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

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ABSTRACT

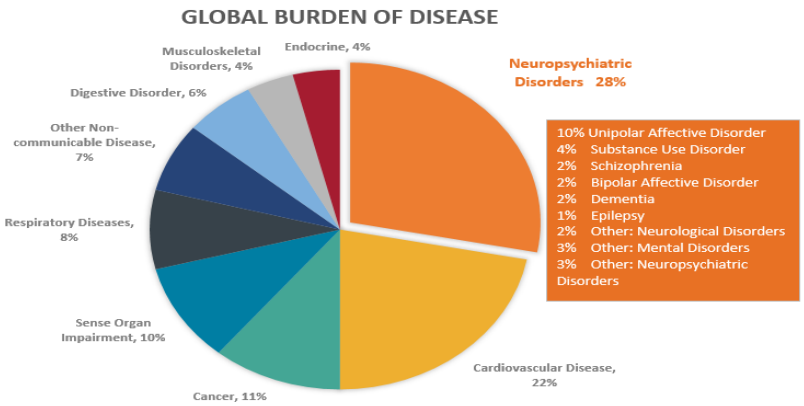
Aim:- The aim of study was to examine the effect of Various drugs Therapy on health related quality of life of Alcohol Dependent Patients. **Methodology:-** This hospital based prospective cohort study include individuals who diagnosed as Alcohol Dependence and initiated Various Drug Therapy were follow 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 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.

KEYWORD:- Quality of life, Alcohol Dependence,Various Drug Therapy, Adverse Drug Reactions.

1. 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.[35] These tend to be male having high perceived stress and anxiety with dissatisfication and poor quality of life, lack of social support, economic strains, and chronic stress.[40]

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.[29]



Quality of Life QoL is an important parameter that provides an insight into how a disorder impact life of those affected World Health Organization[46] 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". It is an important parameter that provides an insight into how a disorder effects life of those affected.[11,26,28]

A review of Quality of Life (QOL) research on patients with alcohol dependence syndrome (ADS) states that Quality of Life (QOL) of alcohol dependent subjects is very poor but improved as a result of abstinence, controlled or minimal drinking. The important factors in Quality of Life (QOL) of alcohol dependent subjects are psychiatric comorbidity, social environment, and disturbed sleep.[31] Knowing about Quality of Life (QOL) of alcohol dependent patients may help to frame policies for their treatment, rehabilitation, and control of alcohol use, and improve Quality of Life (QOL) for this huge population of hopeless patients.[12,15,16]

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.[6,7] However, this approach is sometimes too limited because it does not capture adequately information on how a patient adapts to treatment and lifestyle changes.[8] In cur-rent practice standards, the QoL of alcohol-dependent patients is not measured systematically, even though this is relevant to the psychosocial context of the interventions and to describing how actively patients will participate in their own care.[30,32,42] Studies dedicated to the analysis of QoL of alcohol-dependent patients have already yielded valuable information, whether measuring basal QoL, its improvement during patient care, or its influence on alcohol-dependence itself . Most of these studies have found QoL to be decreased considerably in alcohol dependent patients, but little information is available on how QoL changes during a therapeutic intervention.[28]

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Dependence is a state in which a person requires a steady concentration of a particular substance to avoid experiencing withdrawal symptoms.[14,15,30]

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] About 60% of all injuries to the emergency ward was due to alcohol.[2] The prevalence of alcohol use in India is reported to be 21.4%.[3] States with the high prevalence of alcohol use are Chhattisgarh (35.6%), Tripura (34.7%), Punjab (28.5%), Arunachal Pradesh (28%) and Goa (28%). Alcohol use is quite common in India both rural and urban areas with prevalence rates as per various in rural studies varying from 23% to 74% in males and at the rate 24% to 48%in females in certain sections and communities.[30]

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.[4] 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. in a dose of 100 mg/day appears to be relatively well-tolerated with the most common adverse effects being dizziness, paraesthesia and anorexia.[39]

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.[41]

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.

It blocks EEG arousal from stimulation of the brain stem reticular formation. It takes several hours for peak blood levels to be reached and the half life of the drug is between 24 to 48 hours. After the drug is discontinued plasma levels decline slowly over a period of several days. It excreted in the urine.[47]

Research question

What are the impact of Various Drug Therapy on Quality of Life of alcohol dependence patient and what are the adverse drug reactions associated with this.

2. AIMS AND OBJECTIVES

The objective of the current analysis has to describe the evolution of QOL in males and females with alcohol dependence and determine the adverse reactions 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.

Secondary objective

To determine the Adverse Drug Reaction of Various Drugs Therapy of Alcohol Dependent patients after three, nine and eighteen weeks of initiation of Drug Therapy.

3. Review of literature

Quality of life of an individual with alcohol dependence found significant impairment particularly with respect to their mental health and social functioning.[7,8,9,10,11,12]

The study indicates that Quality of life particularly the mental aspect improves during treatment of alcohol dependence.[13,14] It would also be helpful to observe the dynamics of quality of life changes over an extended period.

Quality of life in alcohol dependent patients changes with SF-36 questionaire have two major component one is Mental component and second is Physical component.[27,37]

In some studies mean mental component summary score improved in each individual clusters. Among the three patient clusters the mean mental component summary score was highest indicating better QOL among those who were mostly abstainers , intermediate for moderate drinkers and lowest among patients who were mostly heavy drinkers.[25,27]

The mean mental component summary score improvement were seen by month three and generally maintained or increased further during the rest of the previous studies.

Previous studies the relation between treatment for alcohol dependence and changes in QOL of Physical component was not clear cut as the changes in Mental component.[14,16,17] Although some studies have found in an improvement in Physical QOL after treatment.[15]

Measurement of a Patients Quality of Life QoL requires a different approach to that typically used in clinically research, where the clinician is responsible for rating the health condition of the patients subjective perception of their state of health and life using a standardised questionnaire. Subjective perceptions of the patient may indeed by quite different from the physician perception of the health status of the patient.[41] Patient reported outcome measures such as QoL may be useful in orienting choice between different treatment options since effective therapy should not only improve the clinical state and prognosis of the patient but also their QoL. The initial QoL of patients could also affect the prognosis of various disease states.[42]

Nowadays practice standards, the QoL of alcohol-dependent patients is not measured systematically, even though this is relevant to the psychosocial context of the interventions and to describing how actively patients will participate in their own care.[25,27,28] Previous Studies dedicated to the analysis of QoL of alcohol-dependent patients have already yielded valuable information, whether measuring basal QoL, its improvement during patient care, or its influence on alcohol- dependence itself.[21,36,37] Most of these studies have found QoL to be decreased considerably in alcohol- dependent patients, but little information is available on how QoL changes during a therapeutic intervention.[25,28] Some studies have identified factors associated with a poor QoL at the beginning of treatment in alcohol-dependent patients but these have not been investigated in a systematic way predictors of changes in QoL.[28] The variables associated with an improvement in QoL of patients during care and the influence of QoL on the prognosis of alcoholism are unknown.[22,23,27]

The aims of this study in a clinical setting is to determine the change in QoL of alcohol-dependent patients during a 18 week outpatient programme to identify the variables associated with QoL in alcohol- dependent patients before detoxification, and how they changes during a 18 week outpatient programme. Alcohol dependent patients treated with available drugs like Topiramate, Baclofen and Chlordiazapoxide at Psychiatry Department Of Mathura Das Mathur Hospital Jodhpur. Side effects of Topiramate the most frequently is paresthesia. Other Adverse Effects found with Topiramate are Anorexia and Concentration Problems.

Side effects of Baclofen are Confusion, Dizziness, Headache, Nausea, Sweating, Trouble Sleeping, Weakness, Overly tired.

Symptoms of Baclofen Overdose include Blurred Vision, Convulsion, Trouble Breathing, Severe Weakness, Muscle Pain, Pale or Blue lips.

Side effects of Chlordiazapoxide are Drowsiness, Tiredness, Dizziness, Nausea, Vomiting, Constipation, Blurred vision, Swelling, Skin rash, Irregular menstrual periods and Headache.

Adverse effects due to overdose of Chlordiazapoxide are Confusion, Depression, Hyperactivity, Hallucination, Slurred speech and Trouble walking.

No specific instrument has yet been developed to asses the changes in QOL in individual with alcohol dependence.[18]

In this study determination of changes in QOL of Alcohol Dependence is measure by using a free version of SF-36 transformed questionnaire.

World Health Organization (WHO) defined adverse drug reaction as- "A response to a drug which is noxious and unintended, and which occurs at doses normally used in human for the prophylaxis, diagnosis, or for the modification of physiological function" (ADR)

The term "adverse effect" encompasses all unwanted effects; it makes no assumptions about mechanism, evokes no ambiguity, and avoids the risk of misclassification. An adverse effect is seen from the point of view of the drug, whereas an adverse reaction is seen from the point of view of the patient. An adverse event is an adverse outcome that occurs while a patient is taking a drug, but is not or not necessarily attributable to it.

The Adverse drug effects of Topiramate, Baclofen and Chlordiazapoxide were taken from the Alcohol dependent patients at Third, Ninth and Eighteenth Weeks and filled in ADR form.

The SF-36 scores for the eight dimensions that are Mental Health (MH), Role limitations attribute to Emotional Problems (RE), Social Functioning (SF), General Health (GH), Bodily Pain (BP), Role limitations due to Physical Problems (RPF), Physical Functioning (PF) and Vitality (VT) were significantly lower on Baseline than at after Eighteenth week. The scores of the eight dimensions of Alcohol dependent patients were similar to the General population at the Eighteenth week of the study.

The study confirms the poor Quality of Life QoL of Alcohol dependent patients at the time of zero day or Baseline and enabled us to identify a number of sociodemographic and clinical variables linked to QoL. It also demonstrate the positive impact of treatment care on short term improvement in QoL of alcohol dependent patients.

The study findings if communicate to patients could enhance their motivation to taken out patient programme.

The study results are better to compare with other studies due to different follow-up time instead this initiation of psychosocial support and the management of somatic or psychiatric comorbidities in patients undergoing alcohol detoxification as a strategy to improve QoL.

However the treatment effect on Quality of Life have not received nearly as much attention as clinical measures of Alcohol Dependent Patients. Patients and their relatives increasingly expect improvements not only their symptoms, but beyond that improvements of their functioning and Quality of Life.

Like Various drugs therapy Alcohol dependent patients needed Psychotherapy and Rehabilitation or De-addiction centre for a better results for improving their Quality of Life and removing dependency of Alcohol.

The study is different with other studies because the changes in Quality of Life QoL of Alcohol dependent patients are taken with various drugs and at distinct weeks.

Types: Adverse drug reactions classified into six categories.

Table 1: Classification of adverse drug reactions.

Type of Reaction	Mnemonic	Features
A: Doserelated	Augmented	-Common -Related to the pharmacologic action of thedrug -Predictable -Low mortality
B: Non-doserelated	Bizarre	-Uncommon Not related to the pharmacologic action ofthe drug -Unpredictable -High mortality
C: Dose related and time related	Chronic	-Uncommon -Related to the cumulative dose

D: Time related	Delayed	-Uncommon -Usually dose related -Occurs or becomes apparent sometime after use of the drug
E: Withdrawal	End of use	-Uncommon -Occurs soon after withdrawal of the drug
F: Unexpectedfailure of therapy	Failure	-Common -Dose related -Often caused by drug interactions

Causality assessment: The Food and Drug Administration (FDA) defined the causality assessment as determination of whether there is reasonable possibility that the product 1s etiologically related to the adverse experience. Causality assessment includes for example the assessment of temporal relationship, de-challenge and rechallenge information, association (or lack of association) with underlying disease. and the presence (or absence) of a more likely cause and physiologicalplausibility.

De-challenge: The clinical decision to withdraw/discontinue a drug treatment after a possible ADR has occurred. A de-challenge is 'positive" or suggestive' if the reaction abates partially or completely, when the drug is withdrawn and it consider to negative or against if the reaction does not abate when the treatment is stopped.

Rechallenge: The Food and Drug Administration defines rechallenge as the reintroduction of product suspected of having caused an adverse experience following a positive de-challenge. Failure of product, when reintroduced, to produce signs and symptoms similar to those observed when the suspected drug was previously introduced implies a negative rechallenge, while recurrence of similar signs and symptoms upon reintroduction of the suspected drug implies a positive rechallenge.

There are 2 stages of causality assessment

1) Causality assessment- Ist stage: Assessment of individual case reports.
2) Causality assessment-2nd stage: Interpretation of aggregateddata.

Currently worldwide varieties of causality assessment scales exist, to attribute clinical events to drugs in individual patients or in case reports, each with their own advantage and limitations. Most commonly used causality assessment scale is includes mainly two scales:

1) WHO-UMC causality categories
2) Naranjo ADR probability scale

WHO-UMC causality categories: As per

Table 1: WHO-UMC causality categories.

Causality term	Assessment criteria
Certain	• Event or laboratory test abnormality, with plausibletime relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, Pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specificmedical disorder or a recognized pharmacologicalphenomenon) • Rechallenge satisfactory, if necessary
Probable/Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake
	• Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking orunclear
Unlikely	• Event or laboratory test abnormality, with a time todrug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausibleexplanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information isinsufficient or contradictory • Data cannot be supplemented or verified

Naranjo ADR probability scale: As per **Table 2**

Table 2: Naranjo ADR probability scale.

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve whenthe drug was discontinued or a specific antagonist was given?	+1	0	0	
4. Did the adverse event appear when thedrug was re-administered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that, on their own, could have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to betoxic?	+1	0	0	
8. Was the reaction more severe when thedose +1was increased or less severe whenthe dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by anyobjective evidence?	+1	0	**0**	
Total Score	ADR Probability Classification			
9	Highly Probable			
5-8	Probable			
1-4	Possible			
0	Doubtful			

Alcohol dependent patients treated with various drug therapy. In Mathura Das Mathur Hospital Drugs used for Alcohol dependence are Topiramate, Baclofen and Chlordiazapoxide. Adverse drug reactions have become an important challenge in today's modern medicine. These associated with above drugs are dizziness, paraesthesia, sedation, postural hypotension, gastrointestinal, weight gain, depression and others.

4. MATERIALS 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 (ANNEXURE 2) and Hindi (ANNEXURE 3). Patients who gave written informed consent were then included in the study.

Measurment
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 (MCS). 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).

Table 4: Items with Domains of SF-36.

Sr. No.	Eight Domains Of SF-36Sub scale	Numberof Items	Included Question Number of SF-36 Questionnaire
1	Physical Functioning (PF)	10	3-12
2	Role limitations due toPhysical Problem(RP)	4	13-16
3	Role limitations due Emotional Problem(RE)	3	17-19
4	Energy /*F*atigue (E/F)	4	23,27,29,31
5	Emotional Well-being(EWB)	5	24-26,28,30
6	Social Functioning (SF)	2	20,32
7	Bodily Pain (BP)	2	21,22
8	General Health (GH)	5	1,33-36

A free version of SF-36 Transformed Questionaire are weighted sums of the questions in their section. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The lower the score the more disability. The higher the score the less disability i.e., a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.

The Result of SF-36 Transformed Questionaire could be get by Manual in which zero to hundred marks give for every questions and then calculate average in Percentage. The other method is online in which Orthotool kit used for result in this method put the answers in this kit and calculate the result by average in Percentage.

Study bias
An important limitation in previous study was the Attrition Rate (The rate of shrinkage of number or size). Although the sensitivity analysis compensated for the effect of loss to follow-up.

Follow-UP
At baseline (day 0), as when come to follow up or at 3rd week, 9th week and 18th week after baseline through patient self or Telephonically.

Sample size
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

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

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

= 19 + 2 = 21

Where,

N = Sample size $\left(Z_{1-\alpha_2}\right)$ = 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:-

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

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

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

t = statistical t-value

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.

5. RESULTS

1) Characteristics of study population

The characteristics of the 50 patients are shown in Table 1. Fourty five men and Fifteen 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 5: Characteristics of the study population.

Variable	Number (%)
Age	32 ±10
Sex ratio (Male/Female)	2.33
Work	44(6)
(Employed/Unemployed)	
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 patient

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 6: Prescribed drugs for treatment of alcohol dependent patients.

Prescribed drug	Patients
Tab. Topiramate 50 mg BD	25
Tab. Baclofen 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 7). 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 7: Score of SF-36 each domains before treatment in Alcohol Dependent patients.

Domain	Mean before treatment(O-Day)	Mean of healthyperson	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 8: SF-36 scores for patients completing 18-weeks of treatment.

Domain	Baselinescore	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 7 & 8 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 31

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 9: 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%

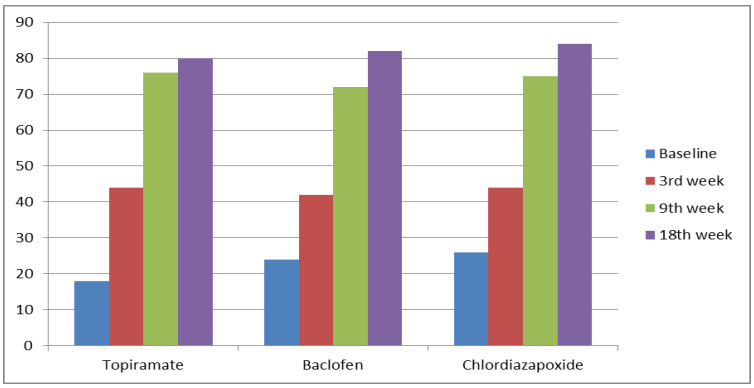

Figure 1: Mean Sf-36 score in % with Prescribed drugs.

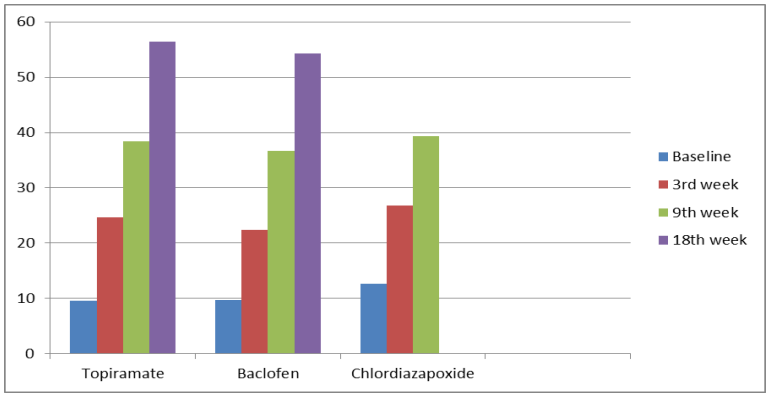

Figure 2: Mean Physical Function PF changes with prescribed drugs.

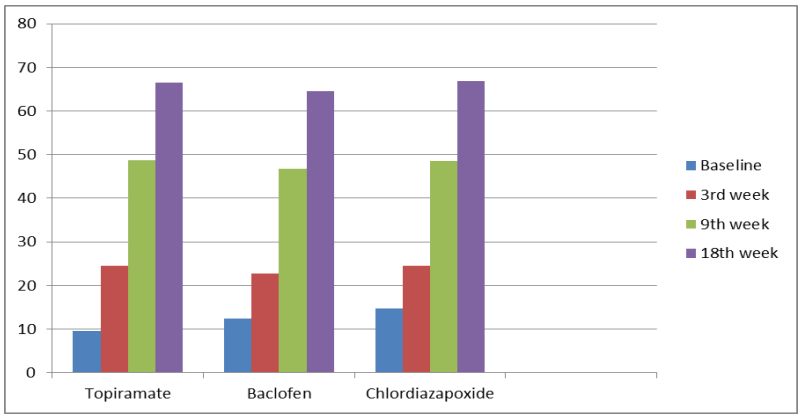

Figure 3: Mean Role Physical Limitation (RP) changes with prescribed drugs.

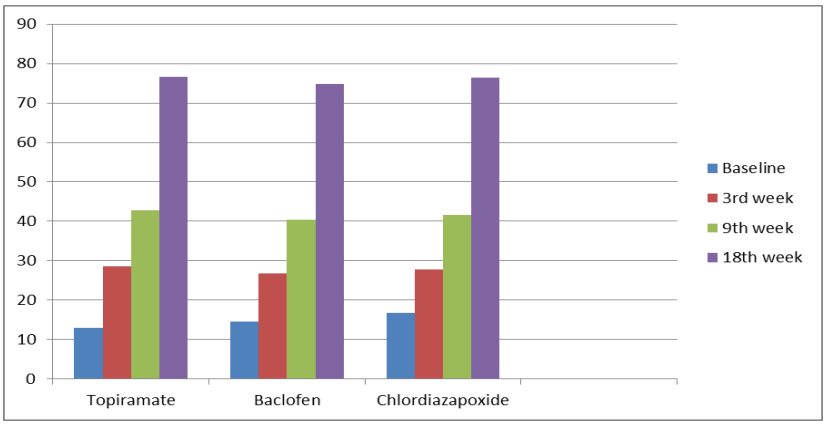

Figure 4: Mean Role Emotional Limitation (RE) changes with prescribed drugs.

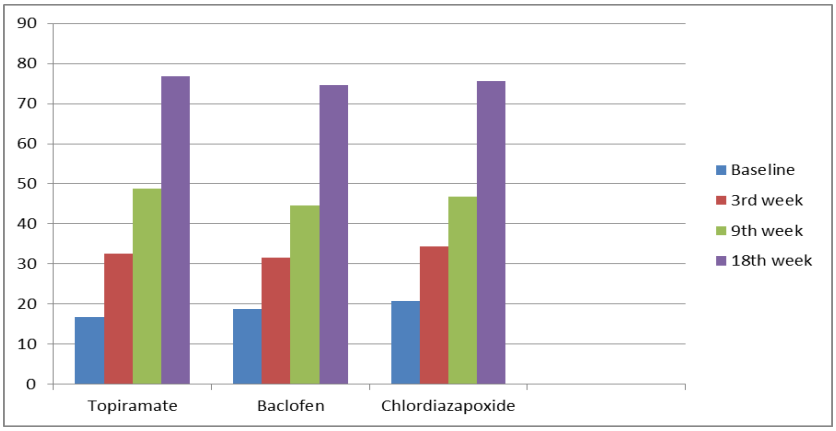

Figure 5: Mean Energy/ Fatigue (E/F) changes with prescribed drugs.

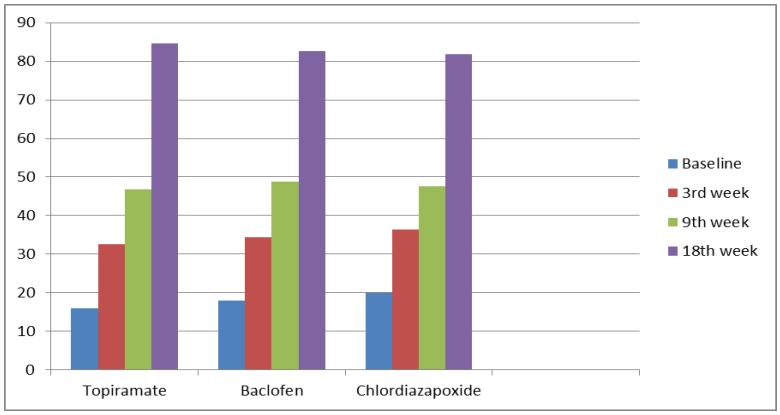

Figure 6: Mean Emotional well Being (EWB) changes with prescribed drugs.

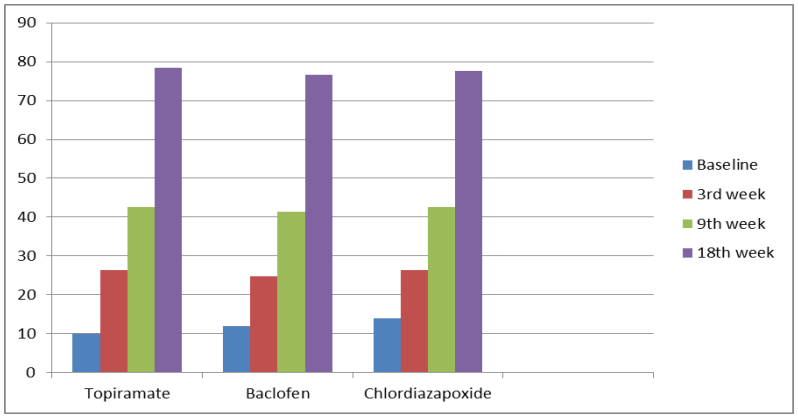

Figure 7: Mean Social Functioning (SF) changes with prescribed drugs.

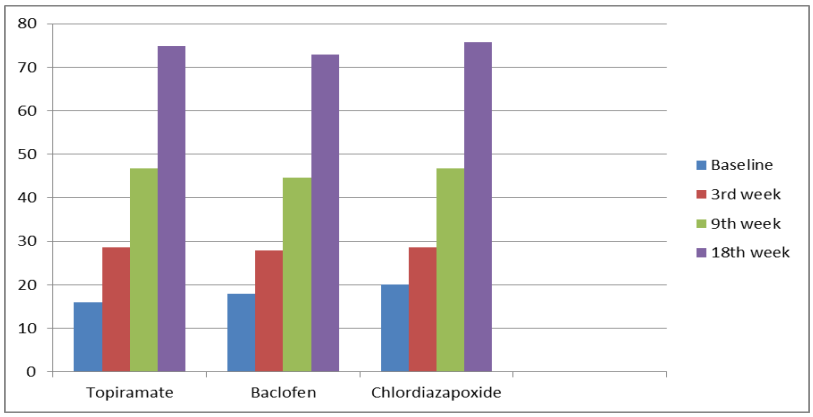

Figure 8: Mean Bodily Pain (BP) changes with prescribed drugs.

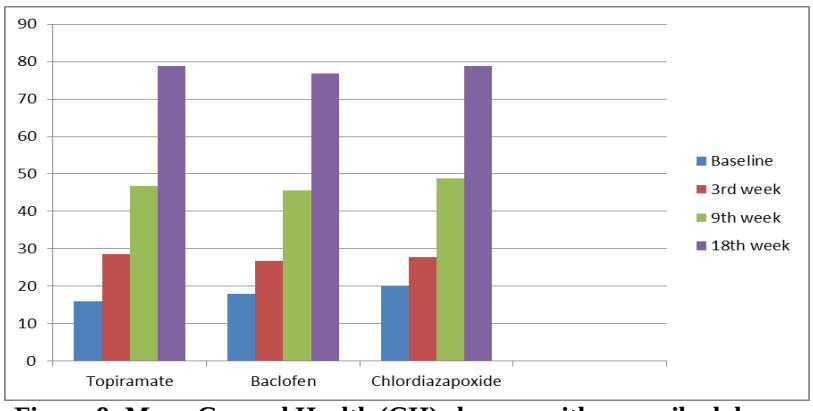

Figure 9: Mean General Health (GH) changes with prescribed drugs.

Adverse drug Reactions (ADR)

Frequency and percentage of observed adverse drug reaction associated with various drugs therapy for Alcohol dependence patients are showed in Table 12. Maximum ADR observed was 26.84%. Topiramate shows maximum adverse drug reactions among group of various drugs.

Commonest ADR was nausea and Headache.

Table 10: ADR with Prescribed Drugs.

ADR	Topiramate	Baclofen	Chlordiazapoxide	Total
	(25)	(15)	(10)	(50)
Nausea	03	01	01	05
Diarrhoea	01	01	--	02
Vomiting	02	01	--	03
Headache	03	01	--	04
Weakness	--	--	01	01
Dizziness	01	01	--	02
Sweating	01	--	01	02
Paraesthesia	01	--	--	01

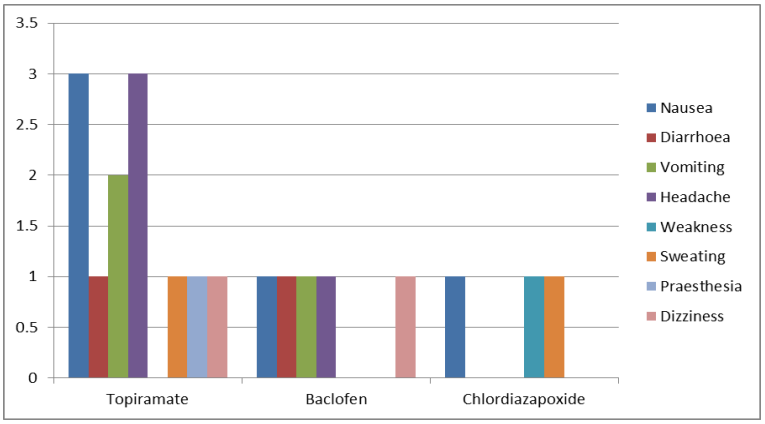

Figure 10: ADR with Prescribed drugs.

6. 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.[34]

Alcohol Dependence is associated with significant reduction in Quality of Life.[25,28]

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),[48] Chikkerahally GDMD 39.09 years (2019),[32] Marsha Y Morgan et al (2004) 43 years[43] and 42 year in Miller M et al (2011) study.[15] 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).[48]

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).[53] Faller S et al (2015)[33] and Chikkerahally GDMD. (2019)[32] 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)[33] and Shrivastava S, Bhatia M study (2013)[53] which were completely difference with Pierre Lahmek et al study (2009) that in patient of alcohol Dependence were diagnosed and Treated.

In This study improvement in Quality of Life by various drugs therapy statistically significant similar with Marsha Y Morgan et al (2004),[43] Pierre Lahmek et al (2009)[48] and Faller S et al (2015)[33] and shows increasingly improvement in Quality of Life with acute and follow-up treatment. Topiramate is better choice for treating Alcohol dependence Patients as like in the study of Johnson B et al (2007)[6] and Florez G et al (2008)[7] study.

In the study of Pierre Lahmek et al (2009)[48] and Marsha Y Morgan et al (2004)[43] scale used for assessment the changes in Quality of Life of Alcohol dependent Patients is similar to Present study that is Medical Outcome Study (MOS) Short Form (SF) Questionnaire results shows that

all area of Health Related Quality of Life improved with acute and follow up Treatment.[27,43]

In This study most common ADR was Nausea that is not in accordance with Marsha Y Morgan et al (2004),[43] Pierre Lahmek et al (2009)[48] and Faller S et al (2015)[33] in which most common ADRs were insomnia. Headache more common with Topiramate common in Miller M et al (2011)[15] This study shows Nausea common with Topiramate and weakness with Chlordiazapoxide.

Limitation of the study

- The results of this study may be limited by the type of questionnaire used for Quality of Life (QoL) measures, all questionnaire were self disclosure with potential risk of misinterpretation or bias in the responses.
- The other limitation of this study is that it did not investigate how involved patients were in treatment decision or the patient- physician relationship, that could further explain the results of patients adherence to therapy or treatment satisfication.
- The results of the design of the study can not ask to what extent the increase in Quality of Life of due to various drugs therapy exclusively because concomitant treatment were given in combination (e.g. psychotherapy).
- 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.

7. ACKNOWLEDGEMENTS

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8. Conflict of interes

No conflict of Interest.

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