

Effect of Liv.52 on Different Bio-Chemical Parameters in Alcoholic Cirrhosis

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ABSTRACT

Liv.52, has significantly improved the biochemical parameter in patients of alcoholic cirrhosis. There was a significant improvement in total protein, serum albumin, blood volume and liver function tests, after 6 weeks of treatment with Liv.52. Acetaldehyde is known to suppress albumin synthesis by the liver cells. Liv.52 improves serum albumin level by causing rapid elimination of acetaldehyde formed during ethanol metabolism and preventing cellular binding of acetaldehyde. This has caused expansions of blood volume and contraction of extracellular fluid space leading to relief from oedema and ascities.

INTRODUCTION

Alcohol abuse can adversely affect almost all organs of the body. However, the liver is particularly susceptible to injury because it is the site responsible for the most part of ethanol oxidation¹. While ethanol and even more importantly its metabolites appear to be primarily responsible for the toxic effects of alcohol, other alcohols, aldehydes and organic molecules in alcoholic beverages may also contribute to tissue toxicity². Cirrhosis has been ranked as one of the leading causes of death in alcoholics³ and an effective specific intervention is necessary to combat this major health problem.

The majority of individuals who misuse or abuse alcohol will develop some toxic changes in their liver at some stage of their drinking career⁴. The alcoholic liver injury appears to progress from fatty change through alcoholic hepatitis to cirrhosis⁵. Approximately 75% of patients with alcoholic cirrhosis die as a result of their liver disease; hepatocellular carcinoma develops in approximately 20% of individuals with alcoholic cirrhosis and development of this tumour may account for upto 1/3 of liver deaths^{6,7}.

In the liver ethanol is oxidised to acetaldehyde, a metabolite potentially more toxic than ethanol itself⁸. The toxicity of acetaldehyde derives from its greater reactivity and lipid solubility and its toxic effects on hepatic organelles such as mitochondria⁹ and microtubules¹⁰. Acetaldehyde binds covalently to hepatic proteins, which in turn have been known to be a critical event in causing liver injury after chronic ethanol consumption^{11,12}.

Acetaldehyde formed during the metabolism of ethanol is being increasingly incriminated as an offending agent. It has several toxic effects on hepatic cells, helps accumulation of lipids and decreases the capacity of the liver to synthesise albumin. It also inhibits its own metabolism thus establishing a vicious cycle in chronic alcoholics and precipitating liver cirrhosis in susceptible individuals.

The treatment of patients with alcoholic cirrhosis poses a great difficulty for the attending physician. Oral or intravenous amino acids, colchicine, testosterone and anabolic steroids have been used with conflicting results¹³.

Liv.52, an Ayurvedic liver preparation, has been found to be very useful in patients of alcoholic hepatitis. It causes rapid elimination of acetaldehyde from blood in chronic alcohol users¹⁴ thereby preventing the binding of acetaldehyde to liver cells, which may be responsible for the protective effect of Liv.52 in alcohol liver disease. A significant decrease in hepatic fibrosis and a favourable change in the architecture

of the liver were reported following Liv.52 treatment in children with cirrhosis of liver¹⁵. A numerical increase in the total mass of functioning hepatocytes was noticed in cirrhosis patients following Liv.52 treatment¹⁶.

Keeping in mind the above information on Liv.52, an open clinical trial was conducted to evaluate the efficacy of Liv.52 in some patients with alcoholic liver cirrhosis.

MATERIAL AND METHODS

Twenty adult male patients aged between 45-55 years with history of chronic alcoholism were selected for this study. The duration of this study was of 6 weeks. The mean duration of alcohol intake was 5 years. The patients were evaluated clinically and with laboratory indices of routine liver function tests for assessing the severity of liver disease. Diagnosis of cirrhosis was based on clinical and biochemical parameters, namely the presence of an enlarged, firm liver and liver function tests showing serum albumin less than 3 gm%, reversal of albumin – globulin ratio and serum bilirubin more than 1.5 mg%. The ultrasonography showed enlargement of liver with fibrosis. The blood volume and serum albumin estimation done as follows:

10c of I 131 tagged with human serum albumin was injected intravenously from a calibrated syringe. Blood samples were drawn about 15-20 minutes after the administration of human serum albumin. The heparinised blood samples were then transferred to a media bottle. Haematocrit percentage was determined by the Wintrobe method (Wintrobe, 1961). Blood samples were then centrifuged at a speed of 3000 rpm and the plasma separated by a micropipette. 2cc of the plasma was transferred to a specially designed glass container with a minimum capacity of 3cc. 10c of I 131 Human Serum Albumin was diluted in 500 cc of distilled water for preparation of a standard sample. Counting was done in a well-type scintillation counter. In few cases three blood samples of the same subjects were taken at intervals of 10, 20 and 30 minutes. The observed values for the radioactivity of the plasma samples were plotted against time on semilog paper and the line kept fitting the points was extrapolated back to zero time. But in majority of subjects only single sample were collected at 10 minutes by using a dilution formula (Dacie and Lewis 1966).

CALCULATIONS

$$\text{Plasma volume} = \frac{\text{Radioactivity of standard} \times \text{Dilution factor} \times \text{Volume injected}}{\text{Radioactivity of post injection sample (converted to 0 time)}}$$

The total blood volume was estimated by multiplying the plasma volume by

$$\frac{100}{100 - \text{haematocrit percentage (corrected P.C.V.)}}$$

The correction factor 0.91 was used in all the cases. The above correction factor was used as it has been observed that venous haematocrit, overestimates the proportion of red cells in circulating blood as a whole, because proportionately R.B.C. volume is substantially lower in capillary bed-than the venous blood, (Wintrobe (1961)). It has been observed that the average value for body haematocrit is nearly 91 per cent of large vessel haematocrit (L.V.H.). The relation is fairly constant in normal as well as in most of the diseased conditions, therefore, the correction factor 0.91 was used in all cases of blood volume estimation.

The patients were instructed to abstain from alcohol or smoking for atleast one week before and also during the study period. They were not administered any drug known to affect microsomal drug metabolising enzymes activity.

The patients were advised to take Liv.52 at a dose of 2 tablets three times a day, for six weeks. The total protein, albumin, globulin, plasma and RBC volume along with liver function tests were repeated at the 3rd and 6th week and the final observations were compared with the initial and 3rd week readings. Statistical analysis was done by using unpaired student's 't' test.

RESULTS

After six weeks of treatment with Liv.52, a significant rise in total protein and albumin was observed. There was a significant rise in the plasma volume and all liver function tests showed significant improvement, specially Gamma Glutamic Transpeptidase (GGT), which is specific for alcoholic hepatitis. Patients on Liv.52 showed marked improvement in appetite. However no significant improvement in body weight was noticed within the short duration of the trial.

DISCUSSION

A variety of agents have been used to treat alcoholic cirrhosis but it is difficult to evaluate the effectiveness of drugs in conditions such as alcoholic liver disease which tends to progress slowly, which is so profoundly affected by other variables such as drinking behaviour. In addition, patients who are unable to control their drinking habits are unlikely to be compliant with treatment making the evaluation of any therapeutic effect more difficult still.

Effect of Liv.2 on Different Biochemical Parameters in Alcoholic cirrhosis (N=20)			
Parameters	Initial values	After 3 weeks	After 6 weeks
Total protein (gm%)	5.23 ± 0.17	5.47 ± 0.44	5.82 ± 0.17
Albumin (gm%)	2.21 ± 0.21	2.61 ± 0.18	2.97 ± 0.21***
Globulin (gm%)	3.02 ± 0.31	2.96 ± 0.34	2.85 ± 0.48
Plasma volume	34.38 ± 1.42	37.38 ± 1.26	38.81 ± 1.50*
RBC Volume	28.41 ± 1.68	29.36 ± 1.71	29.96 ± 1.71
Serum bilirubin (mg%)	1.67 ± 0.22	1.40 ± 0.23	1.23 ± 0.18
Alkaline phosphatase	66.35 ± 6.59	55.90 ± 4.39	48.70 ± 4.61*
SGOT	61.80 ± 2.55	55.30 ± 4.59	53.20 ± 3.03*
STPT	56.40 ± 2.06	47.70 ± 4.73	42.20 ± 5.97*
GGTP	79.60 ± 5.51	66.10 ± 6.61	60.10 ± 6.35

* $p < 0.05$, *** $p < 0.001$ as compared to the initial readings.

Cirrhosis of liver is the third most frequent cause of death in alcoholics. Acetaldehyde, the first metabolite of ethanol, is responsible for many of the ethanol-induced alterations of hepatic structure and function. It has several toxic effects on hepatic cells and helps accumulation of lipids and decreases the capacity to synthesise albumin. This decrease in serum albumin causes contraction of blood volume and expansion of extra-cellular fluid space. The contraction of blood volume leads to enhanced sodium and water retention leading to ascites and oedema. It also reduces hepatic blood flow and causes ischaemia of the liver, which is known to cause parenchymal damage and may be contributing to aggravation of the cirrhotic process.

Severe protein malnourishment can favour immunoincompetence, infections and exacerbates hypoalbuminuria and ascites.¹⁷ Earlier clinical reports on Liv.52 mentioned an increase in serum albumin in patients with malnutrition¹⁸ and also in patients with liver cirrhosis. It has been observed that these beneficial action of Liv.52 is due to rapid elimination of acetaldehyde formed during ethanol metabolism and there by preventing its cellular binding¹⁹.

A significant improvement in the biochemical parameters has been observed in the present study after six weeks of treatment with Liv.52 in patients of alcoholic cirrhosis. The rise in serum albumin seen in this study is rather small compared to the feeling of well-being experienced by the patients. The rise in serum albumin causes expansion of blood volume is returned to near normal. Thus, Liv.52 prevents the progress of liver cirrhosis by inhibiting the toxic effects of acetaldehyde and the rise in serum albumin and increase in plasma volume may restore hepatic blood flow and relieve anoxaemia. This dual action of Liv.52 may

arrest or even reverse the course of alcoholic liver cirrhosis. Liv.52 may arrest or even reverse the course of alcoholic liver cirrhosis. Liv.52 also exerts a protective action on the liver as indicated by a significant reduction in the levels of SGOT, SGPT, bilirubin and GGTP.

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