PROFILE OF LIVER DYSFUNCTION IN ALCOHOL DEPENDENCE

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ABSTRACT

Ninety two patients of alcohol dependence were studied for liver function at a specialised drug dependence treatment centre. Biochemical laboratory evidence of liver dysfunction was found in a very large number of patients, including the patients who had no clinical signs or symptoms. The findings from this retrospective study are discussed in the context of the earlier studies from other settings in India.

Key Words: Liver Dysfunction - Alcohol Dependence - Specialised Settings.

Introduction

Liver is the most commonly affected organ with longterm use of alcohol. As such, assessment of the functional state of the liver is important as a part of the overall health assessment during treatment for alcohol dependence. Biochemical assay of indicators of liver function in the peripheral blood sample is the technique readily available and employed. Histopathological assessment of biopsy samples becomes necessary in some clinical settings and has been carried out in research studies.

Review of literature

Detailed information on alcoholic liver disease across different settings has been available from the western countries for sometime (Edmondson, 1963; Lelbach, 1975; Pimstone & French, 1984). The relationship between alcohol dependence and a high frequency of alcoholic liver damage or dysfunction has been generally agreed upon. It has also been suggested, to the contrary, that subjects who develop alcoholic liver disease are usually different from those who become dependent (Wodak et al, 1983).

Useful, necessary information has been available from the studies on alcoholic liver disease from India in the recent years. These studies have ranged from biopsy reviews in department of pathology (Rajwanshi, 1983) through alcohol dependence sample in a psychiatric hospital (Shankar et al, 1986; Ray et al, 1988) to general hospital sample of alcoholic patients (Sarin et al, 1988). No information is available, as yet, on the extent and nature of liver dysfunction in patients seeking treatment at the centres specifically dealing with treatment of drug dependence (including alcohol dependence). In view of the fast emerging network of these specialised treatment centres, the need for such information is undeniable.

Aims The present study was carried out with the aims of

1) Studying the profile of liver dysfunction in patients of alcohol dependence at a specialised treatment centre, and

2) Studying the correlation of liver dysfunction with alcohol use variables.

Material & Methods

Patient satisfying the DSM-III-R criteria for Alcohol Dependence admitted to the inpatient facility of the Drug Dependence Treatment Centre of AIIMS, located at the Deen Dayal Upadhaya Hospital in Harinagar, Delhi between Jan'89 & Dec'89 formed the universe of the study. Patients between the ages of 18 and 60 years and with adequate information on clinical and laboratory variables were included retrospectively. Patients with any parenteral drug use or longterm medication (eg. Phenothiazines, antidiabetics, anti-tuberculars, antiepileptics, antibiotics) were excluded. Patients with history suggestive of infective hepatitis in the past were also excluded from analysis. Detoxification during the inpatient treatment was carried out with diazepam in the dose range of 20 to 60 mgs per day or Chlordiazepoxide in the dose range of 50-120 mgs per day, along with vitamin supplements. Information on alcohol use pattern comprised of duration of use in years, duration of dependence in years and ethanol index (average daily amount of ethanol consumed for the preceding one month in grams per day). This information has been collected.
during the inpatient assessment with detailed interviews.

Peripheral venous blood samples were collected in an early morning fasting state, within 72 hours of the last dose of alcohol. After extracting the serum sample, biochemical analysis was carried out for levels of serum total bilirubin (STB), serum glutamic oxaloacetic transaminase (SGOT), serum γ-glutamyl transpeptidase (SGGT) on Hitachi 704 autoanalyser with diagnostic kits from Boehringer Mannheim. These tests are carried out as part of routine laboratory services at the centre.

Results.

Sample Description

A total of ninety two male patients had been included in the sample, they had a mean age of 36.9±8.3 (S.D.) years. The mean duration of alcohol use was 13.6±6.7 years and the mean duration of dependence was 6.6±4.75 years. The patient sample has a mean Ethanol Index of 199.3±99.3 gms.

Abnormal Biochemical Indicators:

The mean values of all the four biochemical indicators of liver function in the total sample of ninety two were well above the normal laboratory range. The number of patients with raised values of serum total bilirubin was 39 (42.3%) and 74 (80.5%) patients had elevated SGOT values. SGPT & SGOT were above the normal range in a larger number of patients 87 (94.7%) and 89 (96.7%) respectively. (Table 1). All the patients with elevated bilirubin levels had raised levels of one or more of the three enzymes viz SGOT, SGPT & SGGT. Only one patient (1.07%) had all the four indicators within the normal range.

| Table 1 Biochemical Indicators of Liver Function |
|-----------------------------------------------|
| Test                  | mean±S.D. (n=92) | Normal Range | Number (%) of patients with abnormal test |
|-----------------------|-----------------|---------------|------------------------------------------|
| STB (mg/dl)           | 0.96±1.1        | 0.1-0.8       | 39 (42.3)                               |
| SGOT (IU)             | 91.2±77.5       | up to 20      | 89 (96.7)                               |
| SGPT (IU)             | 73.3±69.1       | up to 15      | 87 (94.5)                               |
| SGGT (IU/L)           | 220.5±402.3     | up to 40      | 74 (80.5)                               |

Severity of Liver Dysfunction:

The categorisation of patients for severity of liver dysfunction was carried out according to the extent of derangement of any one of the enzymes in respect of the Standard Deviation for that enzyme in the total sample of ninety two. Thus, patients who has elevation of any one of the enzymes beyond two standard deviations from the mean, were categorised to have severe dysfunction. Patients with elevation of one of the enzymes between one and two standard deviations from the mean, were considered to have moderate dysfunction. All the other patients who has derangement of enzyme levels within one standard deviation difference were considered to have mild dysfunction. (Table 2)

| Table 2 Severity of Liver Dysfunction |
|--------------------------------------|
| n        | %       |
| None     | 1 (1.07) |
| Mild (within one S.D. difference)    | 77 (83.72) |
| Moderate (between one & two S.D. difference) | 9 (9.78) |
| Severe (more than two S.D. difference) | 5 (5.43) |
| Total    | 92 (100) |

Note: The severe & moderate categories were separated from the mild, based on elevation in any of the three enzymes.

Clinical evidence of liver dysfunction:

Seventy eight patients (84.79%) with laboratory evidence of liver dysfunction had no symptoms or signs suggestive of such a dysfunction.

Correlation with alcohol use variables:

On Pearson's product moment correlation coefficients, no significance was found between any of the alcohol use variables and the four biochemical indicators. (Table 3)

| Table 3 Correlation Coefficients(r) between biochemical indicators and alcohol use variables |
|-----------------------------------------------|
| r      | Duration of use | Duration of Dependence | Ethanol Index |
|-------|-----------------|------------------------|--------------|
| STB   | 0.093           | -0.037                 | 0.072        |
| SGOT  | -0.036          | -0.036                 | 0.039        |
| SGPT  | 0.186           | -0.030                 | 0.060        |
| SGGT  | 0.163           | 0.065                  | -0.050       |

Critical value (2 tail, 0.05) = 0.20486. n = 92.
Discussion

Our sample consisted of patients of alcohol dependence admitted to a specialised drug dependence treatment centre. There was no obvious evidence of malnutrition in these patients and gross haematological and biochemical indicators like haematocrit, total protein and albumin values were largely within the normal range. The patients had no historical or examination findings suggestive of any other liver disease. Thus, it is reasonable to view the findings from this sample to be reflecting the profile of liver function in alcohol dependence.

Adequate evidence exists regarding elevated biochemical indicators of liver function in alcoholics as compared to controls (Edmondson, 1975; Leebach, 1975; Ray et al., 1988; Sarin et al., 1988). As such, we did not consider the need for comparison with normal controls necessary. Such a comparison was also not considered relevant to the aims of the present study. The present study is essentially based on a single group design. Its findings can be seen in the context of two other studies from India. One of these studies reported on patients of alcoholism from the general psychiatry wards of an academic psychiatric hospital, (NIMHANS,) at Bangalore (Ray et al., 1988) and the other study reported findings on patients admitted to the deaddiction unit of the department of Psychiatry or referred by them for admission to the department of Gastroenterology at the G.B. Pant Hospital, Delhi. (Sarin et al., 1988). In the NIMHANS sample SGOT was elevated in 60% SGPT in 35% and SGGT in 47% of 83 patients (Ray et al., 1988). In the G.B. Pant Hospital, sample of 56 patients, four (7.1%) had raised levels of serum bilirubin; 32(57.1%) has raised SGPT levels, 34 (60.7%) had raised SGPT levels and 39 (69.6%) had elevated levels of SGGT (Sarin et al., 1988). In our present sample, serum bilirubin was raised in less than half (42.3%) the patients, but the elevated enzyme levels were found in a very large number of patients. Seventy four patients (80.5%) has raised values of SGGT, 87 patients (94.5%) elevated SGPT and 89 (96.7%) had elevated SGOT values. The higher proportion of patients in our sample with biochemical evidence of liver dysfunction as compared to the other two study samples from India is worthy of note. There can be no reason to believe that the laboratory sensitivity differs across three academic centres to such an extent. In all the three studies the assessments have been carried out in the early part of treatment, within a few days of the abstinence. It becomes necessary to consider that the different settings of the studies may have contributed to the differences in the rates. Specialised treatment centres for drug dependence may draw more patients seeking treatment primarily for alcohol dependence. A large proportion of the patients in the present sample has evidence of mild liver dysfunction. The distribution of the biochemical values in the total sample is seen to have a wide variation for serum bilirubin and SGOT, as evidenced by standard deviation values being larger than the mean values. Such is not the case with distribution of SGOT & SGPT values. The other two studies do not provide information on the severity of the biochemical evidence of dysfunction, but in both the studies the standard deviation values do exceed the mean values often. A wide variability of the values across patients of alcohol dependence is seen to be a common finding. The two earlier studies did assess the histopathology to diagnose alcoholic liver disease and stratify the extent of the disease. In the study by Sarin et al., liver biopsy was obtained in 87.5% of the patients. On biochemical tests, one or the other test of liver function was found to be abnormal in 44(78.6%) patients. The figure increased to 45(81.4%) patients if one looked for the total number of patients in whom either liver function tests or liver histology was abnormal (Sarin et al., 1988). This information supports our view that assessment of histopathology is not crucial to a clinical research study of the extent and profile of liver dysfunction in alcohol dependence. It certainly can add to the information and classification of alcoholic liver disease. In the present study, liver biopsy information is not available. We believe that such biopsies will not be feasible at most of the drug dependence treatment centres and as a first step, the requirement is to generate data from some such centres to be useful to the clinicians at all such centres.

In our sample, 98.3% of the patients has abnormality on one of the biochemical indicators of liver function, with mild elevation of the values being more common. We do not have detailed information on the severity of dependence but not significant
correlation of the liver dysfunction was found with the Ethanol Index, duration of use or duration of dependence.

Seventy eight patients (84.8%) had no clinical symptoms or signs of liver dysfunction. The assessment had been carried out as a part of the routine inpatient care which includes a detailed inquiry and examination of health status by the team. It needs to be admitted that a checklist of specific symptoms and signs would have added to the rigour of the assessment. It is apparent, although, that a majority of the patients had laboratory evidence of liver dysfunction, in the absence of any clinical evidence. The presence of such a large group of patients with "Subclinical dysfunction deserves attention. In one of the earlier studies, there is evidence of such a dysfunction in the absence of clinical symptoms or signs in 34 of 56 patients. (Sarin et al, 1988).

The information from this paper is likely to be useful for clinicians and other staff members at the drug dependence treatment centres in India. The observation that most of the alcohol dependence patients at such centres are likely to have liver dysfunction commonly of mild nature is a finding to take note of. It is also important to remember that a majority of these patients had subclinical dysfunction. As such, routine biochemical assessment of liver function in all patients of alcohol dependence, including those who have no clinical signs or symptoms would seem mandatory. The degree of liver dysfunction may not necessarily be related to the amount or duration of alcohol use.

Conclusions
1) 98.3% of the sample of alcohol dependent patients had biochemical evidence of liver dysfunction. 2) Majority of these patients had mild dysfunction and in the absence of clinical evidence of dysfunction.

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