



Alcohol Abstinence, Adherence, and Attitudes toward Disulfiram Treatment for Alcohol Dependence among Patients Attending a Tertiary Care Setting in North India

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Abstract

Background: Disulfiram is the first Food and Drug Administration (FDA)-approved drug for the treatment of alcohol dependence, primarily acting as a deterrent agent. The available literature on disulfiram treatment for alcohol dependence among individuals in low-income and middle-income countries is scarce, while numerous factors impact the acceptance and adherence to such treatment.

Methods: The study utilized a purposive sampling methodology. The participants were contacted by telephone at 4 weeks, 12 weeks, and 24 weeks after the initiation of disulfiram treatment. Alcohol abstinence was calculated using the self-reported total alcohol-free days, and adherence and attitudes toward disulfiram treatment were measured using the Treatment Compliance Assessment Scale (TCAS).

Findings: The participants had a mean age of 39.30 ± 7.7 years. Nearly 62% and 46% of the subjects reported maintenance of alcohol abstinence after initiation of 12 and 24 weeks of disulfiram treatment, respectively. The proportion of non-adherent subjects increased from 36.3% to 57.2% during the 12-week and 24-week follow-up periods. Attitudes toward disulfiram treatment varied significantly across different time points. A strong positive correlation was observed in the alcohol abstinence, adherence, and attitude scores at different time points ($P < 0.01$).

Conclusion: The present study's findings unveiled that nearly 60% and 40% of the study subjects were maintaining alcohol abstinence and adherence at 12 weeks and 24 weeks after initiation of disulfiram treatment, respectively. Disulfiram could be a viable psychological tool for alcohol abstinence, but objective measurements are required to underpin its utility in this setting.

Keywords: Disulfiram, Alcoholism, Attitude, Therapy

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Introduction

Alcohol predates all human memory, enduring through generations, nations, epochs, and ages. Man discovered alcoholic beverages in prehistoric times, used in human societies since the beginning.¹ Approximately two billion individuals consume alcohol across the world, with about one-third likely to experience one or more diagnosable alcohol use disorders. It is recognized that countries with historically low alcohol use rates are now observing an upward trend in consumption.² According to the World Health Organization (WHO) estimates for Southeast Asian countries, alcohol use accounts for more than 1 in 20 deaths in the world and the WHO Southeast Asia Region, with per capita consumption steadily rising since 2000. Alcohol-related deaths surpass those caused by tuberculosis, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), and

diabetes combined. Notably, more than one in every five tuberculosis deaths is attributed to alcohol use.³ Excessive alcohol use poses significant health and social risks, contributing to over 60 different disorders, including fetal alcohol syndrome, liver disease, neurological disorders, cardiovascular and cerebrovascular diseases, anemia, and various cancers.^{4,5} Considering the health burden associated with alcohol-related deaths from cancers, liver diseases, and road traffic accidents, it is anticipated that by 2050, alcohol will become a significant predictor of health and economic burdens in Indian society.⁶

Disulfiram stands as one of the oldest molecules and was the first Food and Drug Administration (FDA)-approved medication for treating alcohol dependence. It is typically prescribed for middle-aged male subjects with alcohol dependence, who possess relatively intact social stability and supervisory systems, following the



acquisition of written informed consent.⁷ Common disulfiram-ethanol reactions (DERs) include flushing, sweating, nausea, vomiting, palpitations, dyspnea, tremors, confusion, restlessness, drowsiness, and hypotension, which may manifest within 5-15 minutes of alcohol ingestion. General complications in the absence of alcohol use encompass headache, weakness, and dizziness.⁸ Numerous studies have explored the efficacy of disulfiram, and there is convincing evidence to suggest the major role of supervised disulfiram in alcohol addiction treatment.^{9,10} Evidence also indicates instances where disulfiram has been covertly added to food items with the consent of caregivers and marketed as a traditional medicine by faith healers, potentially exposing clients to adverse drug reactions.^{11,12} Interestingly, both physical and psychiatric complications associated with disulfiram treatment were identified as significant predictors for poor medication adherence. A meta-analysis highlighted disulfiram's efficacy compared to controls in maintaining abstinence or preventing relapse, as evidenced by open-label trials. However, serious adverse events were more frequently reported for disulfiram compared to controls, emphasizing the necessity for regular patient follow-up during this therapy.¹³ It is noteworthy that disulfiram stands as the most economical prophylactic drug for alcohol dependence, underscoring its significance for individuals in low-income and middle-income countries.¹⁴ Nevertheless, literature regarding the status of disulfiram treatment for alcohol dependence in India remains limited. Therefore, the investigators examined alcohol abstinence, adherence, and attitudes toward disulfiram treatment among patients attending a tertiary care setting in North India.

Methods

Study and participant characteristics

The study was conducted in the State Drug Dependence and Treatment Center (SDDTC), Department of Psychiatry, PGIMS, Rohtak, a tertiary care hospital in North India. The center provides emergency services and outpatient and inpatient services for individuals with substance use disorders. The center routinely prescribes 250 mg of supervised disulfiram to patients with alcohol use disorder. Patients who were registered and received treatment for alcohol use disorder from October 2019 were retrospectively collected, and patients undergoing disulfiram therapy for alcohol use disorders were included. The data were collected from September 2022 to November 2023. The inclusion criteria were considered for the present study: (a) Subjects with a clinical diagnosis of alcohol use disorder as per ICD-10 diagnostic criteria established by a psychiatrist with a prescription of disulfiram, (b) having mobile connection and the ability to understand Hindi (c), and having no cognitive impairments and the ability to communicate with the

researcher. However, those who refused to participate and those with co-morbid psychiatric diagnoses of psychosis or organic brain disorders were excluded.

Outcome measures

In this study, alcohol abstinence was calculated using the self-reported total alcohol-free days after initiation of disulfiram treatment. Adherence and attitudes toward disulfiram treatment were measured using the Treatment Compliance Assessment Scale (TCAS). The TCAS is a seven-item clinician-rated questionnaire to measure two factors, namely medication compliance (items 1, 2, and 3) and attitudes toward current treatment (items 4, 5, 6, and 7). The scale has demonstrated good reliability and validity in the outpatient treatment setting.¹⁵ In addition, situational confidence in high-risk scenarios was evaluated using the Brief Situational Confidence Questionnaire (BSCQ). This scale is recognized for its validity and reliability in assessing an individual's confidence to resist eight high-risk alcohol use-related situations. These situations include dealing with unpleasant emotions, physical discomfort, experiencing pleasant emotions, testing personal control, resisting urges and temptations, managing conflict with others, handling social pressures, and navigating pleasant times with others.¹⁶

Data collection

For this study, a consultant psychiatrist and psychiatric social worker in the study center screened patients for eligibility. They provided a list of eligible patients who agreed to a follow-up after initiation of disulfiram treatment. Following participant selection, socio-demographic and clinical characteristics were gathered. The study employed a purposive sampling method, and all subjects received a participant information sheet detailing the study and informed consent forms. The available case reports from India suggest that many subjects reported adverse effects and discontinued disulfiram within 4 to 12 weeks of the initiation of treatment.¹⁷ Further, most of the open-label trials in India evaluated the 24 weeks of efficacy of disulfiram treatment.¹⁸⁻¹⁹ Therefore, in order to compare the existing data, the study participants in the present study were contacted by telephone at 4 weeks, 12 weeks, and 24 weeks of follow-up. Out of the 135 participants initially contacted, 110 subjects remained available at the end of the observation period (24th-week follow-up). Other subjects were excluded with reasons such as death ($n = 3$; all three subjects were non-adherent to disulfiram, and the reason for the death was a multi-organ failure due to excessive alcohol use), change of disulfiram treatment ($n = 7$), and refused or not available ($n = 15$).

Statistical Analysis

Socio-demographic and clinical variables were expressed

in frequency, the percentage for categorical variables, and mean and standard deviations (SD) for continuous variables. A chi-square test assessed the relationship between socio-demographic variables and screening tool scores. The Kolmogorov-Smirnov test was used to determine the normal distribution of data, and Spearman's rank-order correlation was employed to determine the correlation of selected outcome variables. A *P* value of 0.05 or less was used as the level for statistical significance, and all the analyses were performed using SPSS 15.0 version.

Results

General characteristics

The participants' mean age was 39.30 ± 7.7 years, and more than half were in the age group above 40 years (54.5%). Nearly 7% of the subjects were illiterate, and 35.5% had undergone education up to a higher secondary standard. Most of them were married (95.5%) and belonged to the Hindu religion (95.5%), as it was the dominant religion according to the study setting. Approximately half of the participants were self-employed (50.9%), and 31.5% were unemployed. Nearly 10% and 33% had monthly incomes of more than 25000 and less than 10000, respectively. Most of the subjects reported having no co-morbid illnesses (93.6%). The mean age of onset of alcohol use was 24.24 ± 6.2 years, and a major proportion of the subjects had the initial age of drinking from 20 to 29 years. In addition, most of the subjects had a total duration of alcohol use of more than 5 years (95.5%). Half of the participants did not report any complications, and 46.4% of experienced subjective anxiety following 24 weeks of disulfiram treatment. Furthermore, nearly 10% of the subjects underwent supervised disulfiram treatment (Table 1).

Alcohol abstinence, adherence, and attitudes toward disulfiram treatment

A significant proportion of subjects maintained alcohol abstinence during 4 and 12 weeks of observation periods (75.4% and 62%). However, only 46% of the subjects reported maintenance of alcohol abstinence after 24 weeks of initiation of disulfiram treatment. Nearly 22.7% of the subjects were non-adherent following four weeks of disulfiram treatment. However, during subsequent follow-ups, the proportion of non-adherent subjects increased from 36.3% to 57.2% during 12 and 24 weeks, respectively. Similarly, the mean adherence scores were observed as 4.60 (SD=1.05), 4.61 (SD=1.03), and 4.26 (SD=0.80) across 4, 12, and 24 weeks of disulfiram treatment, respectively. Further, there was a significant difference in attitudes toward disulfiram treatment across time points in which the mean attitude scores were noted as 8.58 (SD=2.63), 6.35 (SD=1.77), 6.29 (SD=1.79) at 4, 12 and 24 weeks, respectively.

Table 1. Socio-demographic characteristics of study subjects (N=110)

Demographic variable	N	%
Age (y)		
20-29	8	7.3%
30-39	42	38.2%
Above 40	60	54.5%
Mean \pm SD: 39.30 ± 7.7		
Education		
Illiterate	8	7.3%
Primary	24	21.8%
High school	29	26.4%
Higher secondary	39	35.5%
Graduate and above	10	9.1%
Marital status		
Married	105	95.5%
Not married	5	4.5%
Religion		
Hindu	105	95.5%
Sikh	05	4.5%
Occupation		
Unemployed	35	31.8%
Agriculture	12	10.9%
Self-employed	56	50.9%
Government employee	7	6.4%
Income (Per month)		
<10000	37	33.6%
10000-15000	26	23.6%
16000-25000	35	31.8%
Above 25000	12	10.9%
Presence of co-morbid medical illness		
No	103	93.6%
Yes	07	6.4%
Age of onset of alcohol use (y)		
Below 19	17	15.5%
20-29	68	61.8%
30-39	20	18.2%
Above 40	05	4.5%
Mean \pm SD: 24.24 ± 6.2		
Total duration of alcohol use		
Less than 5 years	05	4.5%
5-10 years	85	77.3%
> 10 years	20	18.2%
Adverse reactions following disulfiram treatment		
Nil	56	50.9
Anxiety	51	46.4
Others	03	02.7
Supervision for disulfiram treatment		
Self	97	88.2%
Spouse	10	9.1%
Other family members/friends	03	2.7%

Correlations of alcohol abstinence, adherence, and attitudes toward disulfiram treatment

A Spearman's rank-order correlation analysis was conducted to explore the relationship between alcohol abstinence, adherence, and attitudes toward disulfiram treatment (Table 2). Significant findings emerged, revealing a robust positive correlation between adherence scores and alcohol abstinence across various time points ($P < 0.01$). Additionally, a substantial positive correlation was evident between adherence and attitude scores, demonstrating statistical significance ($P < 0.01$). However, participants' age was not correlated with adherence to disulfiram treatment at different time points except for adherence at 4 weeks ($r = 0.207$, $P = 0.030$).

Relationship between selected socio-demographic variables and high-risk situations to alcohol use

A chi-square test was employed to ascertain any potential association between high-risk situations toward alcohol use and selected socio-demographic variables. The social pressure to use (37.3%) and urges and temptations (24.5%) were the most common self-reported high-risk situations toward alcohol use. Urges and temptations were reported as high-risk situations among those with income of more

than 15000 than those with less than 15000 ($P < 0.01$). Besides, social pressure to alcohol use was more common among lower-income and unemployed individuals. The association proved to be statistically significant ($P < 0.05$). None of the other variables showed any association between high-risk situations toward alcohol use and selected socio-demographic variables ($P > 0.05$; Table 3).

Discussion

The current study examined adherence and attitudes toward disulfiram treatment, as well as alcohol abstinence, at 1-month, 3-month, and 6-month intervals. The mean age of the participants in this study was 39.30 ± 7.7 years, and more than half were in the age group of above 40 years. It is commonly reported in the literature that the mean age of individuals seeking treatment for alcohol use disorders is around 35 years.²⁰⁻²² In the present study, we observed that the mean age of onset of alcohol use among patients was 24.24 ± 6.2 years. However, it is worth noting that data regarding the mean age of initiation of drinking can vary significantly across different study contexts. For instance, Nair et al documented changing trends in the Indian setting, with the mean age of onset declining from 24 to 17 years.²³ Similarly, Reddy et al reported an

Table 2. Spearman correlation of relationship between adherence and attitude towards disulfiram treatment

Adherence	Baseline adherence (r, p)	Adherence-4 weeks (r, p)	Adherence-12 weeks (r, p)	Adherence-24 weeks (r, p)
Age of subjects in years	0.207, 0.030*	0.166, 0.083	0.167, 0.080	0.110, 0.254
Attitude to disulfiram treatment	0.675, 0.001**	0.672, 0.001**	0.679, 0.001**	0.562, 0.001**
Alcohol abstinence	0.772, 0.001**	0.757, 0.001**	0.752, 0.001**	0.588, .001**

* $P < 0.05$, ** $P < 0.001$.

Table 3. Relationship between selected socio-demographic variables and high-risk situations to alcohol use

High-risk situations towards alcohol use	Socio-demographic variables								
	Age (f)		X ² , df, p	Occupation (f)		χ ² , df, P	Income (f)		χ ² , df, P
	<40 years	>40 years		Unemployed	Employed		<15000	>15000	
Unpleasant emotions									
No	47	43	0.51, 1, 0.31	42	48	1.84, 1, 0.17	51	39	1.2, 1, 0.27
Yes	11	09		06	14		14	06	
Pleasant emotions									
No	54	44	0.71, 1, 0.39	45	55	0.83, 1, 0.36	58	42	0.54, 1, 0.46
Yes	04	06		03	07		07	03	
Urges and temptations									
No	41	42	1.50, 1, 0.22	34	49	0.98, 1, 0.32	57	26	12.8, 1, 0.001*
Yes	17	10		14	13		08	19	
Conflict with others									
No	44	41	0.32, 1, 0.56	41	44	2.76, 1, 0.09	49	36	0.63, 1, 0.426
Yes	14	10		07	17		16	08	
Social pressure to use									
No	37	31	0.10, 1, 0.74	24	44	4.51, 1, 0.03*	47	21	8.07, 1, 0.05*
Yes	21	20		23	18		17	24	

* $P < 0.05$

early onset age of 18.9 years.²⁴ However, reports suggest the late age of initiation of drinking (the late 30s).²⁵ This difference could be attributed to various factors, such as bias in expressing the exact age of initiation of drinking, demographic and geographic factors, etc. In the present study, out of the 110 participants, 93% had basic education, most of them were married (95.5%), and most patients belonged to lower socioeconomic status (90.8%), which is consistent with the available data in the Indian setting.²⁶ In the present study, most of the subjects were married, which is relatively different from Western studies in which the patient's marital status is being separated or divorced. This discrepancy might be due to the cultural differences of patients undergoing alcohol addiction.²⁷ Nearly 31% of the individuals in the present study were unemployed. Previous studies have observed that the majority of the participants seeking treatment for alcohol dependence were skilled workers.^{28,29} Many subjects in the present study reported having no co-morbid illnesses (93.6%). Findings of a study reported that tuberculosis, hypertension, and diabetes were present in 20% of the patients undergoing alcohol addiction treatment.²⁹

Approximately 10% of the subjects in the present study received supervision during disulfiram treatment provided by significant family members, such as spouses and mothers. The existing literature indicates that supervised disulfiram therapy plays a superior role in alcohol de-addiction settings^{30,31} because supervised disulfiram may act not only as a deterrent agent but also as a strong reinforcing agent for cognitive and behavioral change. Supervised disulfiram therapy proves significantly more effective for patients whose condition would deteriorate rapidly in the event of an early relapse.³² Half of the participants in the present study did not report any complications, and 46.4% experienced subjective anxiety following disulfiram treatment. The literature indicates that psychiatric adverse events and de novo convulsions are common adverse reactions to disulfiram treatment without alcohol challenge in the Indian setting. The severity of adverse effects associated with DERs was predominantly linked to surreptitious use.¹⁷ It is worth noting that DERs were more frequently reported when prescribed by faith healers and non-psychiatrist allopathic practitioners without patients' knowledge.³³ In the present study, disulfiram was prescribed by a psychiatrist, and informed consent was taken from the subjects. This could be the possible reason for relatively minor complications among the current study participants.

The present study noted that nearly 75% and 62% of the subjects maintained alcohol abstinence following disulfiram therapy during 4 weeks and 12 weeks of initiation of treatment, respectively. It also demonstrated that approximately 46% of the subjects remained abstinent from alcohol at 24 weeks of disulfiram treatment. The available data on alcohol abstinence following disulfiram

treatment are inconclusive due to various reasons. Prasad et al. reported that 81.7% (58/71) of outpatients attending a tertiary care center in South India maintained total alcohol abstinence after six months of disulfiram treatment.³⁴ In an observational study, Sidana et al. reported superior alcohol abstinence rates for disulfiram compared to other pharmacological agents during a 6-12-month period among subjects in Northern India.³⁵ A series of open-label trials by De Sousa et al found that supervised disulfiram treatment yielded better outcomes in promoting alcohol abstinence than naltrexone or acamprosate therapy. At the end of the trial, they reported that 86% to 88% of the subjects remained abstinent following 8-12 weeks of disulfiram treatment, which is higher than the current study's findings.^{18,19} Disulfiram helps maintain alcohol abstinence for those who have relapsed several times with conventional treatment. Therefore, the frequency and outcomes of previous alcohol addiction treatment may be considered while discussing alcohol abstinence following disulfiram treatment.

In the present study, all the subjects had varying proportions of adherence at different levels. For instance, 11% were non-adherent following one week of disulfiram treatment, and nearly 36% were non-adherent to disulfiram at 12 weeks of follow-up. A study in South India revealed that 76.5% of individuals adhered to disulfiram 60 days after the initiation of treatment.³⁶ Various factors determine the adherence to disulfiram treatment. One of the primary reasons for non-adherence to disulfiram treatment is related to the DER, suggesting the need for education regarding staying away from using alcohol and other products that may interact with disulfiram.³⁷ Attitudes toward disulfiram treatment is of paramount importance in the alcohol addiction setting because it is an effective predictor of adherence, relapse, and other health-related outcomes. Disulfiram is widely described as 'an aversive agent; however, in reality, it is a deterrent agent that deters alcohol drinking by acting as a reminder to avoid the DER consequences. In addition, it facilitates the individual to prevent exposure to cues and situations that normally lead to relapse.³⁸ Based on subjective measurements, the findings of the present study revealed a mean attitude score of 8.56 (SD = 2.59), suggesting favorable attitudes toward treatment in this setting. The available evidence demonstrates the under-use of disulfiram as compared to other pharmacological agents in the alcohol de-addiction drug. This could be due to the low cost of the drug and related lack of funding and research for disulfiram in the pharmaceutical industry, exaggeration of fear of adverse drug reactions, traditional or anti-medication propaganda in substance abuse treatment, etc.³⁹ In conjunction with these data, a survey unveiled that physicians prescribed disulfiram for less than 15% of their patients with alcohol use disorders.⁴⁰ Remarkably, it is noteworthy that the prescribing

physician can employ disulfiram as a psychological tool to instill motivation by inducing fear of drinking. Similar to other treatment methods in addiction, failure, and success are observed as correlated with the level of motivation.⁴¹

Limitations

To the best of our knowledge, the current research is the most recent study conducted in India that compares alcohol abstinence, adherence, and attitudes toward disulfiram treatment over different observation periods ranging from 4 to 24 weeks in the last 5 years. However, generalizations of the study findings were limited because of methodological limitations, such as sampling bias, respondent bias, etc. The outcome measures rely solely on self-reported tools. The researcher restricted the study to subjects attending a single de-addiction center in North India, thereby increasing the risk of sample contamination.

Conclusion

The present study's findings demonstrated that nearly 60% and 40% of the study subjects were maintaining alcohol abstinence and adherence at the 12 weeks and 24 weeks of the initiation of disulfiram treatment, respectively. Disulfiram could be a viable psychological tool to promote alcohol abstinence, but detailed objective measurements are required to underpin its efficacy and safety in this setting.

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Authors' Contribution

Conceptualization: Jaison Joseph & Deepika C Khakha.

Data curation: Jaison Joseph.

Formal analysis: Jaison Joseph.

Investigation: Jaison Joseph.

Methodology: Jaison Joseph.

Project administration: Jaison Joseph.

Resources: Jaison Joseph, Deepika C Khakha.

Software: Jaison Joseph.

Supervision: Deepika C Khakha.

Validation: Deepika C Khakha.

Visualization: Jaison Joseph.

Writing—original draft: Jaison Joseph.

Writing—review & editing: Deepika C Khakha.

Competing Interests

The authors declared no potential conflicts of interest concerning the research, authorship, or publication of this article.

Ethical Approval

The study received approval from the Biomedical Research Ethics Committee at Pt. B. D. Sharma Post Graduate Institute of Medical

Sciences, University of Health Sciences, Rohtak (Reference No. BREC/19/87, dated 21/10/2019). Subjects participated in the present study purely voluntarily. Detailed information regarding the study was provided to eligible subjects through a patient information sheet, and informed consent was obtained. Participants were informed of their right to withdraw from the study at any stage, and confidentiality was strictly maintained throughout the study. The researcher's contact details were provided to the participants, and subjects were provided the freedom to contact for any treatment-related assistance during the study period, if any.

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