EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH
www.ejpmr.com

QUALITY OF LIFE OF ALCOHOL DEPENDENT PATIENTS TREATED WITH VARIOUS DRUGS THERAPY: A HOSPITAL BASED COHORT STUDY IN WESTERN RAJASTHAN

Rishiraj Sharma*[1], Monika Sharma[2] and Anusuya Gehlot[3]

[1]Resident, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur.
[2]Senior Demonstrator, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur.
[3]Senior Professor, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur.

*Corresponding Author: Rishiraj Sharma

Resident, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur.

ABSTRACT

Aim:- The aim of study was to examine the effect of Various drugs Therapy on health related quality of life of Alcohol Dependent Patients. **Methodology:-** This hospital based prospective cohort study include individuals who diagnosed as Alcohol Dependence and initiated Various Drug Therapy were follow up for 18th weeks of period. A Student paired t-test was used to examine change in score of eight domains of SF-36 Questionnaire in health related quality of life. This study was conducted in Department of Pharmacology and Psychiatry, Dr. S. N. Medical College, Jodhpur, Rajasthan. **Results:-** A total of 50 patients met the study inclusion criteria. The results of the SF-36 questionnaire showed that more than 90% of the patients with Alcohol Dependence who had taken Various Drug Therapy for 18 weeks of duration, experienced an improvement in the eight domains of SF-36 sub-scale of health relate quality of life. The results of SF-36 showed a statistically significant improvement in scores. **Conclusion:-** Alcohol Dependence has a substantial effect on health related quality of life. There was significant improvement in all domains of SF-36 suggesting overall improvement in quality of life.

KEYWORDS: Quality of life, Alcohol Dependence, Various Drug Therapy.

INTRODUCTION

Alcohol dependence, a common psychiatric disorder in the general population, has a significant impact on health. According to Global Status Report on Alcohol,[1] alcohol use disorders accounted for 1.4% of the global disease burden. Some people are more likely to experience the consequences of alcohol use.[2]These tend to be male having high perceived stress and anxiety with dissatisfaction and poor quality of life, lack of social support, economic strains, and chronic stress.[3] Das, Balakrishnan, and Vasudevan reported that in a developing country like India, over 20% of all disability adjusted life years are lost chiefly because of poor health status of the people, marked nutritional deficiancies, and widely prevalent alcohol addiction.[4] Quality of Life QoL is an important parameter that provides an insight into how a disorder impact life of those affected World Health Organization defined -Quality of Life (QOL) is an "individual's perceptions of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns".[5] It is an important parameter that provides an insight into how a disorder effects life of those affected.[6-8]

In alcohol-dependent patients, most published reports have investigated the effects of alcohol intervention strategies on objective clinical or psychological criteria such as alcohol intake, biological variables, severity of dependence, motivation for change, somatic or psychiatric comorbidities.[9,10]

Dependence is a state in which a person requires a steady concentration of a particular substance to avoid experiencing withdrawal symptoms.[11-12] Alcohol dependence is the second most common psychiatric condition. WHO has estimated that alcohol accounts for 4.5% of all disease burdens worldwide.[1] Alcohol is the 3rd leading cause of Disability in the developed world. A total of 5.3 % of all deaths worldwide are caused by alcohol every year.[1] Pharmacological approaches to the treatment of Alcohol Dependence Disulfiram, Acamprosate, Naltrexone, Topiramate, Baclofen and Chlordiazapoxide etc.

Disulfiram was the first medication approved by FDA to treat alcohol dependent patients. It has been used in the treatment of alcohol dependence with consistently successful results in individual.[14] Drug Disulfiram inhibit Aldehyde dehydrogenase enzyme (ALDH)

causing a rapid rise of acetaldehyde in th blood when alcohol is consumed. The result is called a disulfiram-alcohol reaction. It helps patients learn this new non drinking behaviour, this ability to exercise self-control.[5] Unlike other medications approved to treat alcohol dependence, It does not affect brain opiate, γ-aminobutyric acid or glutamate receptor directly. Pharmacological treatment given for Alcohol Dependence are Topiramate, Baclofen and Chlordiazapoxide at Mathuradas Mathur Hospital Jodhpur.

Topiramate: It is a potent anti-epileptic with strong neuroprotective properties. It has many proposed targets of action, including facilitation of GABA-A receptor activity and reduction in glutamate activity in a-amino-3-hydroxy-5-methyl-4- isoxazolepropionic acid and kainate receptors. Like many other drugs proposed for the treatment of alcohol dependence, it is thought to reduce mesolimbic dopaminergic activity. It is beneficial in heavy drinking and the number of drinks per drinking.

Baclofen: It is a selective c-aminobutyric acid (GABA)-B receptor agonist which was originally approved for the treatment of spasticity associated with multiple sclerosis and spinal cord lesions. 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. Baclofen in doses up to 30 mg/day prevent relapse or reduce drinking in people with alcohol dependence.

Chlordiazepoxide: It is a benzodiazepine that is used to treat anxiety, sedative, appetite-stimulating and weak analgesic. It may also be used short term to treat Acute Alcoholism or withdrawal.

Aims and objective
The objective of the current analysis has to describe the evolution of QOL in males and females with alcohol dependence to Various Drug treatment during a 18 weeks of period after initial assessment for alcohol related treatment in Psychiatry department MDM hospital Jodhpur.

Primary objective
To determine in any changes in Quality of Life (by using A free version of SF-36 transformed score) of alcohol dependent patients after baseline, three, nine and eighteen weeks of initiation of Various Drugs Therapy.

MATERIAL AND METHODS

Study Design
This is a hospital based Cohort Study.

Study Setting
This study will be carried out at the department of Pharmacology in collaboration with department of Psychiatry, Mathuradas Mathur Hospital, Dr. S.N. Medical College, Jodhpur.

Participants
Alcohol depenent patients diagnosed by the Psychiatrist in Out Patient Department of Psychiatry Mathuradas Mathur Hospital, Dr. S. N. Medical College Jodhpur.

Study Variables
They are age, gender, works, duration of alcohol dependence, family history, current smoker, daily alcohol intake.

Quantitative Variables
Factors that predict baseline Quality Of Life include duration of alcohol dependence, intensity of alcohol use, employement status, age, gender and psychiatric history, including the presence of personality disorders and alcohol induced anxiety disorder.

Study Period
This study will be conducted after approval from Institutional ethics committee.

Inclusion Criteria
Newly diagnosed Alcohol dependence patients above eighteen years age of male and female gender in Psychiatry department, MDM Hospital, Dr. S.N. Medical College Jodhpur.

Exclusion Criteria
- Pregnant and lactating mothers
- Comorbid Psychiatric illness
- Drug like Metrotinidazole and other medication misuse
- A History of Legal Problems
- Other comorbid medical conditions like hyperthyroidism, HIV patient etc.
- Patient who refused to follow-up

Institutional ethical approval
The study protocol was approved by the Department of Pharmacology and subsequently by the Institutional Ethics Committee of Dr. S. N. Medical College, Jodhpur, Rajasthan (ANNEXURE 7).

Informed Consent
Patients were made to understand the entire purpose of the study, their rights and the procedure of the study, with the help of the patient information sheet which was available in both English and Hindi Patients who gave written informed consent were then included in the study.

Measurements
A Free version of SF-36 transformed questionnaire that consists of eight scaled scores, physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Component analyses showed that there are two distinct concepts measured by the SF-36: a physical dimension, represented by the Physical Component Summary (PCS),

and a mental dimension, represented by the Mental Component Summary. The physical health measure includes four scales of physical functioning (10 items), role-physical (4 items), bodily pain (2 items), and general health (5 items). The mental health measure is composed of vitality (4 items), social functioning (2 items), role-emotional (3 items), and mental health (5 items).

Sample Size: 50
Sample size was calculated at alpha error 0.05 and study power 90% using the below formula for difference in paired mean in a single sample

$$N= \frac{(Z_{1-\alpha/2}+ Z_{1-\beta})^2 \times \sigma^2}{d^2} + \frac{(Z_{1-\alpha/2})^2}{2}$$

$$= \frac{(1.96+ 1.28)^2 \times 4^2}{3^2} + \frac{(1.96)^2}{2}$$

$$= 19 + 2 = 21$$

Where,
N = Sample size
$(Z_{1-\alpha_2})$ = Standard normal deviate for Type 1 error (taken as 1.96 for 95% confidence interval)
$Z_{1-\beta}$ = Standard normal deviate for Type 2 error (taken as 1.28 for 90% study power) σ = pooled standard deviation of estimated psychological domain (taken as 4 as per reference article)
d= minimum expected difference in psychological domain from baseline. (taken as 3 as per reference article)
Sample size was calculated to be a minimum of 21. This was enhanced to 50 to cover all the domains of WHO QOL.

Statistical Methods
Categorical variables will be expressed as frequency and percentage and will be analyzed using chi square test. Quantitative variables will be expressed as mean and standard deviation and before after analysis will be done using paired t test for two times / repeated measure ANOVA for multiple times. Comparison of mean between two groups will be done using independent sample t test. A p value <0.05 will be taken as statistically significant. All statistical analysis will be done using appropriate statistical software.

We got two paired mean, before (at 0-day =baseline) and after (at 18-weeks =end point) initiation of various drug treatment. With the help of following formula we calculated t-value statistically:-

$$\overline{D} = \frac{\sum D}{N}$$

$$t = \frac{\overline{D}}{S.E} = \frac{M_1 - M_2}{S.E}$$

$$t = \frac{\sum D}{\sqrt{\dfrac{N \times \sum D^2 - (\sum D)^2}{N - 1}}}$$

t = statistical t-value 26 **D** = difference (effect size) M1 = Mean before treatment M2 = mean after treatment
S.E. = standard error
N = total number of samples (patients)
The t-table value was measured at degree of freedom (N -1),95% confidence interval and alpha error 5% in two tail test. P-value less than 0.05 was considered significant.

RESULTS

Characteristics of study population
The characteristics of the 50 patients are shown in Table 1. 45 men and 15 women were included, 30 (60%) patients had a history of abuse or dependence on sedatives at sometime in their life. Alcohol induced anxiety disorder present in 45(90%) patients. Due to alcohol consumption 42(84%) patients have Liver disease. The average age of patients were 32±10.

Table 1: Characteristics of the study population.

Variable	Number (%)
Age	32 ±10
Sex ratio (male/female)	2.33
work (Employed/Unemployed)	44(6)
Duration of alcohol consumption(years)	3
Alcohol intake per day	20ml
Types of alcohol source	Whisky, Rum, Vodka
Current smoker	42(8)
Psychiatric history	40(10)
Family history	30(20)
Personality disorder	36(14)
Alcohol induced anxiety disorder	45(5)

2. Prescribed Drugs for Alcohol dependent patients

Alcohol dependent patients treated with prescribed drugs are Topiramate, Baclofen and Chlordiazapoxide at Psychiatry department of Mathura Das Mathur Hospital Jodhpur.

In 25 patients those alcohol intake per day more than others treated with Tab. Topiramate 50 mg BD were given. In 15 patients those alcohol intake per day less than others treated with Tab. Baclofen 20 mg BD were given and 10 patients those were recently dependence of Alcohol treated with Tab. Chlordiazapoxide 10 mg TDS.

Table 2: Prescribed Drugs for Treatment of Alcohol dependent patients.

Prescribed drug	Patients
Tab. Topiramate 50mg BD	25
Tab. Beclofen 20 mg BD	15
Tab. Chlordiazapoxide 10 mg TDS	10

At 0-Day (before treatment), baseline score of mean of quality of life shows deficit in quality of life as compared with normal score of healthy person which was done by Medical Outcome Study (MOS) SF-36 by RAND Corporation (Table 3). In this we used student paired t-test to calculate t value. Calculated t- value was greater than critical t-value. Therefore statistically significant difference between means, hence Null Hypothesis (Ho) was rejected (M1 i=M2, M1 =Mean before treatment and M2 =Mean of healthy person).

Table 3: Score of SF-36 each domains before treatment in Alcohol Dependent patients.

Domain	Mean before treatment(O-Day)	Mean of healthy person	Difference	t-value
PF	09.53	70.61	-61.08	-83.57
RP	08.83	52.97	-44.14	-47.35
RE	13.64	65.78	-52.14	-26.38
E/F	17.13	52.15	-35.02	-38.75
EWB	16.35	70.38	-54.03	-59.73
SF	13.68	78.77	-65.09	-38.75
BP	24.64	70.77	-46.13	-28.46
GH	17.54	56.99	-39.45	-32.67

The final aim of this study was to investigate whether Alcohol dependence treated drug therapy improve different aspect of quality of life during the study. Mean test (before treatment) and retest score (after treatment) for each domain were compared in same patient (N =50) using student paired t-test. Calculated t-value is higher than t-critical value . All domain show significant increase in quality of life score, demonstrating that quality of life improve in 18-week following the start of various drug. Hence, alternative hypothesis(Ha) was accepted (M3 >M1, M1 =mean before treatment and M3 =mean after 18-weeks of treatment).

Table 4: SF-36 scores for patients completing 18-weeks of treatment.

Domain	Baseline score	Final score	Difference (Effect size)	t-value
PF	09.53	79.68	-70.15	-34.78
RP	08.83	86.85	-78.02	-42.35
RE	13.64	87.78	-74.14	-27.46
E/F	17.13	83.25	-66.12	-20.37
EWB	16.35	85.58	-69.23	-38.57
SF	13.68	78.74	-65.06	-35.64
BP	24.64	76.86	-52.22	-25.12
GH	17.54	76.68	-59.14	-27.81

Table 3 & 4 shows increasingly improvement in each domains of Quality of Life of Alcohol Dependent patients after initiation of various drug therapy.

Quality of Life of Patients on Baseline, third, ninth and at Eighteenth week

The SF-36 Scores for the eight dimension were lower on zero day or Baseline than at eighteenth week.The average score for the eight dimension were respectively

taken of Drug Topiramate, Baclofen and Chlordiazapoxide at Baseline, Third week, Ninth week and Eighteenth week described in Table 9.

Table 5: Changes in Mean SF-36 Score in percentage of Prescribed Drugs.

Drug	SF-36 Scores			
	Baseline	3rd week	9th week	18th week
Topiramate	18%	44%	76%	80%
Baclofen	24%	42%	72%	82%
Chlordiazapoxide	26%	44%	75%	84%

DISCUSSION

This study investigated the effects of Various drug therapy on Quality of Life of Alcohol dependent patients. Foster JH et al study (2000) found that Quality of Life (QoL) measurement has gained increasingly importance in medicine and is increasingly being implemented in clinical study and health policy.[15] Alcohol Dependence is associated with significant reduction in Quality of Life,[8] In This study the mean age of Alcohol dependent patients was 32 ± 10 years which is near to 41 years in Pierre Lahmek et al study (2009),[16] Chikkerahally GDMD 39.09 years (2019)17, Marsha Y Morgan et al (2004) 43 years and 42 year in Miller M et al (2011) study.[12] It is not in accordance with 46 years in Foster JH et al study (2000).[34] In Present study most of the Alcohol dependence patients were Male (61%) which is near to Pierre Lahmek et al (65%) (2009).[16]

The present study shows that most of the Alcohol dependent patients statistically significant deficit in Quality of Life, it is similar with study of Srivastava S et al (2013),[18] Faller S et al (2015).[33] and Chikkerahally GDMD. (2019),[17] by using The World Health Organisation Quality of Life (WHOQOL-BREF) assessment instrument.

In This study Alcohol Dependent Patients diagnosed and treated in out patient department like Faller S et al (2015),[19] and Shrivastava S, Bhatia M study (2013),[18] which were completely difference with Pierre Lahmek et al study (2009) that in patient of alcohol Dependence were diagnosed and Treated.

Limitation of study- The study included small sample size and short duration of follow-up of four and half month, Longer duration of follow-up and big sample size could have predicted the impact of certain treatment related variables on QoL. The other limitation of this Study was that this study was conducted in a single centre only. A study with large sample and multiple centre is needed to investigate changes in Quality of Life (QoL) following Alcohol dependence treatment.

CONCLUSION

In This study majority population of Alcohol dependent patients were male gender as compared to female the sex ratio was 2.33 and Mean age was 32 ± 10 years. This study suggests that there was a significant improvement in all dimensions of Quality of Life of Alcohol Dependent Patients after a 126 day Out- patient programme. This study shows that the QoL scores of alcohol dependent patients on treatment at hospital were much lower than those of a general reference population. The score for the psychological dimension were reduced more than those for the physical dimensions, in particular the scores for role limitations due to emotional problems and social functioning. This study has shown that the initial QoL of the patients was associated with several factors, stemming, from the alcoholic disease itself , its consequences, and from somatic and psychiatric comorbidities. The severity of dependence appeared to be the alcohol related variables that had the strongest impact on QoL. Heavy drinkers had a poorer Qol than other alcohol drinkers whereas smaller regular drinkers had a better QoL. In 25 patients those have drink more quantity of alcohol that 90ml or above were given Tab. Topiramate 50 mg BD show rise in QoL from Baseline to Eighteenth week. In 15 patients those have small drink of alcohol below 90 ml were given Tab. Baclofen 20 mg BD also rise QoL from Baseline to Eighteenth week. 10 patients those were recently addicted from alcohol and have drink below 50 ml also rise QoL from Baseline to Eighteenth week.

All patients were treated with drugs show better QoL and the score rise from week by week. Drug Topiramate is better for heavy and long term drinkers instead Drug Baclofen is better for low and short time drinkers. Drug Chlordiazapoxide or Librium is better for recently alcohol addiction patients.

ACKNOWLEDGEMENTS

Conflict of Interest
No conflict of Interest.

BIBLIOGRAPHY

1. WHO. Global status report on alcohol and health, 2018.
2. Foster JH,PowellJE,Marshall EJ, Peters TJ.Quality of life in alcohol dependent subjects a review.Qual Life Res., 1999; 8: 255-61.
3. Jacob T, Seilhamer RA, Alcoholism and family interaction. Recent Dev Alcohol, 1989; 7: 129-24. [PubMed]

4. Daeppen JB,Krieg MA, Burnand B, et al. Mos-sf-36 in evaluating health- related quality of life in alcohol-dependent patients.Am J Drug Alcohol Abuse, 1998; 24: 685-94.

5. Perkins HW. Gender patterns in consequences of collegiate alcohol abuse: A 10- year study of trends in an undergraduate population. J Stud Alcohol, 1992; 53: 458-62. [PubMed]

6. Daeppen JB Kreig MA Burnard Bet al. MOS-SF-36 in evaluating health- related quality of life in alcohol dependent patients Am J Drug Alcohol Abuse, 1998; 24(6): 85-94. [PubMed].

7. Collaborating Centre for International Drug Monitoring editor. The importance of Pharmacovigilance: Safety Monitoring of Medicinal Products Geneva WHO, 2002.

8. Daeppen JB Faouzi M Sanglier T et al.Drinking patterns and their predictive factors in CONTROL: a 12-month prospective study in a sample of alcohol-dependent patients initiating treatment Alcohol Alcohol, 2013; 48(1): 89-95.

9. Johnson BA, Rosenthal N, Capece JA, Wiegand F, Mao L, Beyers K, et al. Topiramate for treating alcohol dependence. JAMA, 2007; 298: 1641-51.

10. Florez G, Garcia-Portilla P, Alvarez S, Saiz PA, Nogueiras L, Bobes J. Using topiramate or naltrexone for the treatment of alcohol dependence patients. Alcohol Clin Exp Res., 2008; 32: 1251-1259.

11. Morgan MY Landron F LehertPfor the New European Alcoholism Treatment Study GroupImprovement in quality of life a#er treatment for alcohol dependence with acamprosate and psychosocial support Alcohol Clin. Exp. Res., 2004; 28: 64-77.

12. Miller M, Book W and Stewart S. A medical treatment of alcohol dependence: A systemic review.Int. J. Psychiatry Med, 2011; 42(3): 227-266.

13. Das SK, Balakrishnan V, Vasudevan DM. Alcohol: Its health and social impact in India. Natl Med J India, 2006; 19: 94-9.[PubMed]

14. Anton RF, Moak DH, Latham PK. The obessice compulsive drinking scale: a new method of assessing outcome in alcoholism treatment studies. Arch Gen Psychiatry, 1996; 53: 225-231. [PubMed]

15. Foster JH, Peters, Marshal EJ Quality of Life measures and outcomes in alcohol dependent men and women alcohol, 2000; 22: 45-52.

16. Lahmek P et al.Determinants of improvement in quality of life of alcohol- dependent patients during an inpatient withdrawal programme.Int. J. Med. Sci., 2009; 6(4): 160-167.

17. Chikkerahally GDMD. Assesment of quality of life in patients with alcohol dependence syndrome. Open J Psychiatry Allied Sci., 2019; 10: 57-63.

18. Shrivastava S and Bhatia M.Quality of life as an outcome measure in the treatment of alcohol dependence.Indian J. Psychiatry, 2013 Jan-Jun; 22(1): 41-46.

19. Faller S et al. Factors associated with a quality of life decrease in alcoholic patients who sought treatment. J Addict Res Ther, 2015; 6: 232.