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Original Research

Assessment of efficacy of Lorazepam and chlordiazepoxide in alcohol dependence syndrome

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ABSTRACT:

Background: Worldwide, alcohol use is a significant risk factor for both illness and mortality. The present study was conducted to compare efficacy of Lorazepam and chlordiazepoxide in alcohol dependence syndrome. **Materials & Methods:** 62 patients with alcohol dependence syndrome were divided into 2 groups of 31 each. Group I patients received lorazepam 8 mg/day and group II received chlordiazepoxide 80 mg/day.The severity of alcohol dependence was assessed using the Severity of Alcohol Dependence Questionnaire (SADQ). The CIWA-Ar was used for quantification of withdrawal symptoms. Liver function tests were performed at baseline and at the end of the study. **Results:** At baseline and end of study, total bilirubin (mg/dL) was 1.04 and 1.01, direct bilirubin (mg/dL) was 0.26 and 0.27, alkaline phosphatase was 66.9 and 67.4, total proteinwas 6.90 and 6.92, serum albumin was 4.15 and 4.12, serum globulin was 2.87 and 2.05, SGOT was 41.8 and 41.1, SGPT was 45.9 and 45.8 in group I respectively. In group II total bilirubin (mg/dL) was 0.85 and 0.88, direct bilirubin (mg/dL) was 0.25 and 0.27, alkaline phosphatase was 77.3and 77.5, total proteinwas 6.52 and 6.59, serum albumin was 4.31 and 4.26, serum globulin was 2.18 and 2.15, SGOT was 55.2 and 51.3 and SGPT was 68.3 and 67.5 respectively. The difference was significant (P< 0.05). At baseline CIWA-Ar scores in group I was 24.3 and at end was 1.4. In group II, it was 24.1 at baseline and 1.5 at end of study. The difference was significant (P< 0.05). **Conclusion:** Lorazepam and chlordiazepoxide both work equally well to lessen the symptoms of alcohol withdrawal.

Keywords: alcohol, Liver function tests, SGPT

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INTRODUCTION

Worldwide, alcohol use is a significant risk factor for both illness and mortality. An estimated two billion individuals drink alcohol worldwide, and of those, around 76.3 million are thought to be affected by at least one alcohol use disorder.[1] Almost 3.2% of all fatalities and 4% of all disability-adjusted life years (DALYs) are caused by alcohol. Studies have indicated that nations with historically low levels of alcohol consumption are now exhibiting considerable increases in consumption patterns.[2] Furthermore, estimates from the World Health Organization (WHO) indicate that up to one-third of men in South East Asian countries drink alcohol, and the proportion of women who do the same is rising.[3]

In the 1960s, alcoholism was identified as a distinct illness. Edwards coined the term "alcohol dependence syndrome" in the 1970s to refer to the physiological, behavioral, and cognitive alterations brought on by alcohol consumption.[4] When an individual with alcohol dependence syndrome abruptly cuts back on their alcohol consumption, they may experience physical and psychological symptoms known as alcohol withdrawal. Benzodiazepines, such as lorazepam, diazepam, and chlordiazepoxide, are currently the recommended medications for treating the symptoms of alcohol withdrawal.[5] With half-lives of 24–48 hours and 20–50 hours, respectively, the first two medications are long-acting, whilst lorazepam is an intermediate medicine with a shorter half-life of 10–20 hours.[6] Diazepam and chlordiazepoxide are well-researched options for treating alcohol withdrawal. Nevertheless, the hepatic enzymes digest them and also generate.[7]The present

study was conducted to compare efficacy of Lorazepam and chlordiazepoxide in alcohol dependence syndrome.

MATERIALS & METHODS

The present study was conducted on62 patients with alcohol dependence syndromeof both genders.All were informed regarding the study and their written consent was obtained.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 31 each. Group I patients received lorazepam 8 mg/day and group II received chlordiazepoxide 80 mg/day. The dose was tapered and at the end of 8 days. The severity of alcohol dependence was assessed using the Severity of Alcohol Dependence Questionnaire (SADQ). The CIWA-Ar was used for quantification of withdrawal symptoms. Liver function tests were performed at baseline and at the end of the study.Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Assessment of liver function test

Parameters	Group I		P value	Group II		P value
	Baseline	End		Baseline	End	
Total bilirubin (mg/dL)	1.04	1.01	0.97	0.85	0.88	0.94
Direct bilirubin (mg/dL)	0.26	0.27	1	0.25	0.27	0.85
Alkaline phosphatase	66.9	67.4	0.17	77.3	77.5	0.21
Total protein	6.90	6.92	0.25	6.52	6.59	0.63
Serum albumin	4.15	4.12	0.47	4.31	4.26	0.85
Serum globulin	2.87	2.05	0.82	2.18	2.15	0.15
SGOT	41.8	41.1	0.05	55.2	51.3	0.01
SGPT	45.9	45.8	0.81	68.3	67.5	0.85

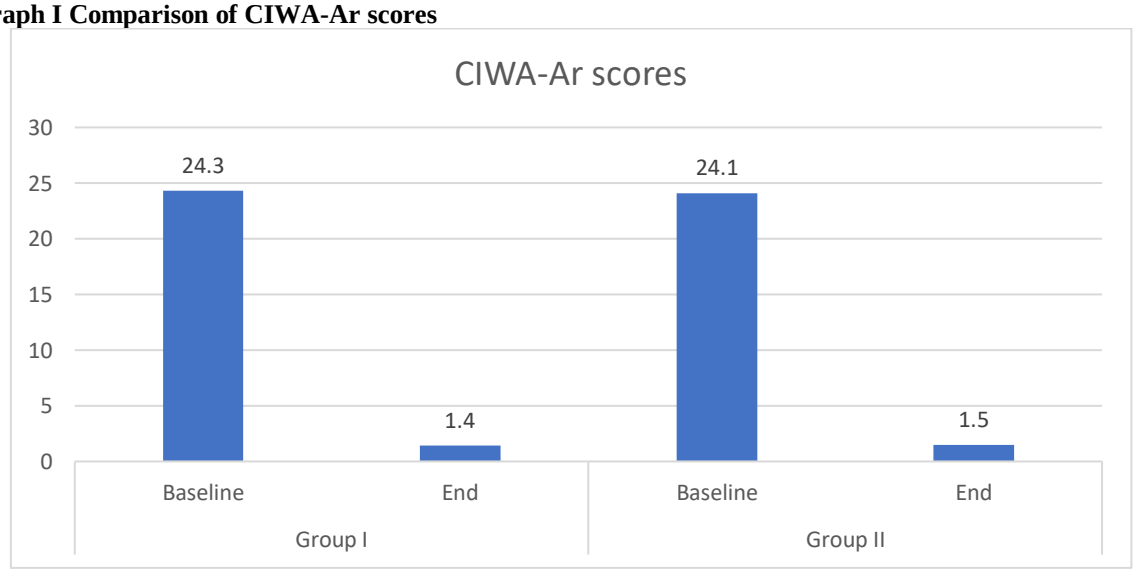
Table II shows that at baseline and end of study, total bilirubin (mg/dL) was 1.04 and 1.01, direct bilirubin (mg/dL) was 0.26 and 0.27, alkaline phosphatase was 66.9 and 67.4, total protein was 6.90 and 6.92, serum albumin was 4.15 and 4.12, serum globulin was 2.87 and 2.05, SGOT was 41.8 and 41.1, SGPT was 45.9 and 45.8 in group I respectively. In group II total bilirubin (mg/dL)was 0.85 and 0.88, direct bilirubin (mg/dL) was 0.25 and 0.27, alkaline phosphatase was 77.3 and 77.5, total protein was 6.52 and 6.59, serum albumin was4.31 and 4.26, serum globulin was2.18 and 2.15, SGOT was55.2 and 51.3 and SGPT was 68.3 and 67.5 respectively. The difference was significant (P< 0.05).

Table II Comparison of CIWA-Ar scores

Parameters	Group I		P value	Group II		P value
	Baseline	End		Baseline	End	
CIWA-Ar scores	24.3	1.4	0.01	24.1	1.5	0.01

Table II, graph I shows that at baseline CIWA-Ar scores in group I was 24.3 and at end was 1.4. In group II, it was 24.1 at baseline and 1.5 at end of study. The difference was significant (P< 0.05).

Graph I Comparison of CIWA-Ar scores



DISCUSSION

Given the severity of the alcohol intake and dependence issue, treating those who exhibit withdrawal symptoms is crucial to aiding in the process of alcohol de-addiction.[8,9] The hepatic enzymes break down both diazepam and chlordiazepoxide into active metabolites that build up in the liver.[10,11] Because of this, these medications may make withdrawal more difficult and raise the possibility of hepatic encephalopathy.[12,13] Conversely, because lorazepam is metabolized via conjugation, a pathway less impacted by liver malfunction than the hepatic microsomal processes, it is less prone to accumulate in the liver.[14,15]The present study was conducted to compare efficacy of Lorazepam and chlordiazepoxide in alcohol dependence syndrome.

We found that baseline and end of study, total bilirubin (mg/dL) was 1.04 and 1.01, direct bilirubin (mg/dL) was 0.26 and 0.27, alkaline phosphatase was 66.9 and 67.4, total proteinwas 6.90 and 6.92, serum albumin was 4.15 and 4.12, serum globulin was 2.87 and 2.05, SGOT was 41.8 and 41.1, SGPT was 45.9 and 45.8 in group I respectively. In group II total bilirubin (mg/dL) was 0.85 and 0.88, direct bilirubin (mg/dL) was 0.25 and 0.27, alkaline phosphatase was 77.3and 77.5, total proteinwas 6.52 and 6.59, serum albumin was 4.31 and 4.26, serum globulin was 2.18 and 2.15, SGOT was 55.2 and 51.3 and SGPT was 68.3 and 67.5 respectively. Ramnujam et al[16]compared and evaluated the safety and efficacy of lorazepam and chlordiazepoxide in patients with alcohol dependence syndrome with symptoms of alcohol withdrawal. Of the 60 patients included in the study, 15 patients each had mild and moderate withdrawal symptoms in the chlordiazepoxide group and 17 and 13 patients respectively in the lorazepam group, based on the SADQ score. At baseline, the mean CIWA-Ar scores were similar in both the treatment groups: 24.77±5.98 in the chlordiazepoxide group and 24.90±6.12 in the lorazepam group. There was a significant intragroup decrease inthe CIWA-Ar scores measured from baseline to the end of 8 days($p<0.0001$) and 12 days ($p<0.0001$) in both treatment groups;however, there was no significant difference between the twogroups. There was no significant difference observed in the liverfunction tests done at baseline and at the end of study period

We observed that at baseline CIWA-Ar scores in group I was 24.3 and at end was 1.4. In group II, it was 24.1 at baseline and 1.5 at end of study. Kumar et al[17] in their study one hundred consecutive consenting male inpatients in a state of moderately severe, uncomplicated alcohol withdrawal at screening were randomized to receive either lorazepam (8 mg/day) or chlordiazepoxide (80 mg/day) with dosing down-titrated to zero in a fixed-dose schedule across 8 treatment days. Double-blind assessments of withdrawal-symptom severity and impairing adverse events were obtained during treatment and for 4 days afterward.One chlordiazepoxide patient developed withdrawal delirium. Lorazepam and chlordiazepoxide showed similar efficacy in reducing symptoms of alcohol withdrawal as assessed using the revised Clinical Institute Withdrawal Assessment for Alcohol scale. During withdrawal, irritability and dizziness were more common with lorazepam, and palpitations were more common with chlordiazepoxide. No difficulties in drug discontinuation or differences in impairing adverse events were observed with either drug.

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that lorazepam and chlordiazepoxide both work equally well to lessen the symptoms of alcohol withdrawal.

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