher rates of sustained recovery.^[8] Furthermore, classic controlled trials have highlighted that structured disulfiram interventions can reduce heavy drinking in high-risk populations, underscoring their value when adherence is ensured.^[9]

The importance of adherence extends beyond disulfiram to the broader context of alcohol pharmacotherapy. The COMBINE study remains a landmark trial in alcohol research, emphasising that medication compliance is among the strongest predictors of treatment response.^[10] Meta-analytic evidence further confirms that disulfiram, when adherence is maintained, significantly improves abstinence outcomes and lowers relapse rates.^[11] Cooperative Veterans Administration studies also reinforced that structured adherence strategies are key to optimising the therapeutic effects of disulfiram.^[12] As reviewed by Garbutt, disulfiram continues to be a relevant and effective pharmacological tool, provided adherence barriers are addressed.^[13]

Taken together, these findings highlight that adherence to disulfiram is not merely a compliance issue but a central determinant of therapeutic success. The present article is part of a larger thesis project conducted to evaluate adherence, therapeutic outcomes and quality of life in patients with AUD receiving disulfiram therapy. For the present paper, the analysis was restricted to two parameters from the thesis: Treatment adherence, evaluated with the Medication Adherence Rating Scale (MARS) and therapeutic response, measured through the AUDs Identification Test (AUDIT). Emphasising these two aspects allowed the study to generate focused evidence that may inform strategies to improve compliance and optimise the clinical effectiveness of disulfiram.

MATERIALS AND METHODS

This study was a prospective observational study conducted to assess adherence and therapeutic outcomes in patients

receiving disulfiram for AUD. The study was conducted over a period of 1 year in the psychiatry outpatient department (OPD). Ethical approval was obtained from the Institutional Ethics Committee before patient recruitment began. Informed consent was obtained from all study participants, ensuring they understood the study objectives, risks and confidentiality measures. Patient anonymity and data privacy were strictly maintained.

The study population consisted of patients diagnosed with AUD who had been prescribed disulfiram as part of their treatment regimen. Patients who met the following criteria were included in the study: Diagnosed with AUD based on DSM-5 criteria, prescribed disulfiram as part of their treatment, aged between 18 and 60 years and those who provided written informed consent to participate in the study. Patients with any of the following conditions were excluded: History of severe allergic reactions to disulfiram or its components, history of severe liver disease or liver failure, severe mental illness or cognitive impairment that could interfere with study participation, pregnancy or breastfeeding, participation in another clinical trial within the past 3 months, patients unwilling or unable to provide informed consent, any contraindication to the use of disulfiram as per clinical guidelines and patients who were receiving other pharmacological treatments for AUD during the study period, except for trazodone (which was permitted for insomnia or depressive symptoms).

The sample size was estimated to detect differences in adherence rates across groups defined by socio-demographic and clinical variables, with 80% power and a 5% level of significance. The calculation was performed using the single-proportion formula, assuming an expected adherence rate of 41.3% based on the study by Walker *et al.*,^[14] with a 95% confidence level and 10% precision. This yielded a sample size of 90.16, which was rounded to 91. Accordingly, a minimum of 91 participants was required, and recruitment continued in the psychiatry OPD until this number was achieved.

Screening and enrolment involved preliminary screening of all patients visiting the Psychiatry OPD with a diagnosis of AUD, followed by clinical evaluation by a psychiatrist to confirm the diagnosis as per DSM-5 criteria. Eligible patients were briefed about the study, and written informed consent was obtained. After consent, baseline data were collected, including demographic details (age, gender, education, employment status, marital status, socio-economic status), alcohol use history (duration of AUD, previous treatments, relapse history) and psychiatric evaluation for co-occurring conditions. Follow-up assessments were conducted at baseline, 1 month and 2 months. Adherence to disulfiram therapy was measured using the MARS, a 10-item tool in which higher scores reflected better adherence. Therapeutic outcomes were assessed using the AUDIT, a 10-item WHO

questionnaire that evaluated alcohol consumption, drinking behaviour and alcohol-related harm. Data were analysed using Statistical Package for the Social Sciences software, with continuous variables expressed as mean \pm SD, comparisons made using the Wilcoxon signed-rank test, and correlation analysis performed between adherence and therapeutic outcomes. A $P < 0.05$ was considered statistically significant.

RESULTS

The study enrolled 91 patients with AUD receiving disulfiram therapy. The baseline demographic and clinical profile is summarised in Table 1. The majority of the patients were in the age group of 30–40 years (57.1%), with a mean age of 34.0 ± 5.80 years. 70.3% of participants were married, and 63.8% belonged to lower or lower-middle socio-economic classes. In most participants (79.1%), the duration of alcohol use was ≤ 5 years, with a mean age of 34.0 ± 5.80 years. This baseline distribution provided a representative profile of young-to middle-aged adults with AUD who were at varying stages of socio-familial and economic functioning.

Adherence to disulfiram therapy, assessed using the MARS, showed significant improvement over time. At the 4-week follow-up, the mean MARS score was 3.57 ± 0.85 , which rose to 5.55 ± 1.18 by the 8-week assessment. Statistical analysis demonstrated that this increase was highly significant (Wilcoxon signed-rank test, $z = 8.56$, $P < 0.001$) [Table 2]. The improvement in adherence over the treatment period is illustrated in Figure 1, where the upward trend clearly highlights the positive shift in compliance with medication.

Table 1: Baseline characteristics of the study population ($n=91$).

Parameter	Category	n (%) / Mean \pm SD
Age (years)	20–30	22 (24.2)
	30–40	52 (57.1)
	40–50	17 (18.7)
	Mean \pm SD	34.0 \pm 5.80
Marital status	Married	64 (70.3)
	Unmarried	27 (29.7)
Socio-economic status	Lower	21 (23.1)
	Lower middle	37 (40.7)
	Middle	32 (35.2)
	Upper middle	1 (1.1)
Duration of alcohol use	≤ 5 years	72 (79.1)
	> 5 years	19 (20.9)
	Mean \pm SD	3.90 \pm 5.49

Baseline demographic and clinical characteristics of patients with alcohol use disorder enrolled in the study. Most participants were in the 30–40-year age group, married and from lower or lower middle socio-economic backgrounds, with the majority reporting alcohol use of ≤ 5 years. SD: Standard deviation

These findings suggest that patients not only initiated but also sustained disulfiram use more effectively as therapy progressed.

Therapeutic outcomes measured using the AUDIT demonstrated a progressive decline in alcohol use severity with treatment. The mean AUDIT score at baseline was 28.18 ± 4.49 , which significantly decreased to 25.19 ± 4.52 at 4 weeks and further reduced to 22.80 ± 4.70 at 8 weeks. Reductions were statistically significant across all intervals: Week 0 to week 4 ($z = 7.82, P < 0.001$), week 0–week 8 ($z = 7.75, P < 0.001$) and week 4–week 8 ($z = 7.45, P < 0.001$) [Table 3]. Figure 2 illustrates the decline in AUDIT scores, reflecting steady improvement in alcohol-related behaviours and a reduction in harmful drinking patterns over the course of therapy. Correlation analysis between adherence and therapeutic outcomes at 8 weeks is presented in Table 4. The association between MARS and AUDIT scores at 8 weeks was weak and not statistically significant ($r = -0.083, P = 0.436$). Likewise, no significant correlation was observed between the duration of alcohol use and either adherence ($r = -0.116, P = 0.275$) or therapeutic outcomes ($r = -0.061, P = 0.563$). These relationships are further illustrated in Figure 3, where the scatter plot with regression line shows no meaningful clustering or trend between MARS and AUDIT scores. This indicates that although adherence and therapeutic outcomes both improved individually over time, they did not significantly correlate with each other in this sample.

Table 2: Effect of disulfiram on medication adherence (MARS Scores)

Time of visit	Mean±SD	Test used	z-value	P-value
Week 4	3.57±0.85	—	—	—
Week 8	5.55±1.18	Wilcoxon	8.56	<0.001

MARS scores at 4 and 8 weeks of disulfiram therapy. Significant improvement in adherence was observed by 8 weeks (Wilcoxon signed-rank test, $P < 0.001$). Significant z-value is ± 1.96 and p-value is < 0.05 . MARS: Medication adherence rating scale, SD: Standard deviation

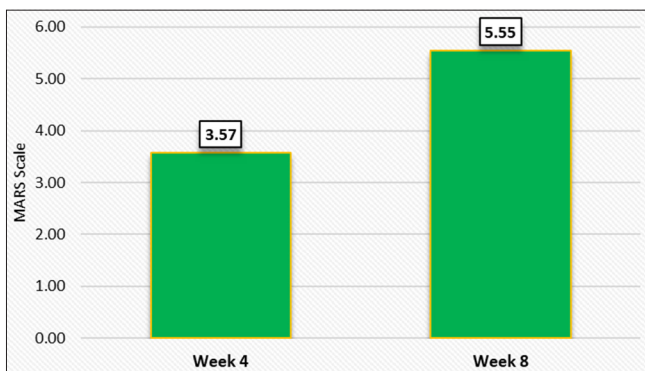


Figure 1: Effect of treatment on alcohol use disorder as per medication adherence rating scale. MARS: Medication adherence rating scale.

DISCUSSION

This prospective observational study assessed adherence and therapeutic outcomes in patients with AUD receiving disulfiram therapy. The baseline profile showed that most participants were young-to middle-aged adults, predominantly married and from lower or lower-middle socio-economic groups. Such socio-demographic clustering reflects the epidemiology of alcohol use in India, where harmful drinking has been strongly linked to urbanisation, marital stress and economic burden, as highlighted in national reports and community-based surveys by Gururaj *et al.*^[5] and NFHS-4 data.^[4] This demographic concentration suggests that AUD in the Indian setting disproportionately affects socially active and economically vulnerable individuals, thereby compounding both personal and societal consequences.

Adherence to disulfiram, measured by the MARS, improved significantly between 4 and 8 weeks of treatment.

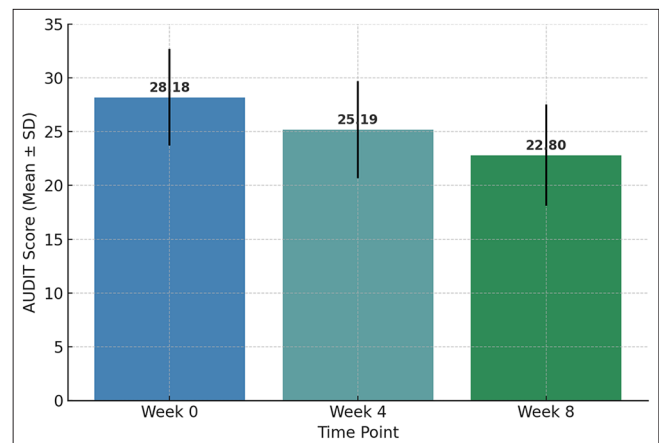


Figure 2: Effect of treatment on alcohol use disorders identification test scores. AUDIT: Alcohol use disorder identification test, SD: Standard deviation.

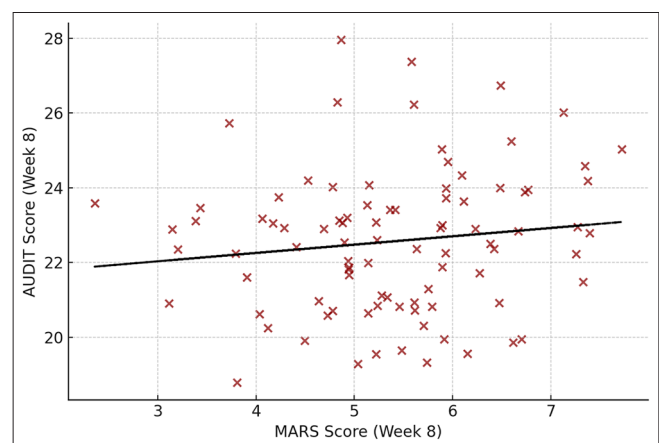


Figure 3: Correlation between adherence and therapeutic outcomes at 8 weeks. Red cross denotes individual data point. Black line denotes line of best fit (regression line). AUDIT: Alcohol use disorder identification test, MARS: Medication adherence rating scale.

Table 3: Effect of disulfiram on therapeutic outcomes (AUDIT scores).

Comparison interval	Mean±SD (start)	Mean±SD (end)	Test used	z-value	P-value
Week 0→Week 4	28.18±4.49	25.19±4.52	Wilcoxon	7.82	<0.001
Week 0→Week 8	28.18±4.49	22.80±4.70	Wilcoxon	7.75	<0.001
Week 4→Week 8	25.19±4.52	22.80±4.70	Wilcoxon	7.45	<0.001

AUDIT scores at baseline, 4 weeks and 8 weeks showing progressive reduction in alcohol use severity with disulfiram treatment (all comparisons significant, $P < 0.001$). AUDIT: Alcohol use disorder identification test, SD: Standard deviation

Table 4: Correlation between adherence and therapeutic outcomes at 8 weeks.

Variable	r-value	P-value
Duration of alcohol use versus MARS	-0.116	0.275
Duration of alcohol use versus AUDIT	-0.061	0.563
MARS versus AUDIT (8 weeks)	-0.083	0.436

Pearson's correlation between adherence (MARS) and therapeutic outcome (AUDIT) at 8 weeks. r-value was calculated using Pearson correlation and p-value was calculated using t-statistic test. No statistically significant associations were observed. MARS: Medication adherence rating scale, AUDIT: Alcohol use disorders identification test

This finding is consistent with earlier observations that structured pharmacological interventions with disulfiram can enhance patient compliance when integrated into regular follow-up care. In a multicentre comparative trial, Laaksonen *et al.*^[7] reported that disulfiram adherence was superior to acamprosate and comparable to naltrexone in early treatment phases, particularly when reinforced by supervision. Similarly, Khan *et al.*^[8] demonstrated in a 7-year follow-up study that sustained adherence to disulfiram was associated with markedly improved long-term abstinence rates. In the present study, although administration was not formally supervised, the progressive increase in adherence suggests that motivational factors and the deterrent nature of disulfiram played a role in reinforcing continued use.

Therapeutic outcomes, evaluated using the AUDIT, revealed a consistent decline in alcohol use severity over the study period, with significant reductions observed at both 4 and 8 weeks. These results align with earlier controlled studies, such as the COMBINE trial, where pharmacological treatment combined with behavioural interventions reduced harmful drinking patterns and relapse rates Anton *et al.*^[10] The meta-analysis by Skinner *et al.*^[11] further supported the efficacy of disulfiram in improving abstinence when patients adhered to treatment. Even early investigations, such as the Veterans Administration Cooperative Study Fuller *et al.*,^[12] demonstrated the value of disulfiram in reducing relapse among compliant patients, despite variable results in unsupervised settings. The progressive decline in AUDIT scores in the present cohort reinforces the concept that disulfiram, though reliant on patient motivation, retains strong therapeutic utility in real-world clinical practice.

Interestingly, correlation analysis revealed that while both adherence and therapeutic outcomes improved significantly over time, there was no meaningful statistical association between MARS and AUDIT scores at 8 weeks. This divergence may be explained by the multifactorial nature of alcohol dependence, where psychosocial determinants and neurobiological adaptations interact to shape outcomes beyond adherence alone. Garbutt^[13] emphasised that while disulfiram is an effective deterrent, its success is optimised when combined with supportive counselling, monitoring and family involvement. Similarly, Kristenson *et al.*^[9] demonstrated in a long-term controlled study that alcohol reduction in middle-aged men was sustained only when combined with structured follow-up and health education. Therefore, the absence of a strong correlation in this study may reflect the short follow-up duration and the lack of intensive psychosocial adjuncts, both of which likely attenuated the direct relationship between adherence and clinical outcomes.

CONCLUSION

While disulfiram therapy was associated with significant improvements in both medication adherence and reductions in alcohol use severity, these gains should not be attributed to the pharmacological action of disulfiram alone. Adherence likely improved due to motivational, behavioural and clinic-based follow-up factors rather than the drug itself. Importantly, although no statistically significant correlation was observed between adherence and therapeutic outcomes at 8 weeks, patients who maintained higher adherence demonstrated a trend towards better clinical improvement over time. These findings suggest that disulfiram remains a valuable deterrent in AUD when integrated with structured psychosocial support, supervision and continuous follow-up to sustain recovery.

Ethical approval: The research/study was approved by the Institutional Review Board at the Institutional Ethics Committee, approval number 3489/Ethics/2024, dated 15th March 2024.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand

that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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