Original Research Article

A comparative study of naltrexone versus baclofen in the management of alcohol dependence

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Abstract

Background: Excessive use of alcohol is a major public health problem. Alcohol dependence represents a set of biological, psychological and social manifestations. Present comparative study was aimed to compare naltrexone versus baclofen in the management of alcohol dependence. **Material and Methods:** Present study was a prospective, interventional study conducted at a government-run tertiary care de-addiction center working among individuals 21-60 years of age, with addiction to alcohol, had moderate-to-high level of dependence, meeting the International Statistical Classification of Diseases-10 (ICD-10) criteria for alcohol dependence. At start of pharmacotherapy, patients were randomly allocated to Group N (Naltrexone) or Group B (Baclofen), by computer generated numbers. **Results:** 30 patients allocated to Group N (Naltrexone) or Group B (Baclofen) each completed study. All patients were male. Majority of patients were from 31-40 years age group, educated upto middle school (7th standard), from urban area, unemployed, single status and living in nuclear family. Sociodemographic characteristics were comparable in both groups and difference was not significant statistically ($p>0.05$). Craving, Alcohol use and relapse were comparable in both groups and difference was not significant statistically ($p>0.05$). Various side effects light headedness, nausea, decreased appetite, gastritis, tremors, palpitations, generalised fatigue and erectile dysfunction were noted in present study, though incidence was more in naltrexone group but difference was not significant statistically ($p>0.05$). **Conclusion:** Naltrexone and Baclofen, both had comparable results with respect to severe and persistent craving, continued problematic use of alcohol and can be considered in pharmacotherapeutic approach to alcohol dependence.

Keywords: Naltrexone and Baclofen, alcohol dependence, craving, relapse

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INTRODUCTION

Excessive use of alcohol is a major public health problem. It causes 5.9% of all deaths globally and is responsible for 5.1% of the DALYs (Disability Adjusted Life Years).[1] Alcohol was reported as the most commonly used substance (apart from tobacco) with 43.9% of the treatment seekers reporting its current use.[2] Alcohol dependence represents a set of biological, psychological and social manifestations. It represents a maladaptive pattern of alcohol use that leads on to clinically significant impairment or distress or both. One can suspect possibility of alcohol dependence when alcohol use turns problematic.[3] Currently, there are four FDA-approved medications for alcohol use disorders (AUD) (disulfiram, oral naltrexone, long-acting intramuscular naltrexone, acamprosate) and a number of non-FDA-approved medications have demonstrated efficacy in randomized controlled trials, e.g. topiramate, baclofen, gabapentin and nalmefene has been approved.[4] Naltrexone and its active metabolite 6b-naltrexol act as opioid receptor antagonists, particularly at the l-opioid receptor. Its excretion is primarily renal. The mechanism of its beneficial effect in

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the treatment of alcohol dependence is not fully understood although it is believed to reduce the reward effects of alcohol by modulating the dopaminergic mesolimbic pathway.[5,6] Baclofen is a selective c-aminobutyric acid (GABA)-B receptor agonist, activation of GABA-B receptors might reduce anxiety and it was for this reason that it was identified as a potential treatment for alcohol withdrawal and dependence.[7] Present comparative study was aimed to compare naltrexone versus baclofen in the management of alcohol dependence

MATERIAL AND METHODS

Present study was a prospective, interventional study conducted at a government-run tertiary care de-addiction center working under department of psychiatry, XXX medical college and hospital, XXXX. Study duration was of 12 months (between January 2021 to December 2021). Study permission was taken from institutional ethical committee. Study was explained to patients and relatives, a written permission was obtained for participation in present study.

Inclusion criteria: Individuals 21-60 years of age, with addiction to alcohol, had moderate-to-high level of dependence, meeting the International Statistical Classification of Diseases-10 (ICD-10) criteria for alcohol dependence.

Exclusion criteria: Individuals with comorbid medical or psychiatric illness. Undergoing any other psychopharmacological interventions during the study period. Individuals with known drug hypersensitivity, epilepsy, pregnancy, lactation, any serious or unstable cardiac, renal, hepatic, hypertensive, pulmonary, endocrine, or neurological disorder. Individuals not willing to participate, counselling and follow up, lost to follow up

Study proforma was designed including demographic details, details of addiction (personal details, drug use pattern, severity of dependence, level of motivation, severity of withdrawal, and degree of craving). The entire data collection was done by a single trained investigator by face-to-face interview of the participants. Routine investigations (complete blood count, blood urea, serum creatinine, and electrolytes) and biological markers for alcohol abuse (liver function tests) were tested at the time of admission and repeated whenever required. Data was collected using the Psychiatric Performa and patients were admitted for detoxification in the de-addiction ward. After detoxification, the treatment under study was initiated among the participants after assessing them for craving, relapse risk, and attitude toward treatment and generally patients were discharged within 2 weeks. In addition to pharmacotherapy, all the patients attended four group therapy sessions which were held once a week. At start of pharmacotherapy, patients were randomly allocated to Group N (Naltrexone) or Group B (Baclofen), by computer generated numbers. Each group had 35 patients. At the end of study, 30 patients from each group completed study. Naltrexone was started at a dose of 25 mg and then built up gradually to 50 mg/day after making sure that the patient was tolerating the medication well till the end of the study period. Baclofen was started with 20 mg tablet once a day. The dose was increased to twice a day after a week after ensuring that the medication was well tolerated.

During the weekly follow-up visits in the 1st month, and bi-weekly follow-up visits for the next 2 months, the participants were assessed for craving, relapse risk, and medication adherence. Craving was recorded in terms of

a. no craving or minimal craving that can be easy to manage,
b. significant cue-associated craving that is often difficult to manage, (moderate craving)
c. severe pervasive craving that cannot be managed (pervasive craving).

During the follow-up, alcohol use was recorded as

a. abstinence (did not consume any amount of alcohol in the past 1 week),
b. intermittent or occasional drinking (consumed <20% of their usual intake per day, never on three successive days, and not having any socio-occupational dysfunction due to alcohol use in the past 1 week)
c. problem drinking or dependent use (i.e., continued use).

In addition, the side effects, if any, during the ongoing treatment were documented through interview and self-reporting, and the necessary modifications in medication were done along with other precautionary measures.

Data was analysed using SPSS version 20 (IBM, Chicago, USA). The quantitative data were expressed as mean and standard deviation. The qualitative data were presented as frequencies and percentages. Pearson's Chi-square test was used to compare data. p value less than 0.05 was considered significant.

RESULTS

30 patients allocated to Group N (Naltrexone) or Group B (Baclofen) each completed study. All patients were male. Majority of patients were from 31-40 years age group, educated upto middle school (7th standard), from urban area, unemployed, single status and living in nuclear family. Sociodemographic characteristics were comparable in both groups and difference was not significant statistically ($p>0.05$).

Table 1: Distribution of sociodemographic characteristics

Parameters	Naltrexone, *n* (%)	Baclofen, *n* (%)
Age (years)		
21-30	5 (16.67%)	6 (20 %)
31-40	13 (43.33%)	12 (40 %)
41-50	8 (26.67%)	7 (23.33%)
51-60	4 (13.33%)	5 (16.67%)
Gender		
Male	30 (100 %)	30 (100 %)
Female	0	0
Education level		
Illiterate	0	1 (3.33%)
Primary	6 (20 %)	4 (13.33%)
Middle	11 (36.67%)	7 (23.33%)
High school	3 (10 %)	6 (20 %)
Higher secondary	5 (16.67%)	7 (23.33%)
Graduate	3 (10 %)	4 (13.33%)
Postgraduate	2 (6.67%)	1 (3.33%)
Residence		
Rural	12 (40 %)	14 (46.67%)
Urban	18 (60 %)	16 (53.33%)
Occupation		
Unemployed	11 (36.67%)	9 (30 %)
Student	3 (10 %)	2 (6.67%)
Daily wager	4 (13.33%)	7 (23.33%)
Farmer	6 (20 %)	6 (20 %)
Businessman	1 (3.33%)	3 (10 %)
Private/government employee	5 (16.67%)	3 (10 %)
Family type		
Joint	6 (20 %)	5 (16.67%)
Nuclear	24 (80 %)	25 (83.33%)
Marital status		
Single	15 (50 %)	13 (43.33%)
Married	11 (36.67%)	14 (46.67%)
Divorced	4 (13.33%)	3 (10 %)

We compared Craving (No craving, Moderate craving and Severe craving), Alcohol use (Abstainers, Intermittent users and Problem users) and relapse at 2,4,8 and 12 week intervals among Group N (Naltrexone) and Group B (Baclofen). Craving, Alcohol use and relapse were comparable in both groups and difference was not significant statistically (p>0.05).

Table 2: Craving and Alcohol use

Characteristic	Naltrexone, *n* (%)				Baclofen, *n* (%)				P value
	Week 2	Week 4	Week 8	Week 12	Week 2	Week 4	Week 8	Week 12	
Craving (%)									
No craving	5 (16.67%)	8 (26.67%)	11 (36.67%)	18 (60 %)	6 (20 %)	9 (30 %)	11 (36.67%)	16 (53.33%)	>0.05
Moderate craving	17 (56.67%)	15 (50 %)	14 (46.67%)	8 (26.67%)	15 (50 %)	13 (43.33%)	12 (40 %)	9 (30 %)	>0.05
Severe craving	8 (26.67%)	7 (23.33%)	5 (16.67%)	4 (13.33%)	9 (30 %)	8 (26.67%)	7 (23.33%)	5 (16.67%)	>0.05
Alcohol use (%)									
Abstainers	8 (26.67%)	12 (40 %)	13 (43.33%)	17 (56.67%)	7 (23.33%)	12 (30 %)	15 (50 %)	19 (63.33%)	>0.05
Intermittent users	13 (43.33%)	12 (40 %)	12 (30 %)	8 (26.67%)	12 (30 %)	10 (33.33%)	9 (30 %)	7 (23.33%)	>0.05
Problem users	9 (30 %)	6 (20 %)	5 (16.67%)	5 (16.67%)	11 (36.67%)	8 (26.67%)	6 (20 %)	4 (13.33%)	>0.05
Relapses	6 (20 %)	5 (16.67%)	5 (16.67%)	5 (16.67%)	5 (16.67%)	4 (13.33%)	5 (16.67%)	6 (20 %)	>0.05

Various side effects light headedness, nausea, decreased appetite, gastritis, tremors, palpitations, generalised fatigue and erectile dysfunction were noted in present study, though incidence was more in naltrexone group but difference was not significant statistically (p>0.05).

Table 3: Side effects

Side effect	Naltrexone (%)	Baclofen (%)
Light headedness	6 (20 %)	3 (10 %)
Nausea	3 (10 %)	0
Decreased appetite	2 (6.67%)	3 (10 %)
Gastritis	3 (10 %)	2 (6.67%)
Tremors	1 (3.33%)	0
Palpitations	1 (3.33%)	0
Generalised fatigue	1 (3.33%)	2 (6.67%)
Erectile dysfunction	1 (3.33%)	0
Total	**12 (40)**	**5 (16.66)**

DISCUSSION

Alcohol dependence is a chronic disorder that may have multiple relapses and remissions, increased mortality and low long-term abstinence rates that lead to increased psycho-social losses. A history of intense, irresistible, compulsive desire to use alcohol (known as craving); a gradual increase in amount of alcohol used over time because of reduction in the effect experienced with previous amount (known as tolerance); and appearance of withdrawal symptoms including sweating, increased pulse rate, hand tremor, nausea, vomiting, insomnia, psychomotor agitation, anxiety, transient visual, tactile, or auditory hallucinations or illusions on stopping or reducing the amount usually consumed are indicators of psychological and physical dependence on alcohol.[3] In study by Arun Kumar *et al.*,[8] 30 alcohol-dependent patients were assigned each to naltrexone, baclofen, and acamprosate group after detoxification. The patients were assessed for craving, relapse risk, and medication adherence using the respective scales and questionnaires. Naltrexone was most effective in decreasing craving and drinking behavior. Baclofen showed best tolerability in terms of liver function tests and least number of side effects reported. Naltrexone group reported the least number of relapses but maximum number of side effects. Rozatkar AR *et al.*,[9] studied 113 male patients, mean age was 41.49 ± 9.75 years, most having a family history of substance use (70.97%), and many reporting binge use pattern in last year (49.46%). Baseline assessment revealed 48.7% of the sample was in precontemplation phase for alcohol use and 70% reported severe and persistent craving. This persistent craving was reported by only 15% of the sample by the end of 4 weeks treatment with baclofen (20–40 mg/day). Thirty-four percent of patients reported continued problematic use of alcohol by the end of 4 weeks. They noted that baclofen reduces craving and alcohol consumption including in those with poor motivation. In study by Shukla L *et al.*,[10] among 549 male cases diagnosed with alcohol dependence who received Acamprosate (201) or Baclofen (348), they noted a strong correlation between doses of baclofen used, average alcohol intake and time to first drink in a selected sample with severe alcohol dependence. Baclofen has been shown to enhance abstinence, to reduce drinking quantity, to reduce craving, and to reduce anxiety in alcohol-dependent individuals in 2 placebo-controlled trials in Italy.[11] In present study, percentage of relapses in the naltrexone and baclofen groups was 16.67 % and 20%, respectively. For naltrexone percentage of relapses was reported in other studies was 20 % (Aruun Kumar *et al.*,[8]), 55 % (Rubio *et al.*,[12]) and 23% (Volpicelli *et al.*[13]). While for baclofen, percentage of relapses was reported in other studies was 50 % (Aruun Kumar *et al.*, [8]), 36% (Gupta *et al.*,[14]) A systematic review with direct and network meta-analysis of 32 double-blind randomized controlled trials (RCTs) there is currently no high-grade evidence for pharmacological treatment to control drinking using nalmefene, naltrexone, acamprosate, baclofen or topiramate in patients with alcohol dependence or alcohol use disorder. Some treatments show low to medium efficacy in reducing drinking across a range of studies with a high risk of bias. None demonstrates any benefit on health outcomes.[15] A simple 5-A strategy of Asking every patient about the use of substances (just as we ask for a history of diabetes or hypertension), Assessing the pattern of use and resulting problems (establishing a link between substance use and presenting problem), Advice (clear strong advice to stop or cut down), Assisting (in the form of specific interventions) and Arranging (by making appropriate referrals when required) is recommended, especially for licit substance use (alcohol and tobacco).

CONCLUSION

Naltrexone and Baclofen, both had comparable results with respect to severe and persistent craving, continued problematic use of alcohol and can be considered in pharmacotherapeutic approach to alcohol dependence. Still, additional clinical trial work is necessary to establish

whether Naltrexone/Baclofen does or does not have therapeutic efficacy in alcohol dependence and, if it does, what factors are predictive of response.

REFERENCES

1. Global status report on alcohol and health 2014. World Health organization, Geenva.
2. Clinical Practice Guidelines for the assessment and management of substance use disorders. Eds: Basu D, Dalal P. Indian Psychiatric Society, Hyderabad, 2014.
3. Standard treatment Guidelines, Management of Alcohol Dependence, Full Background document (Draft), Ministry of Health and Family Welfare Government of India, February 2016
4. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA 2014;311:1889–900.
5. Drobes DJ, Anton RF, Thomas SE, et al. Effects of naltrexone and nalmefene on subjective response to alcohol among non-treatment-seeking alcoholics and social drinkers. Alcohol Clin Exp Res 2004; 28: 1362–70.
6. Anton RF. Naltrexone for the management of alcohol dependence. N Engl J Med 2008; 359: 715–21.
7. Addolorato G, Leggio L, Ferrulli A, et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. Lancet 2007; 370: 1915–22.
8. Arun Kumar, Arvind Sharma, P. D. Bansal, Mamta Bahetra, Harkamal K. Gill, and Rakesh Kumar, A comparative study on the safety and efficacy of naltrexone versus baclofen versus acamprosate in the management of alcohol dependence, Indian J Psychiatry. 2020 Nov-Dec; 62(6): 650–658.
9. Rozatkar AR, Kapoor A, Sidana A, Chavan BS. Clinical experience of baclofen in alcohol dependence: A chart review. Ind Psychiatry J 2016;25:11-6.
10. Shukla L, Shukla T, Bokka S, Kandasamy A, Benegal V, Murthy P, et al. Correlates of baclofen effectiveness in alcohol dependence. Indian J Psychol Med 2015;37:370-3.
11. Garbutt, James and Kampov-Polevoy, Alexei and Gallop, Robert and Kalka-Juhl, Linda and Flannery, Barbara. (2010). Efficacy and Safety of Baclofen for Alcohol Dependence: A Randomized, Double-Blind, Placebo-Controlled Trial. Alcoholism, clinical and experimental research. 34. 1849-57
12. Rubio G, Jiménez-Arriero MA, Ponce G, Palomo T. Naltrexone versus acamprosate: One year follow-up of alcohol dependence treatment. Alcohol Alcohol. 2001;36:419–25.
13. Volpicelli JR, Rhines KC, Rhines JS, Volpicelli LA, Alterman AI, O'Brien CP. Naltrexone and alcohol dependence. Role of subject compliance. Arch Gen Psychiatry. 1997;54:737–42.
14. Gupta M, Verma P, Rastogi R, Arora S, Elwadhi D. Randomized open-label trial of baclofen for relapse prevention in alcohol dependence. Am J Drug Alcohol Abuse. 2017;43:324–31.
15. Clément Palpacuer, Renan Duprez, Alexandre Huneau, Clara Locher, Rémy Boussageon, et al. Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on naltrexone, acamprosate, baclofen and topiramate. Addiction, Wiley, 2018, 113 (2), pp.220-237.

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