Research Article

Understanding of alcoholism induced hepatocellular damage with specific emphasis of selected markers

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Abstract

Introduction: Liver performs many important functions such as uptake, storage, and disposal of nutrients (protein, glucose and fat), drugs and toxins. The liver is responsible for the elimination of 95% of ingested alcohol through metabolism. Chronic alcohol ingestion causes damage to hepatocytes. Various markers have been stated to be useful to diagnose hepatic damage by alcohol. **Aims and Objectives:** to study the alcoholism induced hepatocellular damage with specific emphasis of selected markers. **Materials and Method:** four groups of 10 individuals each were formed. One group was control where as in remaining three alcohol dependent individuals with varying years of chronicity of alcohol consumption were enrolled. Serum GGT, AST, ALT, total protein, albumin, globulin and bilirubin were tested on fasting blood samples of all the study subjects. And were compared. **Results:** increase in serum GGT was observed in alcoholic and it was increasing proportionally with chronicity of alcohol consumption. Similar trend were also observed i9n serum AST and ALT levels and also with AST:ALT ratio. No major change in protein levels was observed. biliribin levels were increased but they were not increasing with the chronicity of alcohol consumption. **Conclusion:** combination of serum GGT, AST, ALT and ratio of AST and ALT can be used for diagnosis of alcohol induced hepatocellular damage instead of any single marker.

Keywords: hepatocellular, emphasis.

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INTRODUCTION

The liver is the largest gland in the body (approximately 1500 grams). It performs many important functions such as uptake, storage, and disposal of nutrients (protein, glucose and fat), drugs and toxins. It also syntheses proteins which are critical for blood clotting and metabolism of substances produced by the body (Vitamins A, B, D, B-12, K).[1] Alcohol is absorbed from all parts of the gastrointestinal tract largely by simple diffusion into the blood. The liver is responsible for the elimination of 95% of ingested alcohol through metabolism.[2] it is known that, a person will eliminate one average drink or 0.5 oz (15 ml) of alcohol per hour.[2] the rate of elimination tends to be higher when the blood alcohol concentration in the body is very high or very low. Also chronic alcoholics may (depending on liver health) metabolize alcohol at a significantly higher rate than average. Finally, the body's ability to metabolize alcohol quickly tends to diminish with age. Ingesting alcohol at a rate higher than the rate of elimination results in a cumulative effect and an increasing blood alcohol concentration. Liver metabolism of alcohol is an active process that commands both metabolic machinery and resources. Alcohol itself induces increased activity in the

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enzyme systems that lead to its metabolism. Alcohol or ethanol is converted by alcohol dehydro-genase, to acetaldehyde, then by acetaldehyde dehydrogenase to acetic acid. Hepatocyte necrosis in acute hepatitis, toxic injury or ischemic injury results in the leakage of enzymes into the circulation.[3] However, in chronic liver diseases such as hepatitis C and cirrhosis, the serum ALT and AST level correlates only moderately well with liver inflammation.[4] Thus, AST and ALT lack some sensitivity in detecting chronic liver injury. Of course, AST and ALT levels tend to be higher in cirrhotic patients with continuing inflammation or necrosis than in those without continuing liver injury. As markers of hepatocellular injury, AST and ALT also lack some specificity because they are also found in skeletal muscle. Levels of these aminotransferases can rise to several times normal after severe muscular exertion or other muscle injury, as in polymyositis or in the presence of hypothyroidism, which can cause mild muscle injury and the release of aminotransferases. Thus the present study was undertaken to study the various markers to identify alcohol induced hepatocellular damage.

AIMS AND OBJECTIVES

To study the alcoholism induced hepatocellular damage with specific emphasis of selected markers.

MATERIALS AND METHOD

Present cross sectional study was conducted to study the changes in various markers in alcohol induced hepatic damage. Four groups were formed containing 10 individual in each group. One group was control which consisted of 10 normal subjects who never had any history of alcohol consumption. Remaining 30 individual were divided in three groups with varying years of chronicity of alcohol consumption.

- Control (n=10): who never had any history of alcohol consumption.
- Group I: had history of alcohol consumption for 5 to 10 years.
- Group II: had history of alcohol consumption for 10 to 15 years.
- Group III: had history of alcohol consumption for 15 to 25 years.

Written informed consent was taken before starting the study. Fasting blood samples were collected from all subjects. Blood samples thus obtained were divided into 2 parts. One was heparinised and the other retained for whole blood estimations. The serum obtained was stored at 4°C till the assays were conducted. The maximum storage period lasted 48 hours.

Following tests were conducted on the collected samples:

a) Serum:

- Gamma glutamyl transferase (GGT),
- Total Protein and Albumin
- Bilirubin, direct and total
- Aminotransferases (AST, ALT)

b) Whole Blood:

- Haemoglobin (Hb)
- Erythrocyte arginase

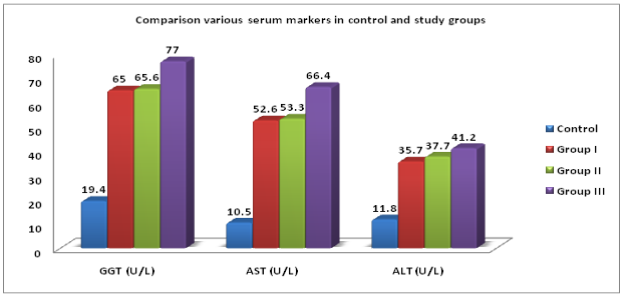
The reagents used in the above estimations were of analytical grade and few biochemical estimations were performed through auto analyzer at University Medical Centre, Mangalore.

RESULTS

Table 1: Comparison various serum markers in control and study groups

Parameter	Group	Mean	SD
GGT (U/L)	Control	19.40	3.80
	Group I	65	7.10
	Group II	65.6	5.96
	Group III	77	6.06
Total Protein (g/dL)	Control	8.07	0.48
	Group I	7.7	0.36
	Group II	7.43	0.82
	Group III	6.32	0.49
Albumin (g/dL)	Control	4.48	0.17
	Group I	4.35	0.19
	Group II	4.00	0.33
	Group III	3.49	0.28
Globulin	Control	3.57	0.53
	Group I	3.42	0.38
	Group II	3.43	0.73
	Group III	2.83	0.57
Total Bilirubin (mg/dL)	Control	0.53	0.15
	Group I	0.73	0.1
	Group II	0.73	0.1
	Group III	0.72	0.09
Bilirubin Direct (mg/dL)	Control	0.14	0.09
	Group I	0.26	0.14
	Group II	0.24	0.14
	Group III	0.26	0.14
AST (U/L)	Control	10.5	2.06

	Group I	52.6	10.4
	Group II	53.3	18.6
	Group III	66.4	31.3
ALT (U/L)	Control	11.8	4.4
	Group I	35.7	7.61
	Group II	37.7	6.61
	Group III	41.2	6.40
AST:ALT	Control	0.98	0.5
	Group I	1.52	0.46
	Group II	1.60	0.50
	Group III	1.65	0.61



The mean Gamma glutamyltransferase (GGT) levels in control group were 19.40U/L. whereas its levels were found to be highly increased in alcoholic. The rise in levels was observed as chronicity of alcoholism increases. The mean total protein in control group was 8.07g/dl. And it was observed that levels were decreasing as duration of alcohol consumption increases. When serum levels of albumin and globulin were measured in control and group and Group I, II and III, it was observed that there levels were decreasing as the duration alcohol consumption was increasing. But the decrease in level was very less. The mean total Bilirubin levels in chronic alcoholics (Gr I=0.73mg/dl, Gr II=0.73mg/dl, Gr III=0.72mg/dl) were increased as compare to control i.e. non alcoholic group (0.53mg/dl). But no difference observed as chronicity of alcoholism increases. Direct bilirubin was also increased in alcoholics. The serum aminotransferases (ALT and AST) levels were compared in alcoholics. It was observed that AST (asparate aminotransferase) in control group was 10.5U/L whereas very high levels were observed in chronic alcoholics. ALT (Alanine amino-transferase) in control group was 11.8U/L whereas very high levels were observed in chronic alcoholics. It was seen that levels of AST and ALT were increasing slightly as the duration of alcohol consumption increases. New parameter in the form of AST: ALT ratio was incorporated in our study. A significant conclusion we could arrive was the fact that an increase in the AST: ALT ratio was observed with increasing degree of alcoholic chronicity in the study groups.

Table 2: Comparison various whole blood markers in control and study groups

Parameter	Group	Mean	SD
Haemoglobin (g/dL)	Control	12.05	1.04
	Group I	11.75	1.04
	Group II	11.44	1.04
	Group III	10.72	1.12
Erythrocyte arginase (µmol urea/min/ml)	Control	0.83	0.20
	Group I	0.75	0.22
	Group II	0.76	0.21
	Group III	0.91	0.18

There was no much difference in Hemoglobin levels of control group and alcoholics. The results of our study indicate no increase in the erythrocyte arginase activity estimated within the 3 study groups.

DISCUSSION

The present cross sectional study was undertaken to study the alcoholism induced hepatocellular damage with specific emphasis of selected markers. The enzyme Gamma-glutamyltransferase (GGT) a chosen marker for alcoholism has established specificity for a long time now. Results of our study indicate a linear increase in the activity of the enzyme with progressive exposure to alcohol spanning over a range of 20 years of alcohol consumption. Gamma-glutamyltransferase (GGT) is a glycoenzyme found in endothelial cell membranes of various organs. It appears to mediate peptide transport and glutathione metabolism. Elevated serum GGT level remains the most widely used marker of alcohol abuse. According to Allen *et al*[5] levels typically rise after heavy alcohol intake that has continued for several weeks. With 2–6 weeks of abstinence, levels generally decrease to within the normal reference range, with the half-life of GGT being 14–26 days. Laboratory tests for evaluating GGT are inexpensive and readily available. GGT may elevate because of increased synthesis or accelerated release from damaged or dead liver cells. It seems to primarily indicate continuous, rather than episodic, heavy drinking, although a few moderate drinkers also produce elevated levels of GGT[6]. Excessive drinking is not the only cause of elevated GGT levels; they may also rise as a result of most hepatobiliary disorders, obesity, diabetes,

hypertension, and hypertriglyceridemia[7]. Thus GGT alone cannot be choosen as specific marker for alcohol induced hepatocellular damage. Serum contains a complex mixture of proteins. The liver is the major source of albumin, fibrinogen and other coagulation factors and most of the α- and β-globulins. The amounts of total protein, albumin and globulin have remained within the normal range, probably a result of lack of microquantitative techniques capable of detecting minute fluctuations. Albumin, quantitatively the most important plasma protein, is synthesized exclusively by the liver. Hypoalbuminemia is not specific for liver disease and may occur in protein malnutrition of any cause.[8] In the present study it was observed that bilirubin (total and direct) was increased in alcoholics as compared to control group. The serum conjugated bilirubin level does not become elevated until the liver has lost at least one half of its excretory capacity. Thus, a patient could have obstruction of either the left or right hepatic duct without a rise in the bilirubin level. Thus total serum bilirubin is not a sensitive indicator of hepatic dysfunction and may not accurately reflect the degree of liver damage.[9,10,11] The serum aminotransferases which was formerly called transaminases are sensitive indicators of liver cell injury.[12] Alanine amino-transferase (ALT) and asparate aminotransferase (AST) activities are estimated in liver disease. Both aminotransferases normally are present in serum in low concentrations. AST is found in the liver, cardiac muscle, the lungs, leukocytes and erythrocytes, in decreasing order of concentration; whereas ALT is present in highest concentration in the liver.[13] Serum AST (asparate aminotransferase) in control group was 10.5U/L whereas very high levels were observed in chronic alcoholics. ALT (Alanine amino-transferase) in control group was 11.8U/L whereas very high levels were observed in chronic alcoholics. According Salaspuro *et al*[14] to enhanced AST levels in alcoholics reflect liver damage, but alcohol consumption per se does not cause elevation. It was seen that levels of AST and ALT were increasing slightly as the duration of alcohol consumption increases. In contrary to our finding Skude and Wadstein[15] state that serum ASAT does not correlate with the length of drinking, but the highest ASAT values have been reported in alcoholics with a history of alcoholism exceeding 10 years. Although in isolation ALT and AST was not particularly useful as a marker of chronic alcohol abuse or of chronic liver disease, the ratio ASAT/ALAT seems to provide meaningful information. An increase in the AST: ALT ratio was observed with increasing degree of alcoholic chronicity in the study groups. Similar finding were also reported by Skude and Wadstein[15], Konttinen[16]. Reichling and Kaplan[17] in their study. No significant correlation could be established with haemoglobin percentage by us. No other haematologic parameters were included in the study, though evidence of a decreased Mean Corpuscular Volume (MCV) has been clearly established. The results of our study indicate no increase in the erythrocyte arginase activity estimated within the 3 study groups. Our results correlate well with the findings of workers in the past that Plasma Arginase is not increased in alcoholics.Thus from the above discussion we can state that no single marker can be used efficiently to diagnose and determine the extent of alcoholism induced hepatocellular damage. Similar conclusion was also drawn by John Allen*et al*[18] and he suggested that since none of the biomarkers currently available offers perfect validity as a reflection of heavy drinking, considerable research has been undertaken to evaluate using them in combination. Thus the combination of serum GGT, AST, ALT and ratio of AST and ALT can be used efficiently to diagnose alcohol induced hepatocellular damage.

CONCLUSION

Thus in the end we conclude that combination of serum GGT, AST, ALT and ratio of AST and ALT can be used for diagnosis of alcohol induced hepatocellular damage instead of any single marker.

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