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Short Comunication

Naltrexone and its Effects on Craving and Alcohol Use among Patients with Alcohol Dependence Syndroms: A Report

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Abstract

Background: Naltrexone is a Food and Drug Administration (FDA)-approved anti-craving agent for the long-term treatment of alcohol dependence syndrome (ADS). However, it may not be equally effective in all patients. This study aims to assess naltrexone treatment response over four weeks in a national-level tertiary care setting.

Methods: Male patients with ADS (n=100) who were initiated on naltrexone were included in the study. The clinical data, including the drinking pattern and craving, were recorded at baseline. At the end of the one-month follow-up, the drinking status and compliance with naltrexone were recorded.

Findings: At the end of one month, more than half of the patients (n=53) were retained in the study. All the treatment-retained patients (n=53) reported naltrexone consumption for more than 24 days in the last month. Those who retained in the study reported significantly less craving among 72% of patients, while an almost 50% reduction in alcohol use was observed.

Conclusion: This study adds to the evidence of outcomes with naltrexone in terms of reduced craving and alcohol use.

Keywords: Alcohol dependence syndrome, Naltrexone, Craving, Alcohol use, Follow-up

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Introduction

Alcohol use disorders constitute one of the most severe public health problems worldwide. Recent epidemiological data suggest that around 16 crore Indians are current alcohol users. Among the current alcohol users, around 2.9 crore are estimated to be affected by alcohol dependence syndrome (ADS).[1] The major challenge in the treatment of ADS is the prevention of relapse. Anti-craving medications are a mainstay in the long-term pharmacological treatment of ADS. Out of all the available medications for reducing alcohol use craving, naltrexone remains one of the most well-studied and recommended medications in India.[2,3] The use of naltrexone is indicated in patients who cannot tolerate other medications.[3] The role of naltrexone in reducing craving and improving the outcome in patients with ADS has been well documented elsewhere, though there is a dearth of such studies from India.[4-7] In India, naltrexone efficacy needs to be explored for a long-growing ADS population. However, there are indications that it may not be equally effective in all patients, and some clinical variables like family history, craving, and amount of alcohol intake are reported to predict the efficacy of naltrexone. In India, where alcohol dependence is a recognized public health problem, it is essential to study naltrexone treatment response among treatment-seeking ADS patients.

Methods

The current study was conducted in a premier tertiary care centre in North India, providing treatment for alcohol dependence free of cost. Male patients seeking treatment for their problematic alcohol use were assessed clinically by a trained psychiatrist for alcohol dependence as per International Classification of Diseases, Tenth Edition (ICD-10) criteria. Patients initiate naltrexone after detoxification on an outpatient or inpatient basis using tapering divided doses of benzodiazepines, usually for about 10 days. The benzodiazepines used for detoxification primarily include diazepam (typically tapering off from initial doses of 50 mg per day) and sometimes lorazepam (given in cases of significant liver dysfunction). Naltrexone is given orally at a standard dose of 50 mg once daily. Those found eligible and initiated on naltrexone 50 mg daily were recruited in the study after taking informed consent. Patients with significant physical/psychiatric co-morbidity were excluded from the study. The patients

were detoxified as per the standard treatment intervention before initiating naltrexone. The patients were followed up one month after treatment initiation. The follow-up assessments included clinical status (retained/not retained) and naltrexone treatment (response reduction of drinking/reduction of craving). Retention in the treatment was defined as the patient visiting the centre at the end of one month and adhering to medication for at least 24 days in the last month.

At baseline, the sociodemographic and clinical profile (the World Health Organization Alcohol, Smoking, and Substance Involvement Screening Test [WHO ASSST], the Readiness to Change Questionnaire [RCQ], the Severity of Alcohol Dependence Questionnaire [SADQ], and the Obsessive Compulsive Drinking Scale [OCDS]), alcohol use pattern (type, quantity, and frequency), and treatment history were collected. Craving was assessed using a self-report questionnaire. At the end of one month of follow-up, an assessment regarding participants' drinking status was carried out using the timeline follow-back method (TLFB). Patients were asked about their drinking behaviours (number of drinking days and number of drinks per day) during the period since the last assessment. The patient self-report about medication compliance (naltrexone only) was also recorded. The study protocol was approved by the Institute Ethics Committee.

The socio-demographic and clinical characteristics were analysed by suitable parametric or non-parametric biostatistics. Further, naltrexone treatment response was assessed using suitable paired data testing. The sociodemographic and clinical profiles were presented as mean (standard deviation [SD]) or percentage. The baseline comparison of variables, including alcohol use pattern, craving, and treatment history among patients retained and not retained on naltrexone, was analysed by an independent sample t-test or Mann-Whitney test. Alcohol use and craving at baseline and one month among patients retained and not retained on naltrexone were compared. The two-sided p-value of 0.05 was considered statistically significant. All the statistical analyses were performed using SPSS 21.0 version.

Results

A total of 100 male patients with alcohol dependence started on naltrexone were included in the study. The patients' mean age (SD) was 36.4 (8.7) years. The majority of the patients (78%) were married and living in joint families (92%). Three-fourths of the patients (75%) worked as skilled personnel, while one-fourth (25%) were either unskilled personnel or students. Moreover, most patients (91%) had a high school or diploma degree.

Data on various addiction indices, namely severity, compulsion to drink, and craving, were recorded. More than 90% of the subjects scored high for alcohol use and moderate (87%) for tobacco use on the WHO ASSIST scores. Most subjects (76%) liked changing their habits under the RCQ action stage. The SADQ score fell under moderate alcohol dependence for 64% of the patients. A large number of patients (60%) were under mild symptoms as per the OCDS.

The patients who were retained (n = 53) in treatment and those not retained (n = 47) were compared (Table 1). The retention rate at the end of one month of naltrexone treatment was 53%. All the treatment-retained patients (n = 53) reported naltrexone consumption for more than 24 days in the last month. It was observed that the two groups did not differ significantly on the baseline parameters like the usual quantity or type of alcohol used, the frequency of drinking, family history of alcohol use, and the time taken to travel to the centre. However, treatment-retained patients were more likely to report craving at the baseline compared to those not retained.

Table 1. Comparison of patients retained and not retained on naltrexone treatment

Variable	Retained (n = 53)	Not Retained (n = 47)	Comparison (*P* value)
Usual quantity of alcohol used at treatment initiation (standard drinks)	10.7 (6.0)	10.3 (5.3)	t = 0.370 (0.712)
Type of alcohol used			
Indian-made foreign liquor	25 (47.2%)	19 (40.4%)	χ^2 = 0.460 (0.498)
Country-made liquor	28 (52.8%)	28 (59.6%)	
Frequency of drinking any alcoholic beverage			
Daily/almost daily	38 (71.7%)	37 (78.7%)	
3-4 times per week	11 (20.8%)	6 (12.8%)	U = 1174 (0.514)
1-2 times per week	4 (7.5%)	1 (2.1%)	
2-3 times per month	0 (0%)	3 (6.4%)	
Craving present on day 0	53 (100%)	43 (91.5%)	(FE 0.045)*
History of psychiatric comorbidity	0 (0%)	0 (0%)	χ^2 = 0.000 (1.000)
Family history of alcohol use disorder	22 (41.5%)	24 (51.1%)	χ^2 = 0.915 (0.339)
Hours of travel time to the centre	2.5 (2.1)	2.9 (2.5)	t = 0.727 (0.469)

* Significant at $P < 0.05$. FE, the Fisher's Exact Test.

Among those retained in treatment, alcohol use and craving were compared at the baseline with that after one month (Table 2). It was found that alcohol use was only once for 5 patients, 2 days for 3 patients, 3 days for 4 patients, 4 days for 1 patient, and 3 patients used alcohol daily or almost daily. The paired sample comparison showed a significant decrease in the number of subjects (86%), reporting alcohol use at one-month follow-up compared to the baseline. The usual amount of alcohol used (among those who used alcohol) (mean[SD]) = 10.7(6)) was significantly reduced to 4.9 (3.2), with a significant decline (50%) in the follow-up period.

Discussion

The present study suggests that the reduction of alcohol use among ADS patients retained in treatment with naltrexone. Only about one-third of the retained participants used alcohol, and among them, the usual quantity of alcohol use and craving was also reduced. The findings are in line with previous studies suggesting that naltrexone is associated with a reduction in rates of relapse and craving.[7,8]

However, a more concerning finding is that by the first month, about half of the patients dropped out of treatment. A previous study from the region also suggests high dropout rates in the initial days of treatment for alcohol use disorders.[9] Previous systematic reviews and meta-analyses of trials with naltrexone in alcohol-dependent patients have reported a significant proportion of patients dropping out of the studies.[7] There are several risk factors ascribed to drop from addiction treatment services, including cognitive deficits, therapeutic alliance, personality characteristics, and age. Motivation for abstinence may also fluctuate with time, and that may determine the dropout from treatment as well. The baseline profiles of treatment-retained and dropped-out patients were totally similar except for craving. Interestingly, those with high baseline cravings were more likely to be retained in treatment. This may indicate that those with high cravings perceived naltrexone to be beneficial and, hence, were retained in treatment.

Findings suggest that many patients with alcohol dependence started on naltrexone may have good outcomes in terms of reduction of alcohol use and craving., making naltrexone a potentially necessary medication in the treatment of alcohol use disorder. The entire 'good' outcome may not be attributed to naltrexone, and other factors like engagement in treatment, therapeutic alliances, and changed family interactions after medication use might also have contributed to patient improvement. Since many patients leave treatment prematurely (about half of the patients in the first month), treatment retention-related factors may also need to be thoroughly studied, and other measures need to be employed to address treatment dropout.

The study's findings should be interpreted considering limited sample size, single-centre experience, no control group, and limited duration of follow-up, but in a naturalistic clinical setting. Withdrawal ratings were not applied, adherence to naltrexone was not formally assessed, and alcohol abstinence was not biologically corroborated. There could have been other potential confounders affecting the outcomes. Despite these limitations, the study provides evidence of naltrexone being effective in patients with alcohol dependence who were retained in treatment. Further studies may look at other factors influencing naltrexone treatment response, including pharmacogenetics and the effect of pertinent environmental and individual life circumstances.

Table 2. Alcohol use and craving among patients retained on naltrexone at baseline and at follow-up (n = 53)

Variable	Baseline	At 1 month	Comparison (*P* value)
Patients reporting alcohol use	53 (100%)	17 (32.1%)	$\chi^2 = 15.000$ (<0.001)*
Mean frequency of standard drinks (SD) in the past 1 month	10.7 (6.0) (n = 53)	4.9 (3.2) (n = 17)8	Z = 6.376 (<0.001)*
Patients reporting craving	53 (100%)	15 (28.3)	$\chi^2 = 36.026$ (<0.001)*

* Significant at $P < 0.05$; McNemar χ^2, Wilcoxon signed rank Z.

Conclusion

A significant reduction in the number of patients reporting alcohol use, along with a reduction in craving and the amount of alcohol used among patients undergoing naltrexone treatment, was observed. This study is from a naturalistic treatment setting and provides further evidence of naltrexone being effective in patients with alcohol dependence who were retained in treatment. These results will help to deliver better treatment management among alcohol-dependent patients.

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Authors' Contribution

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Competing Interests
There is no conflict of interest to declare.

Ethical Approval
The study was approved by the Ethics Committee of the All India Institute of Medical Sciences, New Delhi, India.

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