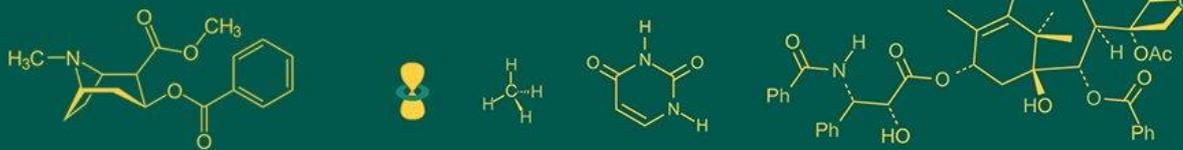


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Biomarkers to assess chronic alcohol consumption: carbohydrate deficient transferrin (CDT) a reliable biomarker

B Vikram, Shruti Mohanty and Archana A Dharwadkar

Abstract

Alcohol abuse is very common all over the world. The biological, clinical and social effects of alcohol abuse have long made evident the need for objective and specific markers for alcohol-related diseases and for early detection of alcohol consumers at risk. Alcohol abusers may exhibit several biochemical alterations, some of which have been used as markers of alcoholism i.e. Alanine Aminotransferase (ALT), Gamma Glutamyl Transferase (GGT) and Carbohydrate Deficient Transferrin (CDT). The present study was taken up to estimate serum biochemical parameters i.e. ALT, GGT and CDT in chronic alcoholics. The study subjects were divided into 2 group's i.e. Group-I was cases and Group-II was controls. Group-I includes (n=30) male chronic alcoholics with a history of alcohol abuse (since 1 year to 11+ years) and aged 25-65 years. Group-II includes (n=30) age-matched, non alcoholics were taken as controls in the study. Biomarkers i.e. ALT, GGT and CDT were assayed in the serum of all study subjects. The present study shown increased serum levels of ALT, GGT and CDT in Group-I as compared to Group-II. There is a significant increase of enzyme activities seen in CDT, when compared to serum GGT, ALT levels of case group. CDT sensitive bio markers which can be used to diagnose alcohol abuse and is superior to GGT, ALT in terms of sensitivity as well as specificity.

Keywords: Biomarkers, alanine transaminase, gamma Glutamyl Transferase, carbohydrate deficient transferrin, chronic alcohol consumption

Introduction

The magnitude of the problem of alcohol abuse has to be seen in light of three basic features of ethanol: It is easy to produce, it is a solvent and it has sedative and euphorizing effects on the central nervous system, similar to those of anesthetics. These characteristics have made ethanol the most widely used centrally acting drug known. Some other basic facts about ethanol are also important: It has immediate and direct biochemical and biophysical effects on cell membranes^[1, 2]. It has basic metabolic consequences through its oxidation^[3, 4].

Susceptibility to Alcoholic Liver Disease: Early epidemiological studies of alcoholic liver disease showed a dose response relationship between cumulative alcohol consumption and the risk of cirrhosis^[5]. In contrast, recent prospective studies have suggested that only about 20% of heavy drinkers will ultimately develop alcoholic cirrhosis, provided their average daily intake regularly exceeds a threshold dose of about 50-60 g. This is consistent with the common clinical experience that some individuals develop alcoholic cirrhosis while still in their early 20s while others escape damage after a lifetime of heavy drinking^[6].

Biochemical markers have been used for detecting and monitoring alcohol abuse such as serum Alanine Transaminase (ALT), γ -Glutamyl Transferase (GGT). Elevated serum Gamma-Glutamyl Transferase (GGT) level remains the most widely used marker of alcohol abuse. Levels typically rise after heavy alcohol intake that has continued for several weeks in response to the acute hepatocellular damage^[7].

A new diagnostic marker has been introduced that appears to fulfill important clinical criteria. It is apparently dependent on ethanol or its metabolism, it appears in serum after regular high alcohol intake and it shows a high sensitivity and specificity. This marker is Carbohydrate Deficient Transferrin (CDT). Asialotransferrin, monosialotransferrin and disialotransferrin are collectively referred to as Carbohydrate Deficient Transferrin (CDT)^[8].

Materials and methods

This study was carried out in the Department of Biochemistry (2013-14) at Kamineni

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Institute of Medical Sciences and Hospital, Narketpally, Nalgonda District, Telangana State, India. The study protocol was approved by the institutional ethics committee. A written informed consent was obtained from all study subjects.

Inclusion Criteria

1. The study subjects were divided into 2 groups i.e. Group-I (Cases) and Group-II (Controls)
2. Group-I (Cases) with history of chronic alcohol consumption (1 year to 11 years+) and n=30. Age between 25-65 years.
3. Group-II (Controls) were age and sex-matched and healthy volunteers and n=30.

Exclusion Criteria

1. Occasional drinkers
2. Patients with systemic illness
3. Smokers and tobacco chewers

For ALT, GGT estimations 5ml of random venous blood sample was collected from the all the subjects in a sterile disposable syringe which was transferred into centrifuge

tubes and could clot for 30 minutes after that sample centrifuged at 3000 rpm for 10 minutes and the supernatant serum was collected and assayed immediately. For CDT estimation 5 ml of random venous blood sample was collected and allowed samples to clot for 30 minutes. And then samples were centrifuged at 3000 rpm for 10 minutes and serum was collected and assayed immediately.

The levels of ALT, GGT in serum were estimated by using the end-point method by Mindray BS-380 Auto analyzer. The levels of CDT in serum estimated by ELISA kit method.

Results

The results of this study shown that the activities of the enzymes ALT, GGT and CDT in serum samples of subjects with chronic alcoholism were higher when compared to the control. (Table no-I & Figure-I).

The statistical analysis was performed using SPSS software version 11.0. The descriptive results were expressed as Mean and Standard Deviation. The significance of the differences in the values of the parameters among chronic alcoholics (Group-I) and controls (Group-II) was evaluated by ANOVA (Analysis of Variance).

Table 1: Comparison of Serum ALT, GGT and CDT levels in Group-I (Cases) with Group-II (Controls)

Parameters	Group-I (Cases)	Group-II (Controls)	p-Value
ALT	117.03±42.19	25.43±6.36	<0.001**
GGT	405.10±135.39	36.47±8.97	<0.001**
CDT	492.05±56.20	41.15±18.88	<0.001**

(p< 0.001)** Highly significant statistically.

Table-I & Figure-I: Shows that there is a statistically significant difference in between both the groups in ALT (IU/L) levels (p<0.001) with 117.03 ± 42.19 in Group-I and 25.43 ± 6.36 for Group-II. In GGT levels (IU/L) (p<0.001)

with 405.10 ± 135.39 for Group-I and 36.47 ± 8.97 for Group-II. In CDT (mg/L) (p<0.001) with 492.05 ± 56.20 for Study Group and 41.15 ± 18.88 for Control Group.

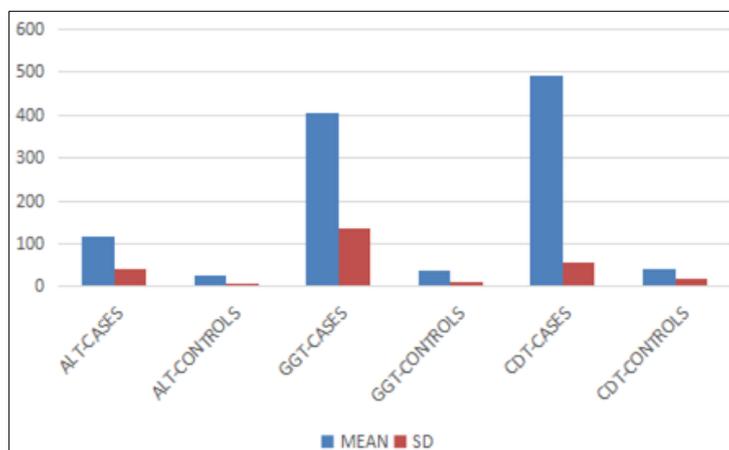


Fig 1: Comparison of ALT, GGT and CDT Enzyme Activities in Group-I (Cases) with Group-II (Controls)

Discussion

The present study selected 30 study subjects (Study Group) who were diagnosed to have harmful alcohol consumption and 30 healthy subjects (Control Group) in the comparable age group. The study population comprised fully of males which may be attributed to the cultural background of the local population.

It is evident that there is a statistically significant difference between the cases and controls for the parameters namely ALT, GGT and CDT. Furthermore, it is observed that CDT and GGT showed a highly significant difference among the

groups when compared to ALT. It shown that all parameters are increased in cases compared to controls and among cases CDT is more.

GGT is a well established marker of liver disease and has been extensively studied in alcoholism. In the present study GGT was found to be significantly increased in the cases when compared to controls. The mean values (IU/L) were 405.10 for cases and 36.47 for control group. Similar highly significant results have been reported earlier [9, 10].

Finally, in the present study serum CDT was elevated in of the cases and GGT was above the reference range in of the

cases. ALT levels in serum of cases increased but the increase was low when compared to the Mean and SD of CDT and GGT.

However, when the two markers are used in combination of those in the case group were found to have fallen in that group. This suggests that when used together GGT and CDT make a better diagnostic tool than used alone. CDT and GGT should, therefore, be considered as complementary rather than alternative markers^[11].

Conclusion

Bio markers revealing chronic alcohol consumption including AST, ALT, GGT and MCV are still used as the standard markers to in defining alcoholism treatment course. CDT, on the other-hand considered to be a relatively new marker that added an extra value to better interpretation of heavy alcohol consumption with higher sensitivity and specificity. CDT result would be of higher value in defining heavy alcohol consumption.

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