Comparative Study of Different Anti Craving Medication for Alcohol Dependence and Their Effect on Relapse Rate

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ABSTRACT

Background

Alcohol use disorder is a chronic medical condition with a multifactorial aetiology. Food and drug administration approved treatment options for alcohol dependence syndrome includes: Naltrexone, Acamprosate, and Disulfiram and Topiramate as an off label drug. The lack of data specific to the Nepalese population pose significant challenges.

Objective

To fill that gap by assessing the effectiveness of Naltrexone, Disulfiram, Topiramate and Acamprosate in relapse prevention

Method

Hospital based cohort study conducted over a period of two months. The total 128 participants were divided into four groups randomly. Patients in the Naltrexone group were prescribed a 50 mg tablet once daily, patients in Topiramate group was given 25 mg up to 100 mg. Acamprosate group, 333 mg one tablet three times a day was given and Disulfiram group received 250 mg once a day and followed up for four weeks. The association between alcohol consumption and sociodemographic characteristics was assessed using Chi-square test. The Statistical Package for Social Science software (IBM SPSS Statistics 21, Chicago, USA) was used for analysis.

Result

Out of 128 participants 23.4% relapsed in 12 weeks follow up. Naltrexone, Topiramate, Disulfiram, and Acamprosate all were equally effective in preventing relapse and there was no statistically significant differences identified among these medications regarding relapse prevention in our study.

Conclusion

This study contributes important new data on the efficacy of Acamprosate in the treatment of alcohol dependence in Nepalese population. The study also support for use of pharmacotherapy for relapse prevention.

KEY WORDS

Alcohol dependence, Anti-craving drugs, Relapse prevention

INTRODUCTION

The return to any form of alcohol use after a time of sobriety or reduced use was defined as relapse.[1] Relapse prevention is an essential part of addiction recovery. The primary goal of alcohol dependence treatment should be patients in attaining either complete abstinence from alcohol or a substantial reduction in alcohol-related problems through decreased alcohol consumption.[2]

Several pharmaceutical options are available for alcohol dependence treatment and management. However, Food and Drug Administration (FDA) approved treatment options for alcohol dependence syndrome includes: Naltrexone, Acamprosate, and Disulfiram. Off label drug use includes: Topiramate, Gabapentin, Baclofen, Ondansetron. Suggested drugs for abstinence are: disulfiram and acamprosate.[3]

In a double-blind, placebo controlled study, Naltrexone, acamprosate, and the combined medication were significantly more effective than placebo. Comparing the course of non-relapse rates between naltrexone and acamprosate, the naltrexone group showed a tendency for a better outcome regarding time to first drink and time to relapse. The combined medication was most effective with significantly lower relapse rates than placebo and acamprosate but not naltrexone. The results of this study support the efficacy of pharmacotherapeutic strategies in the relapse prevention of alcoholism. Naltrexone and acamprosate, especially in combination, considerably enhance the potential of relapse prevention.

The scarcity of direct comparative studies and the lack of data specific to the Nepalese population pose significant challenges. Thus, in this study we aims to fill that gap by assessing the effectiveness and determining the relative effectiveness of Naltrexone, Disulfiram, Topiramate and Acamprosate in treating alcohol use disorder within the Nepalese context.

METHODS

This is the Hospital based cohort study conducted at department of psychiatry, Kathmandu University Hospital, Dhulihel, Kavre, Nepal. It is a tertiary care hospital where patients all over the country get referred for the treatment.

All patients who came to the hospital during one month period for alcohol related problems were screened. The participants were recruited from in-patient clinic and out patient's clinics from 12 June 2025 to 15 July 2025.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval was taken from Institutional Review Committee (IRC) IRC approval No 154/25 Kathmandu University School of Medicinal Sciences (KUSMS). Eligibility criteria were: voluntary written consent, Alcohol Dependence Syndrome diagnosed by consultant psychiatrist according to ICD 10 Diagnostic Criteria for Research, age between 18 and 65 years, and those who were ready for pharmacological treatment with either Naltrexone, Acamprosate, Topiramate or Disulfiram after detoxification. Exclusion criteria were: refusal to give consent, severe psychiatric illnesses in the active phase like depression, psychosis, anxiety disorders, personality disorders, significant suicidal risk, and Clinically decompensated liver disease (jaundice or other signs of liver failure), History of nephrolithiasis, History of glaucoma, Concurrent use of any psychotropic medication and Previous hypersensitivity to topiramate, disulfiram, acamprosate and naltrexone. Mental status examination was done to see if they have any confusion, disorientation, any perceptual abnormalities and any signs of impaired cognitive functioning.

Once they were physically and mentally fit, individual case was assessed for suitable drug. Consent was obtained in the prescribed form from all the participants after explanation of details of the study with maintaining strict privacy and confidentiality. A detailed information regarding age, gender, year of enrollment, family income, address, marital status, family type, religion, year of alcohol use, family history of substance use, family history of psychiatric disorders, concurrent use of any other substance, comorbid psychiatric disorders, previous treatment history for dependence had been taken from predesigned socio-demographic proforma.

The participants were advised to stop drinking, educated them about alcohol-related disorders,psychoeducated about a rationale to take medication, they had been instructed on the importance of medication adherence and also given information regarding side effects of the medications. The participants were divided into four groups. Patients in the Naltrexone group were prescribed a 50 mg tablet once daily with no further increment. Patients in Topiramate group was given up to 100 mg. Acamprosate group, 333 mg one tablets three times a day was given and Disulfiram group received 250 mg once a day and followed up at 4 weeks.

Baseline characteristics for different variables are presented in a table. For each categorical variable, frequencies and percentages are reported, along with the p-value for a χ^2 test of equality of proportions across the categories. The Statistical Package for Social Science Software (IBM SPSS Statistics 21, Chicago, USA) was used for analysis.

RESULTS

As shown in table 1, the mean age of the participants were 40 ± 8.5 years. They were almost equally distributed, 56.3% were age more than 40 years and 43.7% were less than 40 years. We had very less number of females and almost all of them were males (93.8%), majority of participants were educated (87.5%) and employed (64.8%).

Table 1. Socio-demographic variables.

Variables		N=128(%)
Age	Up to 40	72 (56.30)
	41 and above	56 (43.80)
Sex	Male	120 (93.80)
	Female	8 (6.20)
Occupation	Unemployed	45 (24.70)
	Employed	83 (64.80)
Education	No formal	16 (12.50)
	Formal	112 (87.50)
Demography	Rural	62 (51.60)
	Urban	66 (58.40)

As depicted in table 2, out of 128 participants 23.4% relapsed in 4 weeks follow up, more than half (60.4%) had dependency for more than 15 years and 8.6% reported side effects like dizziness, headache, diarrhea and abdominal pain.

Table 2. Alcohol related variables.

Variables		N=128 (%)
Substance use	ADS	95 (74.20)
	Polysubstance	33 (25.80)
Hospital stay	Up to 12 days	85 (66.40)
	13 days and above	43 (33.60)
Relapse	No	98 (76.60)
	Yes	30 (23.40)
Years of Dependency	Up to 15 years	77 (60.20)
	16 years and above	51 (39.80)
History of previous Detox	No	98 (76.60)
	Yes	30 (23.40)
Side effects noted	No	117 (91.40)
	Yes	11 (8.60)

Table 3 shows the association between sociodemographic variables with relapse and we could not established any statistically significant association with any variables. Table 4 shows the alcohol related variables like duration of alcohol use, comorbid substance use, duration of hospital stay, adverse side effects of different drugs and previous history of deaddiction treatment with relapse. We found that history of previous treatment for deaddiction was significantly associated with relapse.

DISCUSSIONS

Alcohol dependency treatment is complex due to its multifactorial etiology, encompassing neurobiological, genetic, psychological, social, and environmental factors.[5]

In Nepal limited studies have been carried out, one study done by Kaul et al. compared Baclofen and Topiramate in the treatment of alcohol dependence syndrome as an anti

Table 3. Socio-demographic Variables and its association with Relapse

Variables		N=128 (%)	Chi-square df p-value
Age	Up to 40	72 (56.20)	0.2 1 0.63
	41 and above	56 (43.80)	
Sex	Male	120 (93.80)	0.5 1 0.45
	Female	8 (6.20)	
Occupation	Unemployed	45 (24.70)	0.4 1 0.49
	Employed	83 (64.80)	
Education	No formal	16 (12.50)	0.6 1 0.43
	Formal	112 (87.50)	
Demography	Rural	62 (51.60)	1.0 1 0.30
	Urban	66 (58.40)	

Table 4. Alcohol related variables and its association with relapse.

Variables		N=128 (%)	Chi-square df p-value
Substance use	ADS	95 (74.20)	0.6 1 0.40
	Polysubstance	33 (25.80)	
Hospital stay	Up to 12 days	85 (66.40)	0.72 1 0.39
	13 days and above	43 (33.60)	
Years of Dependency	Up to 15 years	77 (60.20)	0.76 1 0.38
	16 years and above	51 (39.8-)	
History of previous Detox	No	98 (76.60)	34.7 1 0.0001
	Yes	30 (23.40)	
Side effects noted	No	117 (91.40)	1.3 1 0.24
		11 (8.60)	

craving agent they have found that both drugs are equally effective at six weeks for controlling craving.[6] Baclofen started to show significant improvements after two weeks of trial.[6] Another study from Nepal which compared topiramate and Naltrexone in preventing alcohol relapse and they concluded that Topiramate 100 mg is equally efficacious to Naltrexone 50 mg in terms of maintaining alcohol abstinence and reducing the alcohol daily intake but Topiramate is better than Naltrexone in decreasing craving at 12 weeks.[7]

In our study we found that: Naltrexone, Topiramate, Disulfiram, and Acamprosate all are equally effective in preventing relapse and there was no statistical significant differences identified among these medications regarding relapse prevention. Similar finding reported by Anton et al., a large scale trial (COMBINE), which compared acamprosate, naltrexone, and behavioral therapies, both

individually and combined with each other, against placebo (N = 1383), found that acamprosate had no significant effect on drinking in comparison to placebo, either alone or in combination with naltrexone and/or behavioral intervention.[8] However, another study, a Cochrane meta-analysis of 24 RCTs with 6915 participants found that acamprosate significantly reduced the risk of any drinking and increased cumulative duration of abstinence.[9]

A study by Gerardo et al. suggests both Topiramate and Naltrexone were efficacious in the treatment of alcohol dependence, and the treatment costs were also similar.[10]

Study done by Baltieri et al. found that, although there were no significant differences between topiramate and naltrexone on a many outcome measures, Topiramate was superior over naltrexone on several measures of drinking including time to first relapse, cumulative abstinence duration and heavy drinking weeks.[11]

Meta-analysis published in 2013 concluded that, acamprosate has been found to be slightly more efficacious in promoting abstinence and naltrexone slightly more efficacious in reducing heavy drinking and craving.[12]

When evaluating the effectiveness of drugs, a crucial factor to keep in mind is the equivalent dosage. In a review article by Ricardo et al, findings suggests that Topiramate in the dosage range of 75-300 mg/day, shows beneficial effects in alcohol relapse prevention and in reducing drinking behavior.[13]

Another study on comparing Topiramate with naltrexone for alcohol dependence also found that Topiramate at a mean dose of 200 mg/day was better than naltrexone at a mean dose of 50 mg/day at reducing alcohol intake and cravings throughout the study.[14]

An additional important element for treatment results is genetics. However, a genotype-stratified double blind RCT in Topiramate and Naltrexone showed that Topiramate is at least as effective and safe as the first-line medication, naltrexone, in reducing heavy alcohol consumption, and superior in reducing some clinical outcomes. Neither rs2832407 nor rs1799971 had effects on Topiramate and Naltrexone treatments respectively.[15]

Relapse is a multifactorial phenomenon and factors affecting risk for relapse after treatment include addiction severity, co-occurring psychiatric disorders, employment, Higher Addiction Severity Index (ASI) scores for drug use and employment problems.[16] Study from US which aimed to determine what factors were associated with risk for relapse over a period of one year also reported that higher Addiction Severity Index (ASI) scores for alcohol problems, psychiatric severity, and the greater number of prior alcohol or drug treatment episodes predicted higher risks for relapse.[17] Our study also found that greater number of prior alcohol treatment was significantly associated with relapse.

The prevalence of common psychiatric disorders like mood, anxiety, and thought disorders is higher in people with alcohol use disorder than in the general population. Lifetime prevalence of alcohol use disorder in those with lifetime major depressive disorder ranges from approximately 27% to 40% across epidemiological studies with a median prevalence of 30% across 35 studies.[18] Meta-analysis in 2009 found that, the median lifetime prevalence of alcohol use disorder in patients diagnosed with schizophrenia was 21% and current prevalence in this group was 11%.[19] Psychiatric commodities are the major factors that affects treatment outcomes in alcohol use disorders. However, our study could not establish significant relationship between comorbidities and relapse outcome.

Comprehensive approaches for addressing alcohol use disorder alongside co-occurring psychiatric conditions have been researched, and the overall finding is that they typically produce more favorable outcomes compared to separate treatments.[20]

A new approach to combination pharmacotherapy in the treatment of alcohol use is also being developed. Recent meta-analysis published in May 2025 found that combined pharmacotherapies are more effective than monotherapy in enhancing abstinence rates in AUD treatment. Combination therapies led to an average 4.045% increase in abstinence rates (95% CI: 0.415% to 7.675%) compared to monotherapies. Meta-regression showed a strong positive association between the use of Naltrexone, Acamprosate, and Sertraline-either alone or in combination.[21]

For a number of reasons, we were unable to prescribe combination therapy in our study. One of the reason is that, combination therapy may potentially reduce patients' adherence to treatment; adherence is a critical factor for the successful treatment of substance use disorders. Thus, combined medication regimens may lead to treatment discontinuation. This could be one of the limitation of our study. Other limitations were short treatment duration and follow up and few patients from an inpatient setting, where the opportunity to drink was limited in first few weeks. In addition, patients received behavioral therapy like motivational enhancement therapy, which may have helped reduce drinking and craving severity.

CONCLUSION

This study contributes important new data on the efficacy of acramprosate in the treatment of alcohol dependence in Nepalese population since acamprosate was not available in the past in Nepal. In addition, this study is to our knowledge the first study in Nepal to compare topiramate, disulfiram, acamprosate and naltrexone in the treatment of alcohol dependence patients. The study also supports for use of pharmacotherapy for relapse prevention, although more research with larger sample sizes will be needed to verify these observations.

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