

A PROSPECTIVE STUDY OF TREATMENT OUTCOME IN ALCOHOL DEPENDENCE SYNDROME AT RIMS HOSPITAL, IMPHALS. Bikramaditya Meitei¹, T. Hemchand Singh², S. Hingba Joyson³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: A naturalistic, uncontrolled follow-up study was carried out in 70 male alcohol dependent patients, in the Department of Psychiatry, RIMS, Imphal from May, 2005 to October, 2006. The author is aiming to evaluate the efficacy of TOPIRAMATE as anti-craving agent and also evaluate the treatment outcome at the end of one year. The study has been well designed and carried out meticulously. The severity of alcohol dependence data questionnaires (SADD) and Michigan alcohol screening test (MAST) was applied after detoxification. Out of 70 subjects, 35 subjects were given topiramate as anti-craving drug. At the end of one year follow-up study, 34.3% of the subjects could be classified under the abstinent and non-problem drinker, 34.3% continue to drink but showed improvement in social and occupational functioning and 31.4% showed no improvement.

KEYWORDS: Alcohol Dependence Syndrome, Anti-craving agents & Treatment outcome.

INTRODUCTION: Alcohol dependence and abuse are the most common substance related disorder. 90% of US population has had an alcohol containing drinks once in their life time. Alcohol dependence causes violence, absence from work, job loss, legal problems and quarrel in the family.¹

Alcohol dependence is a major public health problem in many developing countries. In alcohol dependence, the desire to drink alcoholic beverages has become overpowering and urgent. Epidemiological studies conducted in India [show] high prevalence of alcohol dependence.²

The follow up studies in India suggest that the significant number of these patients do respond to intervention.³ It is reported that more than 50% of patients who continued to take antic raving drugs showed good moderate improvement.⁴ Using a postal follow up inquiry reported 37% response rate out of which 50% remained abstinent for more than 2 years.⁵ thought after 1 year 32.5% remained improved during the follow up period. Again another 1 year longitudinal study done by.⁶ positive outcome was noted in 55% of the study sample.

Certain issues are to be addressed while conducting a follow up evaluation. For assessing the efficacy of treatment, an optimum period of 1 year has been advocated.⁷ It is consider that patient's outcome at the end of 1 year predicts later functioning and helps in assessing the efficacy of treatment.⁸ evaluated outcomes in which 8 patients Continue to attend the follow up clinic regularly for 1 year, 28 patients come to the hospital in response to latter and remaining 24 patients were visited at home. There is a debate regarding the usefulness of self-reports using postal questionnaires in assessing the outcome.

Appropriate strategies are to be adapted to obtain more accurate reports from key relatives to substantiate what is given in the self-report. Keeping these issues in mind, this study was designed to evaluate the outcome after 1 year in patients treated for alcohol dependence.

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MATERIALS AND METHODS: The treatment programme consists of a 4 week period of inpatient stay and subsequent outpatient follow up to 1 year. Treatment team consists of a senior consultant psychiatrist, resident psychiatrist, Medical Social Worker and psychiatric nurse.

Initially patients undergo detoxification with benzodiazepines (Lorazepam & Chlordiazepoxide), vitamin (Thiamine) and when necessary, intravenous fluids. After detoxification, the patients attended group therapy sessions. The sessions were conducted once a week. The number of participants fluctuates from 5 to 8, allotted time was one hour. Patients having major physical and psychiatric problems were excluded from this study.

35 patients were offered topiramate after motivation and explaining the drug in details and informed consent was obtained. The dose of topiramate started from 25mg daily and increased upto 200 mg. Another 35 patients were not offered topiramate, 15 patients refused to take and 20 patients couldn't afford the course of treatment (Topiramate).

After discharged patients were advised to attend the follow up clinic. Follow up details including abstinence, any drinking episodes, problems in the social and occupational areas are enquired and recorded. Those who refused topiramate were also advised to come once in a fortnight to meet the psychiatrist for the follow up evaluation. Postal reminders are sent to patients who failed to turn up for follow up for 1month. In case, no response is elicited for 3 consecutive postal reminders, no further reminder is sent.

The alcohol dependence patients from Manipur, meeting the DSM-IV TR criteria.⁹ were included in the study. All patients who underwent the 4 weeks of inpatient treatment programme were from Imphal, Bishnupur and Thoubal district. Thus, seventy patients participated in the study.

The ages of the patients ranges from 18 to 70 years, in which maximum number of patients were married and 13(18.6%) were unmarried, 9(12.9%) had stable employment, 9(12.9%) employed in semi-government and the rest 52(74.3%) were unemployed and 37(52.9%) were under matriculation.

All the patients were male, 60 patients were reported on their own and brought by family members, 3 referred from hospitals and 7 referred from NGOs.

A detailed initial assessment using a semi-structured Performa was done after detoxification and before group therapy sessions. Information was gathered from the patient and a key informant. Socio-demographic details included marital status, education, occupation, employment and socio-economic status.¹⁰ Details were obtained regarding the use of alcohol, including abstinence and treatment in the past and family with a history of alcoholism.

The severity of alcohol dependence data (SADD) Questionnaire was used to measure the severity of dependence.¹¹ The SADD Questionnaire measures both physiological and behavioural features of dependence. The questionnaire consists of fifteen questions and is rated on a four point scale. All questions applied prior to treatment, scale 0-9 indicate no dependence syndrome, 10-19 indicate medium dependence and 20 or more indicate high dependence.

The Michigan alcohol screening test.¹² was used for detection of alcohol related problems. All questions apply prior to treatment and after completion of the study. All the patients were screened for cognitive disturbances by the Mini-mental state examination¹³ and none had significant cognitive impairment.

The outcome evaluation was done after a period of 12 months. Of the initial sample of 70, 8 patients continued to attend the follow up clinic regularly for 1 year. Letters were sent to the remaining patients and their relatives. 33 patients came to the hospital in response to letters.

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The remaining 29 patients were visited at their homes with the help of their relatives and patients, spouse or a key relative were interviewed for the final assessment. Information on alcohol use, dependence features and alcohol related problem was obtained.

The number of months this patient attended follow-up clinic and the duration of topiramate medication was found out from the record and from the relatives.

The outcome was classified into 4 groups, based upon proposals by Healthier and Tebbutt (1989).¹⁴

- 1. Abstinent:** Complete abstinence from alcohol, or not more than 1 drink per month. No problem in the family, social and occupational areas due to alcohol.
MAST scoring 0-2.
- 2. Non- problem drinker:** Not more than one drink per week, and no evidence of the dependence. No problem in the family, social occupational areas due to alcohol.
MAST Scoring 3-5.
- 3. Drinking but improved:** Not more than 1 drink per day, or drinking with evidence of dependence.
MAST scoring 6 or more.
- 4. Unimproved:**

Same drinking pattern or no significant change in the MAST score, or worse, or died due to alcohol related problems.

'Abstinent' and 'Non-problem drinker' groups were considered as patients with favourable outcome whereas 'Drinking but improved' groups as unfavourable outcome. Chi-square test was used to test the significance of difference between proportions and 't' test to test the significance of difference between means. The relationship between the duration of topiramate use and outcome was determined using chi-square test for trend. The patients were divided into 4 ordered categories depending upon the duration of topiramate use.

RESULTS & OBSERVATIONS: At the end of the study, 13 patients were taking topiramate for 12 months, 9 patients taking for 6 months and 13 patients taking topiramate for 3 months only. 33.3% of the patients showed favorable outcome which included abstinent and non-problem drinkers group, 34.3% drinking but improved and 31.4% were in the improved group which included 3 patients who were expired due to alcohol related problems.

Comparison baseline characteristics between patients with favorable and unfavorable outcome

Variables	Favourable outcome	Unfavourable outcome	Total	P- Value
Abstinent	22(31.4%)	26(37.1%)	48(68.5%)	P <0.003
Abstinent in the past	2(2.9%)	20(28.6)	22(31.5%)	
Age of onset of drinking				P<0.000
Below 20 yrs.	6(8.6%)	38(54.3%)	44(62.9%)	
20 yrs. & above	18(25.7%)	8(11.4%)	26(37.1%)	
Duration of alcohol				P<0.006
Below 5 years	7(10%)	5(7.1%)	12(17.1%)	
Below 10 yrs.	14(20%)	18(25.7%)	32(45.7%)	

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10 yrs. & above	3(4.3%)	23(32.9%)	26(37.2%)	
SADD score	24 (Mean 10.875)	46 (Mean 35.8910)	70	P <0.000
With medication	22(31.4%)	13(18.6%)	35(50%)	P <0.000
Without medication	2(2.9%)	23(47.1%)	35(50%)	

Table 1: Shows the Pre-Treatment Variables in favoring of Good Outcome.

MAST	MEAN	NUMBER	STD. DEVIATION	STD. ERROR MEAN	P- VALUE
Before treatment	18.388	67	2.8335	0.3462	P<0.000
After treatment	10.134	67	6.7193	0.8209	

Table 2

DISCUSSION: The important finding at the end of one year is that definite improvement was observed in 34.3%, 34.3 had shown some improvement in social and occupational functioning despite continuing alcohol on a regular basis, 31.4 of the patients have shown any significant change during this follow up period. Reasonable conclusion regarding treatment efficacy can be obtained from this study because of its prospective design, adequate follow up period, well defined and multiple indicators of outcome and reliable data gathering method.

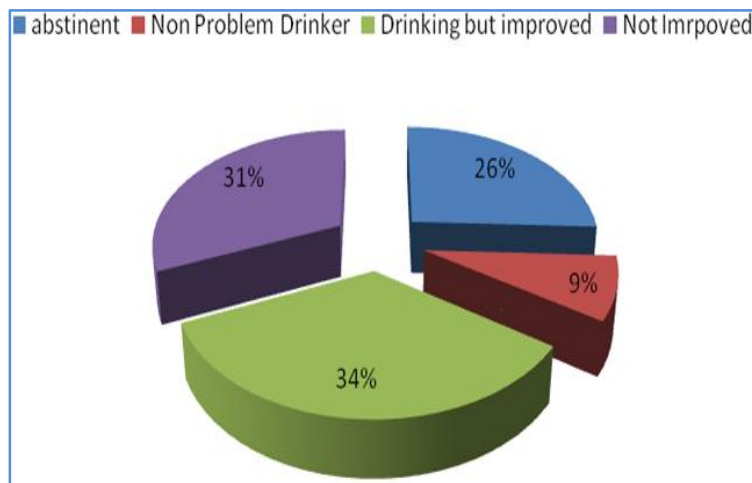


Fig. 1: Shows overall treatment outcome in this study

In this study 70 patients were contacted at the end of follow up period in no attrition from the initial sample. 8(11.5%) of the patients regularly attended the follow-up, 33(47%) responded to letters and 29(41.5%) were contacted through home visits.¹⁵ the follow-up evaluation showed 13.3%, 46.7% and 48% respectively. Effective tracing techniques and low attritions are especially important, since high rates of loss of clients could seriously bias the finding of research.

The outcome was classified into four well defined categories using multiple indicators. Understanding of mechanism behind the successful outcome of the treatment for alcohol dependence can be cause in conclusion in this study. Various socio-demographic and drinking variables have been studied. Older age, lesser duration of drinking, social stability, abstinence in the past, less severe alcohol related problems and better initial level been identified by various research as predicting good outcome.¹⁶

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In this study among the pretreatment variables, previous history abstinence, last onset drinking, short duration of drinking and low dependency (Low SADD score) are favouring for better outcome.

In India,¹⁷ it is found that the previous abstinence pattern, previous treatment patterns, or a history of withdrawal symptoms in the past are not favouring for good outcome.¹⁸ It also revealed the difference in duration of consumption, family history and level of education between acceptors and non-acceptors. Acceptors abstained from alcohol for longer periods than non-acceptors, as did those who completed treatment.¹⁹ concluded that late onset drinkers are in favour of good outcome.

The study clearly indicates that the association between medication with topiramate and favourable outcome was statistically highly significant ($P < 0.000$). Also the duration of anticraving medication with topiramate definitely brought forth a favourable outcome. This possibly explained on the basis of better motivation, which is pointed out as an important factor behind good outcome.²⁰ It revealed the difference in duration of consumption, family history and level of education between acceptors and non-acceptors. Acceptors abstained from alcohol for longer periods than non-acceptors, as did those who completed treatment and²¹ concluded that late onset drinkers are in favour of good outcome.

This study clearly indicates that the association between medication with topiramate and favourable outcome was statistically highly significant ($P < 0.000$). Also the longer duration of anticraving medication with topiramate definitely favour the favourable outcome. This possibly explained on the basis of better motivation, which is pointed out as an important factor behind good outcome.

In topiramate (upto 300mg/day) is more efficacious than placebo as an adjunct to standardized medication compliance management in treatment of alcohol dependence. Also topiramate is superior to placebo by increasing overall well-being and quality of life and lessening dependence severity and its harmful consequences.²²

There is no study in India regarding treatment outcome with anticraving medication, i.e. topiramate. But according to this study it appears that in our population using a pharmacological intervention always enhance the motivation of the individual and makes the hospital visit more purposeful and meaningful for the individual. Topiramate has at least six important mechanisms of action. These include: 1) Facilitation of inhibitory gamma-aminobutyric acid-A ($GABA_A$)-mediated currents at non-benzodiazepine sites on the $GABA_A$ receptor. 2) Antagonism of alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and kainate glutamate receptors. 3) Inhibition of L-type calcium channels and limitation of calcium-dependent second messenger systems. 4) Limitation of activity-dependent depolarization and excitability of voltage-dependent sodium channels. 5) Activation of potassium conductance. 6) Weak inhibition of carbonic anhydrase isoenzymes—CA-II and CA-IV, which are found in both neuronal and peripheral tissues. In renal tubules, carbonic anhydrase isoenzyme inhibition decreases hydrogen ion secretion and increases secretion of Na^+ , K^+ , HCO_3^- , and water, thereby enhancing the likelihood of acidosis and renal stone formation. Topiramate decreases alcohol reinforcement and the propensity to drink.

The shortcomings of the present study are the lack of a control group and random assignment. So the results cannot be generalised. Further no comparison was attempted with an outpatient group. This is because majority of patients would either get admitted or dropout even detoxification is completed.

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Since multiple treatment modalities were employed in the present study, results do not prove the efficacy of any specific treatment methods. Since the study included any patients who completed four weeks of inpatient treatment programme, the study might have included any patients with better motivation. The definite method of determining the efficacy of a particular treatment is randomized, controlled clinical trial, which is extremely difficult to undertake in alcohol research.

Although it is suggesting that outpatient treatment is as good as inpatient treatment, it does not seem to be practical in the Indian situations. Initially external control is necessary to help the patients keep away from alcohol which the hospital seems to provide them. Further the family members of the patients also need a respite for some time. Patients who attend or referred to alcohol de-addiction centres for psychiatric treatment facilities in India are with more severe dependence and who have significant physical and psycho-social impairment who need inpatient care.

CONCLUSION: This study shows the anticraving medications with topiramate were found to be highly associated with favourable outcome. Therefore, the present study had implicated that every effort should be met to maintain the patients on topiramate to improve the prognosis. Further, comprehensive studies incorporating other psychological and social pretreatment variables are needed to elucidate the mechanisms behind successful outcome in the treatment of alcohol dependence syndrome patients. Also future research should include large samples and control group with periodic evaluation to arrive to any reasonable conclusion regarding treatment efficacy.

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