A Study of Oxidative Stress in Alcoholic Liver Disease

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Abstract

The present study was conducted to evaluate the oxidative stress and its subsequent damaging effect in 20 male patients of alcoholic liver disease (ALD). The results were compared with 20 healthy volunteers. Blood samples were collected for estimating malondialdehyde (MDA), transaminases (AST, ALT) and gammaglutamyl transferase (GGT). Serum aspartate amino transferase (AST) & alanine amino transferase (ALT) and their ratio was significantly ($p<0.01$) increased in ALD patients as compared to the controls. Plasma GGT levels were significantly ($p< 0.01$) increased in alcoholics and the enzyme showed a significant positive correlation with MDA which also showed a rise. These results give enough evidence of increased oxidative stress and compromised antioxidant defense system in patients with ALD.

Key Words : Alcoholic liver disease, Lipid peroxidation, Oxidative stress

Introduction :

Alcohol dependence is a severe socio-economic problem and its excess consumption leads to alcoholic liver diseases (ALD). The incidence of ALD is increasing day by day specially in the developing countries including India. ALD has genetic, psycho-social and environmental factors influencing its development and manifestations. [1] It is a progressive condition and is a major cause of morbidity and mortality. [2] Oxidative stress has been implicated in the patho-physiology of a many disease or disorders which are initiated and /or exacerbated by pro-oxidants such as various drugs including alcohol and food additives. [3] Besides, ingested alcohol produces striking metabolic imbalances in the liver [4, 5] it leads to the formation of reactive oxygen species (ROS). [6] Inadequate removal of ROS may cause cell damage by attacking membrane lipids, proteins and inactivating enzymes thus mediating several forms of tissue damage. [7] At present, except for the abstinence of alcohol abuse, there is no effective modality of either prevention or treatment. The present study was planned with the objectives to investigate the oxidative stress in patients of alcoholic liver disease.

Methodology

The study group comprised of 20 male patients of alcoholic liver disease undergoing treatment at SAIMS hospital, Indore. The patients had history of daily alcohol intake for more than five years. Twenty healthy age and socio-economic status matched male volunteers served as controls. Patients suffering from disease of any origin other than alcohol intake were excluded from the study. Heparinised whole blood samples were collected for estimating biochemical parameters. Serum Aspartate transaminase (AST) and Alanine transaminase (ALT) were estimated by Reitman and Frankels method, [8] Plasma malondialdehyde (MDA) by TBARS i.e., Thio Barbituric acid reactive species assay [9] and enzyme gamma- glutamyltransferase according to the method of Szasz. [10]

The data was analyzed using students't' test and the values were expressed as mean $\pm$ S.D. p value less than 0.05 was considered as the significant value.

Results

20 healthy volunteers were compared with the study group comprising of 20 alcoholics. The age distribution was found to be non-significant ($p>0.05$) between both groups, the mean values being 45.15+4.74 (controls), and 48.00+6.27 (alcoholics). The serum AST/ALT ration was significantly ($p<0.001$) increased in alcoholic group compared to group control group (Table 1). Plasma malondialdehyde (MDA) levels were significantly ($p<0.001$) increased in alcoholic group when compared with control group (Table 1). Plasma-gamma-glutamyl transferase (GGT) were found to be increased in alcoholics significantly ($p<0.001$) compared to control group.

Table 1 : Alterations in biochemical parameters in healthy volunteers and alcoholics.

	Healthy volunteers	Alcoholics
Serum AST (IU/L)	18.75±7.14	116.65 ± 44.8*
Serum ALT (IU/L)	22.75 ± 7.50	48.55±18.80*
AST/ALT	0.72 ± 0.09	2.33 ± 0.95*
MDA (mmol/L)	3.48 ± 0.63	7.97 ±1.40*
GGT (IU/L)	11.2 ±4.40	81.8 ± 12.4*

Values expressed in Mean ± S.D
* P value < 0.001 between alcoholics group and healthy volunteers.

Discussion

Free radical mediated damage to macromolecule plays inflammation, carcinogenesis, ageing, drug reaction and toxicity. [11] Ethanol undergoes oxidative metabolism in the cytosol, peroxisome and /or microsomes. Liver injury due to acute or chronic abuse has been proved to be dependent on metabolic products of Ethanol viz. acetaldehyde and ROS account for the various functional derangements

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accompanying alcohol abuse. [4, 11] Induction of cytochrome P450 2E1' (CYP450 2E1) by ethanol increases the generation of ROS which initiates the oxidative stress [12] and which is also potentiated by redox shift associated with ethanol oxidation by alocohol dehydrogenase. [13] Acetaldehyde, a major metabolic product of ethanol by either alcohol dehydrogenase (ADH) or CYP450 2E1 catalyzed oxidation, promotes oxidative stress not only via consumption and inactivation of antioxidants but also by increased generation of free radicals. [14] These facts suggest that oxidative stress may be one of the contributing factor in the pathogenesis of ALD.

Raised levels of serum transaminases observed in the present study may be due to increased permeability of cell membrane following the oxidative damage. Moreover, the ratio of AST/ALT used in discriminating alcoholic liver disease from other liver disorders, [15] was found to be reversed in ALD. The reversal of ratio may be because of release of mitochondrial AST by alcohol itself or through its toxicity by its metabolites and/or oxidative stress.

The present study was conducted to correlate role of oxidative stress as a contributing factor in the pathogenesis of ALD. The significant increase in MDA levels in alcoholics compared to volunteers suggests that alcoholics are subjected to more oxidative stress. [16] The measurement of serum GGT levels is known as a sensitive marker of hepatobiliary disorders [17] and it has been reported to be induced by drugs including alcohol. [18] As GGT is a membrane bound enzyme, oxidative stress induced damage to the membranes of hepatocytes seems to contribute to the increased activity of GGT as observed in the present study. This is substantiated by the observation of positive significant correlation of MDA with the enzyme in alcoholics.

The present study clearly demonstrates that due to alcohol induced oxidative stress the anti-oxidant defense system is compromised. It is reasonable to suggest that apart from the standard medical care for these patients, antioxidant supplement should form a part the physician's prescription. This will help in lowering the oxidative stress and the resulting peroxidation. However, it would be useful to evaluate other aspects of the anti-oxidant defence mechanism such as the antioxidant vitamins in follow up studies. It is expected that in future a more rational treatment plan for the poor victims of alcohol can be devised.

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