



COMPARATIVE EFFICACY OF BACLOFEN AND TOPIRAMATE IN ALCOHOL DEPENDENCE SYNDROME: A 3 MONTHS FOLLOW UP STUDY

Psychiatry

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ABSTRACT

Objective: Craving plays significant role in relapse in patients with alcohol dependence syndrome. Baclofen and topiramate are effective in reduction of craving and maintenance of abstinence in various placebo controlled trials.

Method: It is a retrospective study of patients of alcohol dependence who were admitted in de-addiction ward from January- December 2013. Case record files of patient who completed detoxification and were prescribed either baclofen or topiramate were taken out and analyzed after applying coding plan.

Results: A total of 68 patients fulfilled the inclusion criteria, 40 in baclofen group and 28 in topiramate group. Mean age was 38 years in baclofen group and 41 years in topiramate group. Majority of the patients in both the groups were married and employed. Majority of the patients in both the groups had duration of alcohol dependence between 5-10 years. 32.5% patients in baclofen group did not report craving at 3 months against 14.2% in topiramate group and 47.5% patients in baclofen group remained abstinent at 3 months against 28.5% in topiramate group.

Conclusion: Both baclofen and topiramate are effective in reduction of craving and maintaining abstinence in patients with alcohol dependence syndrome and baclofen fared better than topiramate.

KEYWORDS

Baclofen, Topiramate, Alcohol Dependence

INTRODUCTION: Alcohol dependence is a major public health problem throughout the world. Alcohol dependence often follows a chronic, relapsing course similar to other medical disorders, such as diabetes.¹

Without a pharmacological adjunct to psychosocial therapy, the clinical outcome is poor, with up to 70% of patients resuming drinking within 1 year.^{2,3}

Several drugs combined with psychosocial treatments have been found to reduce alcohol consumption in controlled clinical trials and are currently used clinically for the treatment of alcohol dependence.

In the last decade, GABAergic agents such as Baclofen, a γ aminobutyric acid (GABA) B-receptor agonist and Topiramate, GABAergic anticonvulsants have been recommended for the treatment of alcohol dependence and the prevention of relapse.^{4,5} Baclofen has been shown to reduce alcohol craving and enhance abstinence in alcohol-dependent patients.⁶

Addolorato et al reported that baclofen, 30 mg/d, was significantly better than placebo in increasing total abstinence (71% vs. 29% respectively), decreasing drinking days and reducing craving in 84 individuals with alcohol dependence and cirrhosis studied over a period of 12 weeks.⁷

In a 12-week, double-blind, randomized controlled trial carried out in 63 alcohol-dependent patients, topiramate compared with placebo was associated with a lower number of drinks per drinking day a lower percentage of heavy drinking days and a higher percentage of days abstinent.⁸

In a recent 4 weeks study from India on use of baclofen in alcohol dependence reported that it reduced craving and alcohol consumption in alcohol dependent subjects.⁹

Hence, in the absence of head to head comparison of baclofen and topiramate in alcohol dependence syndrome, the current study is planned to see the effects of these molecules in patients with alcohol dependence syndrome.

METHODOLOGY: Case record files of patients of Substance Use Disorders (SUDs), who were admitted in de-addiction ward of department of Psychiatry, a tertiary care teaching hospital of North India from January 2013-December 2013, were taken out. A total of 229 patients of Substance use Disorders were admitted during this period. Out of which 122 patients were of Alcohol Dependence syndrome (ADS). A total of 110 files could be traced at the time of assessment and were analyzed for socio-demographic, clinical and treatment outcome variables after applying coding plan. Patients having dependence on other substances except nicotine and caffeine,

who did not complete detoxification and did not receive baclofen or topiramate as anticraving agent, were excluded from study.

As a protocol in the department, patients who are having moderate to severe alcohol dependence, fair to good motivation, willingness to get admitted, past unsuccessful attempts to achieve abstinence on OPD basis or history of complicated withdrawals in past and accompanying with family member get admitted in de-addiction ward.

As a standard follow up notes in the case record files, craving is recorded as reported by the patient i) no craving or very minimal craving that can be managed by the patient without any difficulty as '0' or '+' ii) significant craving (moderate craving) that leads to intermittent alcohol use is noted as '++' and iii) severe craving that causes more frequent alcohol use and dysfunction is noted as '+++'.¹⁰

The drug use pattern during the follow up is recorded as (a) abstinence, (b) intermittent or occasional drinking, and (c) relapsed. For the purpose of this study, we defined abstinent user as those who did not consume any amount of alcohol after discharged; intermittent drinking as those who consumed alcohol on 1-2 occasions during last 2 weeks and relapsed means that who returned to original alcohol drinking pattern.

RESULTS:

Out of 110 patients of ADS, 12 patients took premature discharge either without completion of detoxification or not willing for anticraving medicine. Out of remaining sample of 98 patients, 30 patients received other anticraving treatments (combination of baclofen and topiramate (16), fluoxetine(6), acamprosate (2), only non-pharmacological intervention-6) hence, could not be included in final analysis. Final sample consisted of 68 patients of ADS. Baclofen was prescribed in 40 patients and topiramate was prescribed in 28 patients.

Patients who did not come for follow up after discharge from de-addiction ward, were kept under lost to follow up and considered as relapsed for statistical purpose in the final analysis.

Sample dropped out from final analysis (n=30) was comparable on socio-demographic and clinical variables to sample included (68) in final analysis.

TABLE 1. Socio-demographic and clinical profile of patients

Variables	Baclofen (n=40)	Topiramate (n=28)
Age (Mean) in years	38	41
Marital Status, n (%)		
Married	29 (72.5)	22 (78.5)
Unmarried	11 (27.5)	6(21.4)

Occupation,n(%)		
Employed	30 (75.0)	20 (71.4)
Unemployed	10 (25.0)	8(28.5)
Duration of Alcohol use (Mean, in years)	13.5	14.6
Duration of Dependence (in years)		
Less than 5 years, n(%)	12 (30.0)	8(28.5)
5-10 years	23(57.5)	15(53.5)
More than 10 years	5(12.5)	5(17.8)
Family History of Alcohol Use, n (%)		
Present	8(20.0)	7 (25.0)
Absent	32 (80.0)	21 (75.0)

Co-morbid Chronic Medical Illnesses, n (%) (HT, Diabetes Mellitus, Epilepsy)	9 (22.5)	7(25.0)
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Mean age in the baclofen group and topiramate group was 38 and 41 years respectively. Majority of the patients in both the groups were married, employed and having duration of dependence between 5-10 years and co-morbid chronic medical illness (HT, Diabetes Mellitus, Epilepsy) was 9 (22.5%) and 7 (25.0%) in baclofen and topiramate group respectively. Family history of alcohol use in baclofen and topiramate group was 8(20.0%) and 7 (25.0%) respectively.

TABLE 2. Outcome at 1 week, 1 month and 3 months

Variables	Baclofen (n=40)			Topiramate (n=28)		
Mean Dose (in mg)	23			80		
Dose of Lorazepam (Mean)	0.95			1.95		
Craving(post-discharge),n(%)	1 week	1 month	3 months	1 week	1 month	3 months
No Craving (0/+)	23(57.5)	17(42.5)	13(32.5)	14(50.0)	8(28.5)	4(14.2)
Moderate Craving (++)	10(25.0)	15 (37.5)	13(32.5)	5(17.8)	7(25.0)	8(28.5)
Severe Craving (+++)	3(7.5)	2(5.0)	4(10.0)	4(14.2)	5(17.8)	6(21.4)
Lost to follow- up	4(10)	6 (15.0)	10(25.0)	5(17.8)	8(28.5)	10(35.7)
Alcohol use at follow ups	1week	1 month	3 months	1week	1 month	3 months
Abstinent	29(72.5)	21(52.5)	19(47.5)	15(53.5)	12(46.4)	8(28.5)
Intermittent use	6(15.0)	8(20.0)	9(22.5)	6(21.4)	8(28.5)	10(35.7)
Relapsed (includes lost to follow up)	5(12.5)	11(27.5)	12(30.0)	7(25.0)	8(25.0)	10(35.7)

Mean dose of baclofen was 23mg/day and topiramate was 80mg/day and mean dose of lorazepam in baclofen and topiramate group was 0.95mg/day and 1.95mg/day respectively. At the end of 3 months, 32.5% in baclofen group did not report any craving against 14.2% in topiramate group. Similarly 47.5% in baclofen group were maintaining abstinent at 3 months whereas 28.5% in topiramate group were abstinent from alcohol.

DISCUSSION:

In the current study, author tried to look for the change/reduction in craving and abstinence rate in alcohol dependence patients over a period of 3 months after getting them admitted in de-addiction ward for detoxification.

More than 57% of patients in baclofen group at one week of post discharge from hospital reported no craving and which was reduced to 32.5% at 3 months in contrast to 50.0% in topiramate group at week one and which reduced significantly to 14.2 at 3 months. Hence, baclofen clearly fared better than topiramate in reduction of craving from week one to at one and at 3 months.

A study from India also reported that baclofen reduce craving in alcohol dependence syndrome over a period of 4 weeks.⁹

Earlier studies^{7,8} have also reported that baclofen as well as topiramate are significantly better than placebo in reduction of craving in patients with alcohol dependence syndrome. However, there is no study available to compare these two molecules in terms of effect on craving in alcohol dependence.

The mean dose of baclofen and topiramate in our study was 23mg and 80mg per day respectively and which is lower than earlier studies^{7,8}. Additionally, baclofen group required low dose of lorazepam as hypnotic than topiramate group (0.95mg/day vs 1.95mg/day) and which was stopped within one month in both the groups. However, few patients in topiramate group complained about sleep disturbance after discontinuing lorazepam whereas none of the patient in baclofen group reported significant sleep problem after discontinuing lorazepam.

More than 47% of patients in baclofen group could maintained abstinent at 3 months whereas only 28.5% of patients in topiramate group could maintained abstinence and 22.5% of patients in baclofen group were using alcohol intermittently against 35.7% patients in topiramate group. At 3 months 30.0% of patients in baclofen group relapsed against 35.7% in topiramate group.

An earlier study by Sidana et al, 2007 found abstinence rate at 6 months and 12 months in 49 patients with alcohol dependence syndrome who were treated with disulfiram, naltrexone, accamprosate and SSRI and reported that abstinence rate goes down with duration of follow-up.¹⁰

Hence, the results of current study shows that abstinence rate in

baclofen group is clearly better than topiramate group starting from week one to the end of study at 3 months but the percentage of abstinence reduce with duration of follow up and same has been reported in earlier study.¹⁰

Around 30% in baclofen group and 35.7% patients in topiramate group relapsed at 3 months but this subpopulation also includes patients who were lost to follow-up and could not be contacted. It might also be possible that few patients actually achieved abstinence and did not feel the need for follow up or stopped taking medicines. Few other studies have reported even higher relapsed rate at 6 months follow up.^{11,12}

To sum up the findings of current study, it can be concluded that both baclofen and topiramate are effective agents to reduce craving and to achieve abstinence in patients with alcohol dependence syndrome. Baclofen fared better than topiramate in reduction of craving and abstinence at 3 months.

The study also has few limitations as baseline motivation was not assessed and it could be possible that baclofen group might had better motivation and no standard tools were used to assess severity of dependence, craving and abstinence.

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