IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 11 Ser.2 (November. 2019), PP 01-06
www.iosrjournals.org

"A Prospective Observational Study on Effectiveness of Baclofen in Alcohol Withdrawal Syndrome".

Ch. Indira priyadarsini[1],Y. Himabindu[2]
[1] *(Associate professor, department of general medicine, ACSR GOVT medical College, Andhra Pradesh, India).*
[2]*(pharm.D intern department of general medicine, ACSR GOVT medical College, Andhra Pradesh, India).*
Corresponding Auhtor: Ch. Indira priyadarsini

Abstract: *Alcohol abuse is emerging as a global burden and causes a substantial health loss. Alcohol while using causes no significant effects but its abrupt withdrawal causes deleterious effects. In this study baclofen is used as a novel drug to overcome the alcohol withdrawal effects.*
Aim: *The main objective of the study was to determine baclofen as a safe and effective treatment option for alcohol withdrawal syndrome.*
Materials and methods: *A total of sixty nine patients were enrolled in the study by using CIWA-Ar (clinical institute withdrawal assessment) scale in ACSR GOVT medical college from September 2018 to February 2019. Patients who were attended for three follow ups their CIWA-Ar score is measured and noted. CIWA-Ar scale was used only to evaluate physical symptoms.*
Results*: In a total of 69 patients, 28 patients were attended for three follow ups. Among them, 27(39%) patients were in complete abstention with alcohol and the craving (39%) also considerably decreased. Symptoms include nausea (95%), tremors (84%), anxiety(53%), agitation(57%), paroxysmal sweats(67%), tactile disturbances (85%), auditory disturbances (85%), visual disturbances (73%), headache (55%) were decreased significantly. Baclofen notably decreases the anxiety score which shows its anxiolytic effect.*
Conclusion: *Hence forth the results in the study suggests that baclofen may be a brand new treatment to implicate in the treatment area of AWS.*
Keywords: *Alcohol withdrawal syndrome, baclofen, $GABA_B$ analogue.*

Date of Submission: 23-10-2019 Date of Acceptance: 08-11-2019

I. Introduction

According to 2018 WHO (World Health Organization) census, more than 3 million people died as a result of harmful use of alcohol in 2016. This represents 1 in 20 deaths. It representsmore than three quarters of these deaths were among men. More than 5% of the global disease burden is caused due to harmful use of alcohol[11].

In most countries drinking alcohol is socially acceptable and it is legal. It raises levels of HDL (high density lipoprotein) which are associatedwith protection against heart diseases. Red wine 150ml (5oz) per day helps in the prevention of heart disease. Chronic intake of alcohol can damage liver cells and make it dysfunctional. It causes inflammation of liver such as alcoholic hepatitis and cirrhosis. It causes slow and progressive degeneration of nervous system and damages the neurons.

Alcohol dependence is considered as a severe form of alcohol use disorder which manifest when a person develops withdrawal symptoms after cessation of alcohol. This may be due to family pressure, self-motivation, physical ill health or difficulty in procuring alcohol. There is a misconception in regular drinkers that cessation of alcohol causes more problems than continuing it. This is partly true in those who have developed dependence as they may experience withdrawal symptoms including autonomic arousal, hallucinations, seizures and delirium tremens (DT)[8]. Alcohol is a CNS depressant, which influences the inhibitory neurotransmitter gamma-amino butyric acid (GABA).The excitatory (glutamate) and inhibitory (GABA) neurotransmitters are mostly in homeostasis state. Alcohol provokes GABA action, causing decreased CNS excitability. Its long-term effect causes a decrease in the number of GABA receptors (down regulation) which results in the requirement of increasingly larger doses of ethanol to achieve the same euphoric effect, which is a phenomenon known as tolerance. Alcohol in general acts as an N-methyl-D-aspartate (NMDA) receptor antagonist, thereby reducing the CNS excitatory tone. Chronic use of alcohol leads to an increase in the number of NMDA receptors (up regulation) and production of more glutamate to maintain CNS homeostasis.

Baclofen has been used safely for decades as a smooth muscle relaxant. Recent understanding of the pathophysiology of alcohol withdrawal syndrome evolved, leading to the evaluation of baclofen's role for

treatment of AWS. Although data are mixed regarding baclofen's efficacy in AWS, data are consistent in terms of safety. Literature supporting higher doses of Baclofen, mostly case reports and series, has reported the safe use of doses up to 275 mg daily[7]. However, there are very limited safety data utilizing high dose Baclofen in alcohol-dependent patients, and significant adverse events have been reported, including overdose and seizures. Activation of $GABA_B$ receptors by Baclofen may result in local inhibition of surrounding dopamine neurons[2]. Through this mechanism, alcohol-stimulated dopamine release would be reduced, thereby decreasing positive reinforcement from alcohol consumption and aiding in abstinence from alcohol. Evidence also supports Baclofen as a safe maintenance treatment for alcohol dependence, even when patients continue to consume alcohol or resume drinking alcohol. Mesolimbic dopamine neurons, found in the same areas of the brain as $GABA_B$ receptors, are thought to be involved in the mediation of alcohol intake and reinforcement

II. Methods And Materials

Study area:

- The study was carried out in ACSR government medical college, 750 bedded tertiary care teaching hospital, Nellore.

Study population:

- This study involved 69 subjects who were with alcohol withdrawal symptoms.

Study design:

- A prospective observational study

Study period:

- The study period was 6 months from september2018 and February 2019.

Inclusion criteria:

- Patients who were at high risk with withdrawal symptoms.
- Patients who would agree to abstain from alcohol for duration of study,
- Patients who agreed to give their consent to the study.
- Patients with age of above 18yrs

Exclusion criteria:

- Patients with any drug dependence.
- Patients with psychiatric disorder.
- Patients with neurological disorders.
- Not willing to abstain from alcohol during the time of study.
- Not willing to give their consent to the study.

Data collection:

At first baseline data were obtained from patients. Demographic details (age, gender) as well as their alcohol history drinking intensity; duration and type of alcohol; any serious illness if present. Patients were enrolled by using CIWA-Ar scale which constitutes the symptoms of alcohol withdrawal and the score were noted. We conducted three follow ups; at each time CIWA-Ar scale were re-measured and the score were noted.

Statistical analysis:

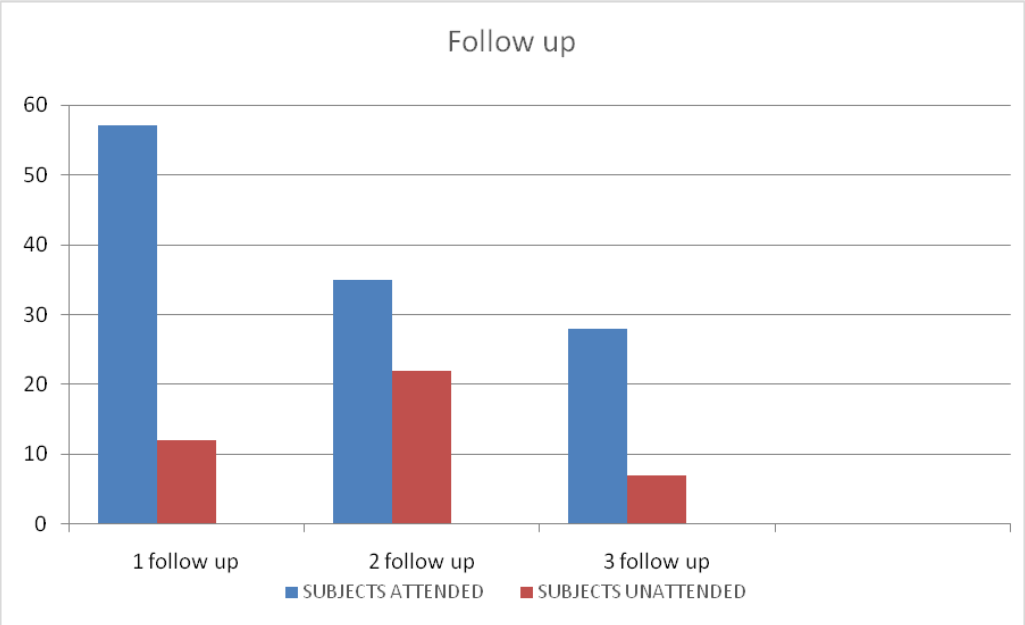
Analysis of decreased severity of symptoms before and after treatment in CIWA-Ar score was performed by 2 way analysis of variance test (ANOVA). This analysis was only considered for those patients who came for all three follow ups. Statistical significance was defined as $p < 0.05$

III. Results

This is a prospective observational study, we included subjects based on inclusion and exclusion criteria by taking the subjects consent in this study period (6months).We collected data and determined the effectiveness of baclofen in 27 subjects, out of 69 subjects 28 subjects were attended 3 follow ups and provided information regarding effectiveness of baclofen and improvement of their quality of life.

Table no 1: Categorisation of Subject's Attendance in Three Follow Ups

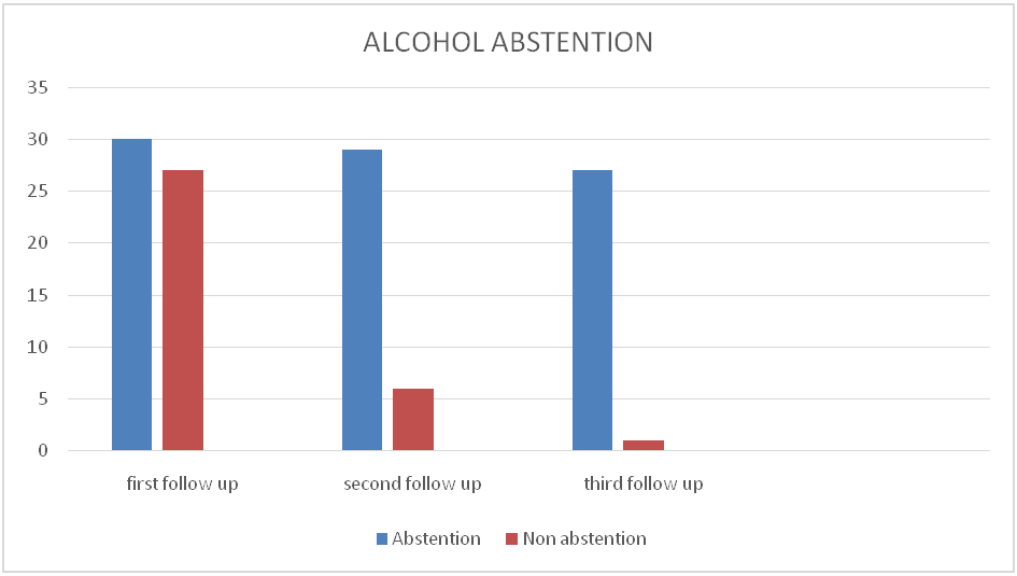
S.NO	Follow up	subjects attended	subjects unattended
1.	1 follow up	57	12
2.	2 follow up	35	22
3.	3 follow up	28	7



Study starts with 69 subjects, but for first follow up out of 69 subjects 57 patients were attended and 12 were dropped .In second follow up out of 57 subjects,35 subjects were attended and 22 subjects were dropped. By the end of the study total of 28 subjects were attended for all three follow ups

Table no 2: Abstention and Nonabstention In Subjects

S.NO	Follow up	Abstention	Non abstention	Total subjects
1.	First follow up	30	27	57
2.	Second follow up	29	6	35
3.	Third follow up	27	1	28

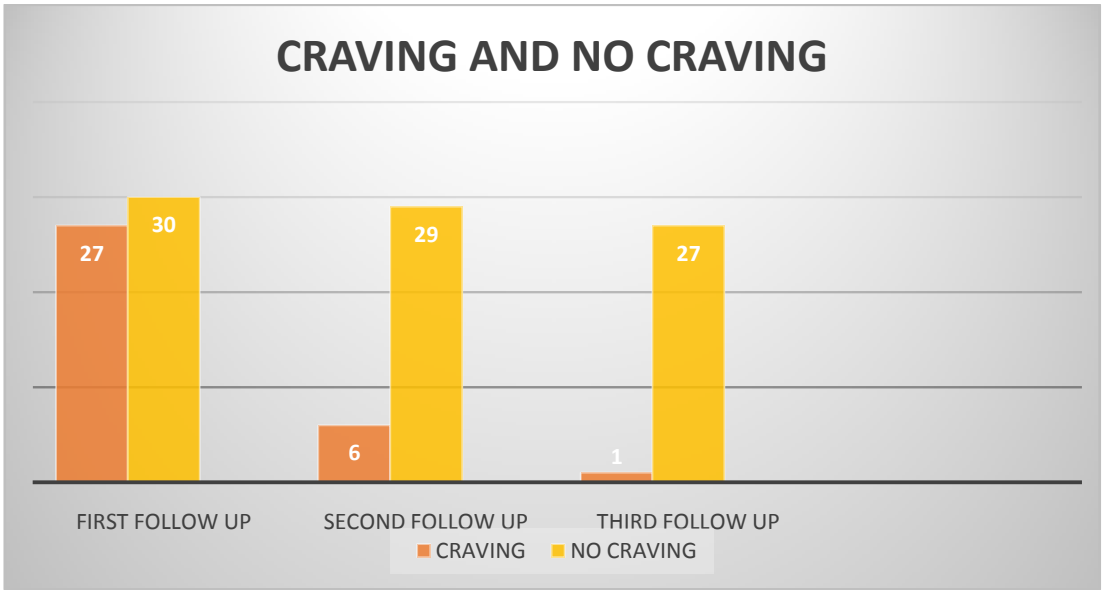


In first follow up out of 57 subjects, 30 subjects were abstained from alcohol remaining 27 subjects were continued to take alcohol. In second follow up out of 35 subjects, 29 subjects were abstained from alcohol remaining 6 subjects were continued taking alcohol .In the third follow up out of 28 subjects 27 subjects in

abstention with alcohol. At the end of the study, out of 57 subjects 27 subjects were completely abstained from alcohol.

Table no 3: Categorisation of Craving and Non Craving in Subjects

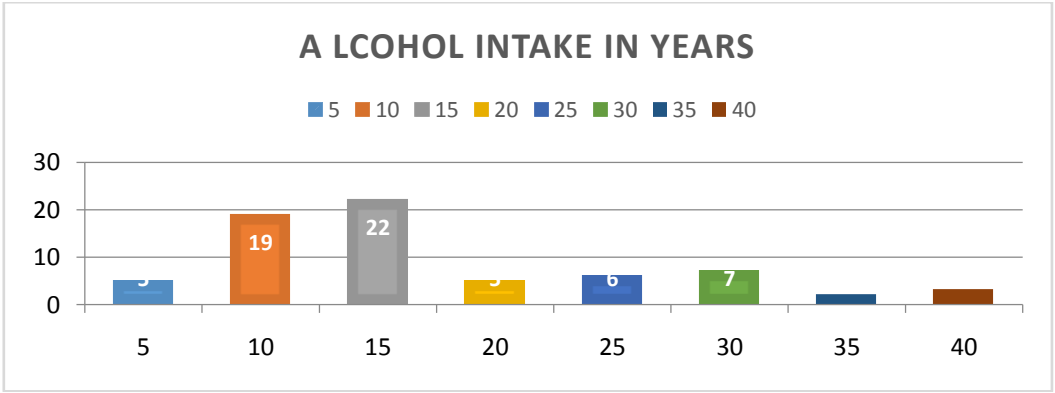
S.no	Follow up	Craving	No craving	Total subjects
1.	First follow up	27	30	57
2.	Second follow up	6	29	35
3.	Third follow up	1	27	28



During the first follow up among 57 subjects, 30 subjects (43%) had no craving for alcohol. In the second follow up, among 35 subjects, 29 subjects (42%) had no craving for alcohol. In third follow up among 28 subjects, 27 subjects (39%) had no craving for alcohol. By the end of the study a total of 27 subjects (39%) had no craving for alcohol.

Table no 4: Duration of Alcohol Intake in study subjects

S.NO	Alcohol intake (in yrs.)	Number of subjects
1.	0-5yrs	5
2.	5-10yrs	19
3.	10-15yrs	22
4.	15-20yrs	5
5.	20-25yrs	6
6.	25-30yrs	7
7.	30-35yrs	2
8.	35-40yrs	3



Out of 57 subjects more than 22 subjects are found to drinking alcohol since 15 years.

Table no 5: subject's age(in yrs)

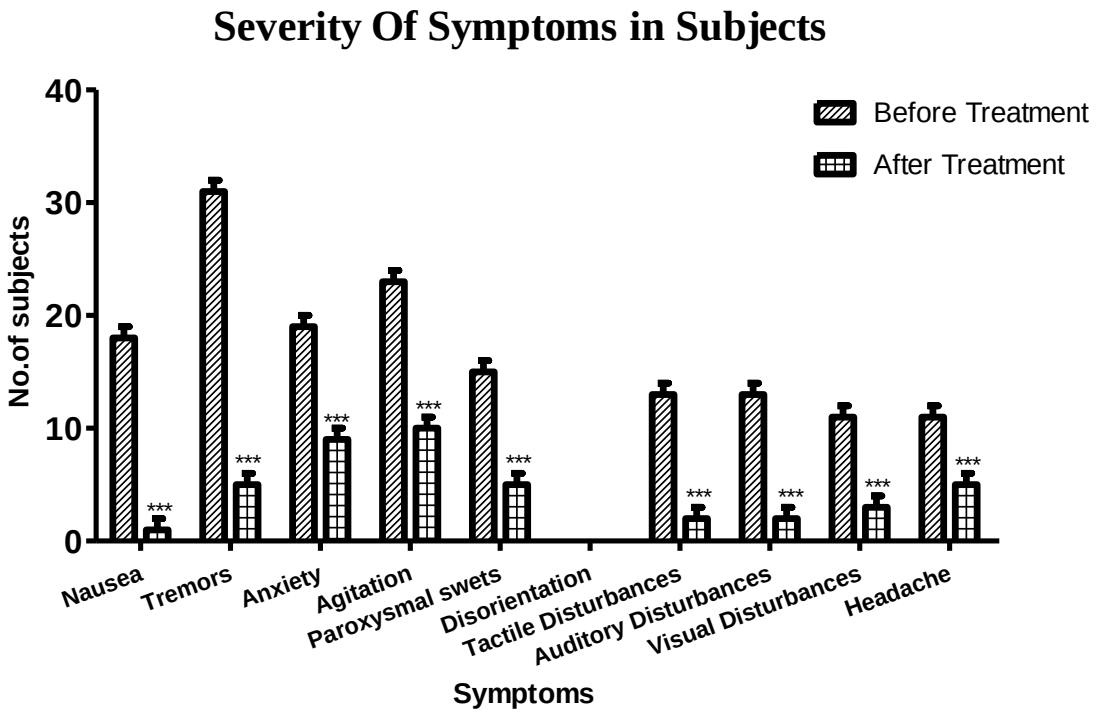
S.no	Age (in yrs)	Number of subjects
1.	18-28	10
2.	28-38	20
3.	38-48	25
4.	48-58	7
5.	58-68	7

Among 69 subjects, 25 subjects are found to be at age between 38-48 yrs.

Table no 6: Severityof Symptoms in Subjects

S.no	Symptoms	Before treatment	After treatment	Improvement in percentage
1	NAUSEA	18	1	95%
2	TREMORS	31	5	84%
3	ANXIETY	19	9	53%
4	AGITATION	23	10	57%
5	PAROXYSMAL SWEATS	15	5	67%
6	DIS ORIENTATION	0	0	0
7	TACTILE DISTURBANCES	13	2	85%
8	AUDITORY DISTURBANCES	13	2	85%
9	VISUAL DISTURBANCES	11	3	73%
10	HEADACHE	11	5	55%

Symptoms include nausea (95%), tremors (84%), anxiety (53%), agitation (57%), paroxysmal sweats (67%), tactile disturbances (85%), auditory disturbances (85%), visual disturbances (73%), headache (55%) were decreased significantly.



statistical analysis : The observed data of this study was analysed by using 2 way ANOVA .The results of this analysis shows that P value < 0.05 as significant with 95% confidence interval,where *** significant compared with before treatment.

IV. Discussion

Benzodiazepines constitute the contemporaneous treatment in alcohol withdrawal syndrome. Apart from these drugs, there is no other class of drugs provide effectiveness as much as benzodiazepines. But the long term use of benzodiazepines leads to dependence and abuse.

So far baclofen is known for its muscle relaxant property. Results obtained in our studymay affix one more indication to baclofen as alcohol withdrawal agent. Being a $GABA_B$ analogue baclofen increases the GABA concentration and decreases the withdrawal symptoms.

The use of baclofen not only limited to AWS but also shows its results in alcohol dependence and addiction. It is also proved to be safe in alcohol liver disorders such as liver cirrhosis.

The evidence supporting the safe and effective use of baclofen for the maintenance treatment of alcohol withdrawal is growing. From the studies which is reviewed here, baclofen shows the evidence of anti-craving and abstention properties of alcohol.

Notable results were achieved in thisstudy which includes craving (39%) and abstention (39%). And symptoms includenausea (95%), tremors (84%), anxiety (53%), agitation (57%), paroxysmal sweats (67%), tactile disturbances (85%), auditory disturbances (85%), visual disturbances (73%), headache (55%) were decreased significantly.

A comparison study conducted by addolorato and his colleagues showed that baclofen has the similar ability as diazepam in decreasing the CIWA-Ar score. They considered 4 items of CIWA-Ar score to determine the effectiveness of baclofen i.e, sweating, tremors, anxiety, agitation which were substantially decreased after treatment. In the current study these 4 items were improved by; sweating (67%); anxiety (53%); tremors (87%); agitation (57%).

A preliminary study in humans by Colombo g and his colleagues stated that baclofen substantially decreased the alcohol intake and patients were in complete abstention with alcohol. In their study; among 20 patients 14(70%) patients were in abstention with alcohol. In this study out of 69 patients 27(39%) patients were in complete abstention with alcohol. They also concluded that baclofen also has a possible role of anti-craving property which supports the anti-cravingeffect observed in the current study.

An open label study by Flannery BA and his colleagues suggested that baclofen is reasonably tolerated in alcohol dependent patients. In their study out of 12 patients, 5(41%) patients were in complete abstention with alcohol. Same in thecase with current study, out of 69 subjects 27(39%) patients were in complete abstention with alcohol.

Addolorato and his colleagues conducted a preliminary clinical study in 10 heavy alcoholic patients. Out of 10 patients, 7 (70%) patients maintained abstinence throughout the study period. In the current study in a total of 69 patients, 27 (39%) patients were in complete abstention with alcohol.

Stallings W and his colleagues conducted a retrospective study in which baclofen is used as prophylactic treatment for alcohol withdrawal syndrome. A total of 17 cases were collected; 12 patients showed improvement and 2 patients showed no improvement. The success rate of prophylactic treatment was 86% .In the current study, out of 69 patients 27 patients were showed positive results in which drug decreased the symptoms by 39%.

V. Limitations

The considerable limitation in the current study was inappropriate follow up. We were unable to follow up some patients due to lack of their proper contact details which was due to their low socio-economic status and their lack of awareness. But we successfully collected data from remaining patients and their improvement in symptoms.

VI. Conclusion

Baclofen showed its promising effects in the treatment for alcohol withdrawal syndrome. These results in the study suggests that baclofen may be a brand new treatment to implicate in the treatment area of AWS.

References

[1]. A Randomized, Open-Label, Standard Controlled, Parallel Group Study of Efficacy and Safety of Baclofen and Chlordiazepoxide In Uncomplicated Alcohol Withdrawal Syndrome By,K.Girish10.1016
[2]. .Baclofen In the Treatment of Alcohol Withdrawal Syndrome: A Comparative Study Vs Diazepam Giovanni addolorato 10.1016/J.Amjmed.2005.08.042
[3]. Baclofen in Managing Acute Alcohol Withdrawal: Preliminary Findings from a Randomised Controlled TrialS.Jegham 10.1016/j.euroneuro.2017.12.102
[4]. Baclofen for the Treatment of Alcohol Use Disorder: The Cagliari StatementRobertaagabio 10.1016/s2215-0366 (18)30303-1
[5]. Baclofen as Add-On to Standard Psychosocial Treatment for Alcohol Dependence: A Randomized, Double-Blind, Placebo-Controlled Trial with 1 Year Follow-UpAlexander M.Ponizovskym.D, Ph.D. 10.1016/J.Jsat.2014.11.007
[6]. Rapid Suppression of Alcohol Withdrawal Syndrome by BaclofenGiovanni addolorato 10.1016/S0002-9343(01)01088-9.
[7]. High-Dose Baclofen for the Treatment of Alcohol Dependence (BACLAD Study): A Randomized, Placebo-Controlled Trial byA.Müller[a]10.1016/j.euroneuro.2015.04.002.
[8]. Clinical management of alcohol withdrawal syndrome: a systematic review
[9]. Effectiveness and Safety of Baclofen for Maintenance of Alcohol Abstinence in Alcohol-Dependent Patients with Liver Cirrhosis: Randomised, Double-Blind Controlled Study Dr Giovanni addolorato 10.1016/S0140-6736(07)61814-5
[10]. Anti-craving Effect of Baclofen in Alcohol-Dependent Patients. Imbert B 2015
[11]. www.who.int/substance_abuse/publications/global_alcohol_report/en/

Ekpenyong, Nnette. "B Scan of Orbit with Its Clinico-Surgical Correlation." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 11, 2019, pp 01-06.