

Liv.52 - A New Therapeutic Agent in the Management of Steatorrhoea of Cirrhosis of the Liver

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The management of cirrhosis of the liver presents a multifaceted problem. It has now been increasingly recognised that a considerable proportion of these cases suffer from steatorrhoea. Recent studies have shown that fat malabsorption occurs in 50-70% of these cases (Fast *et al.* 1959; Baraona *et al.*, 1962, van Goidsenhoven *et al.* 1963 and Sun *et al.* 1967). The malnutrition of these cases is thus not only produced by hepatocellular damage but also by steatorrhoea. Despite several researches on these lines the genesis of steatorrhoea in this condition still remains uncertain and its management, consequently, has also been unsatisfactory.

We therefore undertook a trial of Liv.52 tablets in the management of this crippling complication of portal cirrhosis. Liv.52 tablets, a product of Himalaya Drug Co., consists of 8 ingredients *viz.* Capparis spinosa; Cichorium intybus; Solanum nigrum; Cassia occidentalis; Terminalia arjuna; Achillea millefolium; Tamarix gallica; Mandur bhasma in various proportions.

The combination of these agents is claimed to produce a protective and regenerative effect on hepatic parenchyma, stomachic and chloretic action with a salutary effect on liver glycogen and serum proteins along with some diuretic and anabolic action.

MATERIAL AND METHODS

Thirty clinically diagnosed cases of hepatic cirrhosis were taken from the General Medical wards of S.N. Hospital, Agra. The clinical diagnosis of cirrhosis was confirmed by biochemical tests and by a liver biopsy. A thorough clinical examination was done in each case.

The following investigations were done in each case.

1. *Complete haemogram*:- to include haemoglobin levels, erythrocytic sedimentation rate, general blood picture, absolute values and total and differential leucocytic count.
2. *Liver function tests*:- consisted of Serum Bilirubin, Serum Proteins, Albumin Globulin ratio, Serum Alkaline Phosphatase, Vandenbergh reaction, Thymol Turbidity and Flocculation, Zinc Sulphate Turbidity and Prothrombin time. All these tests were done with standard techniques (Varley 1969).
3. *Ascitic fluid*:- was examined for total and differential cell count and protein content. The study included only those cases whose ascitic fluid was transudate on this examination.
4. *Stool examination*:-for ova and cyst was done in each case.
5. *X-ray Abdomen*:-was taken in each case to look for pancreatic calcification.

6. *Three days faecal fat estimation*:- was done after keeping the patients on a standard diet containing 75 g fat/24 hrs at least 5 days before the test. Total faecal fats were estimated on 3 days collection of stool by Wet method of Vandekamer (1949).

ALLOCATION OF TRIAL TREATMENT WITH Liv.52

Treatment with Liv.52 was allotted on random basis to the cases of cirrhosis with steatorrhoea using random sampling tables.

The haematological examination and liver function tests were repeated after every 15 days and faecal fat estimation was repeated after a 30 days course of Liv.52 tablets in doses of 2 tablets three times a day.

OBSERVATIONS

Out of 30 cases studied for faecal fat excretion, 20 cases showed a total faecal fat content of more than 6 g/24 hrs. The maximum normal limit in control subjects has been found at 5.9 g/24 hrs in our biochemical laboratory. The incidence of steatorrhoea in cirrhosis in this series was therefore 66.6%.

Out of 20 cirrhotic cases with steatorrhoea, 12 were males and 8 females with their ages ranging from 17-60 yrs. Twelve out of these 20 cases were kept on tablet Liv.52 + usual supportive treatment for a total period of 30 days and the remaining 8 cases were kept on the usual supportive therapy without Liv.52 and they served as controls.

Results of Haematological Examination

The tests revealed that there was significant improvements in haematological findings in both test group (12 cases) receiving Liv.52 and control group (8 cases) without Liv.52 as shown in figure 1. The rate of improvement in haemoglobin levels was nearly the same for both groups.

Results of Liver Function Tests

All the 20 cases had hepatocellular failure and had ascites. Out of 12 cases kept on Liv.52 therapy, 8 showed definite improvement in their liver function tests and in other 8 cases without Liv.52 therapy, the improvement in liver function test occurred only in 4 cases and this improvement was also less in extent, that those on Liv.52 therapy (Table 1).

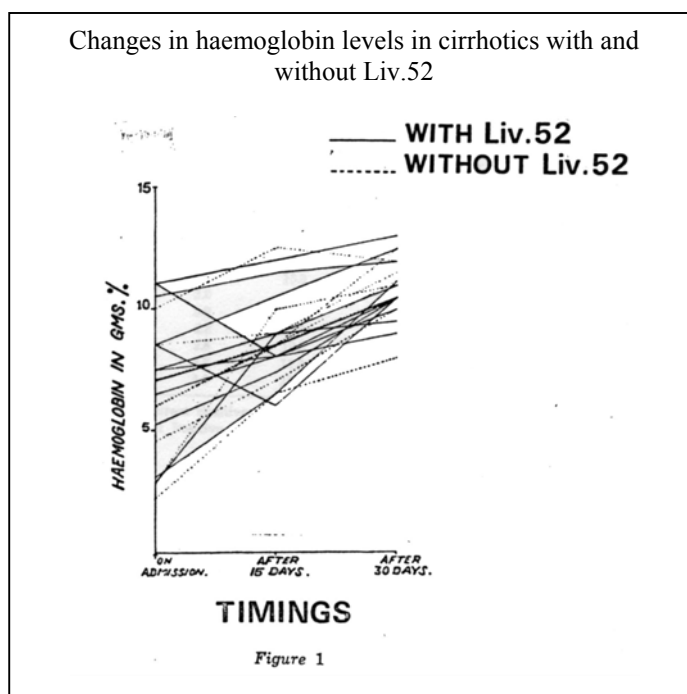


Table 1: Showing results of liver function tests improved in test and control group							
Sl. No.	Timings	Serum bilirubin mg%	Serum Prot		Serum Alk. Phos. Units (K.A.)	Zinc Sulphate turbidity units	Vandenberg Reaction
			Alb. in gm	Glob. in gm			
Results of cases on Liv.52 Therapy							
1.	On Adm.	1.7	3.7	3.0	19.2	15	D.D.P.
	30 days	1.2	4.0	3.2	15.5	19	D.D.P.
2.	On Adm.	1.4	3.0	2.7	19.1	30	Negative
	30 days	0.9	2.6	3.9	19.3	12	Negative
5.	On Adm.	1.7	3.2	3.5	20.3	14	D.D.P.
	30 days	0.8	2.3	4.4	18.3	8	Negative
6.	On Adm.	1.0	2.1	4.2	26.1	16	D.D.P.

	30 days	0.8	3.5	4.0	16.0	8	Negative
7.	On Adm.	2.1	1.7	3.5	20.0	14	D.D.P.
	30 days	0.9	3.7	3.1	17.0	7	Negative
10.	On Adm.	0.7	1.7	5.5	16.0	12	I.D.P.
	30 days	0.8	3.5	4.1	12.5	8	Negative
11.	On Adm.	4.5	1.6	3.4	19.0	12	D.P.
	30 days	1.0	2.8	4.1	14.0	7	Negative
11.	On Adm.	2.0	1.8	3.4	11.0	12	D.P.
	30 days	0.9	3.5	3.2	9.5	5	Negative
Result of Cases without Liv.52							
1.	On Adm.	0.9	2.5	2.9	19.3	14	Negative
	30 days	0.9	3.9	2.7	15.0	8	Negative
4.	On Adm.	1.1	3.2	3.9	11.6	7	D.D.P.
	30 days	0.8	3.2	3.0	18.0	7	Negative
6.	On Adm.	1.0	2.0	4.2	23.0	16	Negative
	30 days	0.9	3.0	3.5	19.5	13	Negative
7.	On Adm.	0.7	1.9	3.8	11.0	10	Negative
	30 days	0.8	2.4	3.9	10.0	8	Negative
Adm. = Admission D.D.P. = Delayed Direct Positive D.P. = Direct Positive I.D.P. = Indirect Positive							

The Results of 3 Days Faecal Fat Estimation

Our study in 20 healthy controls has revealed the maximum faecal fat excretion/24 hrs at a level of 5.9 g/24 hrs has been universally accepted (Sun *et al.* 1967, Sleisenger, 1971). All the 20 cases of hepatic cirrhosis taken for the present study were having their mean faecal fat excretion about 6 g/24 hrs on admission.

Eight out of 12 cases kept on Liv.52 therapy showed a satisfactory reduction in their mean faecal fat excretion/24 hrs. Actually the steatorrhoea disappeared completely in 8 cases but in remaining 4 cases which were in advanced decompensated stage (Case Nos. 3, 4, 8 and 9) reduction in steatorrhoea was only marginal and in 2 cases (Case nos. 8 and 9) there was no reduction in the mean faecal fat excretion per 24 hours.

In the control group (8 cases) without Liv.52 kept on supportive therapy, only 4 cases showed reduction in their mean faecal fat excretion per 24 hours, but this was very slight and out of these 4 cases only in one case the steatorrhoea disappeared completely (= Below 6 g/24 hrs). In the remaining 4 cases there was no effect of one month supportive therapy on their faecal fat levels.

DISCUSSION

Twenty proved cases of hepatic cirrhosis having steatorrhoea (faecal fats more than 6 g/24 hrs) were taken for the present trial. Twelve cases were kept on tab. Liv.52, 6 tablets a day in 3 divided doses for one month and 8 cases were kept on the usual supportive, therapy without Liv.52. In all these cases the haematological examinations and liver function tests were done on admission, and repeated after 15 days and 30 days of therapy while 3 days faecal fat estimation was done on admission and 30 days later after either therapy.

Sl. No.	Faecal fat per 24 hrs. In Test Group (12 cases) on Liv.52 therapy (in gms.)		Faecal fat per 24 hrs. In Control group (8 cases) without Liv.52 therapy (in gms)	
	On Admission	30 days	On Admission	30 days
	1.	6.60	4.40	7.03
2.	7.63	4.20	14.66	12.87
3.	7.67	6.90	8.36	8.11
4.	7.38	6.63	8.43	6.60
5.	8.03	4.87	14.15	10.12
6.	11.14	5.51	6.66	5.10
7.	10.79	4.63	8.13	8.10
8.	13.28	13.10	9.56	9.06
9.	13.28	12.99	–	–
10.	9.93	5.90	–	–
11.	10.46	4.74	–	–
12.	22.80	5.00	–	–

The haematological picture in both these groups improved remarkably and it was because both of these were getting haematinics and good diet.

It was seen that in 8 cases out of 12, where the disease was not very advanced clinically, the improvement in liver function tests was significant (compared to control group of 8 cases), while in 4 cases of advanced cirrhosis there was no improvement showing thereby that Liv.52 has got a significant role in the cases where the disease is early, perhaps due to its anabolic and regenerating effect on the liver tissue. In 4 cases of advanced cirrhosis there was no effect of Liv.52 on the liver function tests because in advanced cirrhosis there is a lot of fibrosis, disorganisation and obliteration of blood vessels and Liv.52 does not act on a fibrosed liver.

Liv.52 therapy caused a marked reduction in daily total fat excretion in 8 of the 12 cases and these cases were completely cured of steatorrhoea, which is highly significant when compared to controls, where only one case was cured of steatorrhoea.

The production of steatorrhoea in cases of hepatic cirrhosis is very controversial. The possible mechanisms include malnutrition secondary to liver disease causing malfunction of small intestine, insufficient bile salt production to achieve normal micelle formation necessary for the absorption of fats and fat soluble substances and presence of abnormal bacterial flora in the small intestine. But the evidence for these mechanisms is not convincing.

A common underlying cause may exist for both liver disease and the malabsorption as exemplified by alcoholism damaging both liver and pancreas, hepatitis virus, affecting many organs of the body including the small intestine or as in mucoviscidosis (Sobel and Wayne 1963, Anderson 1938).

Liver disease may be secondary to malabsorption irrespective of its aetiology but as evidence by Losowsky *et al.* (1969) there is enough proof to suggest that malabsorption is secondary to the liver disease itself.

Some workers have reported structural and functional changes in the small intestine (Astaldi and Strosseli, 1960) but it is not supported by others (Sun *et al* 1967).

Similarly portal hypertension as a cause of steatorrhoea has been excluded as marked fat malabsorption may occur in the absence of portal hypertension (Foster *et al*, 1950 and Sun *et al.* 1967). Correlation between the degree of steatorrhoea and severity of liver damage is also diversely reported (Sun *et al.* 1967, Siurala *et al.* 1960, Summerskill and Moertel 1962).

Abnormalities of histology of the pancreas in patients with liver disease have been reported by several authors (Krishbaum and Shure 1943, Stinson 1952). It has also been shown that pancreatic lesions are more prevalent in alcoholic cirrhotics than non-alcoholics. Many authors have assessed pancreatic functions in liver disease but there is not general agreement at the frequency or nature of the abnormal findings. Our own study of pancreatic enzyme estimation done in cases of cirrhosis with and without steatorrhoea did not reveal any significant difference in the enzyme levels as compared to the results in the normal subjects. The only finding was increased volume of duodenal aspirate in the cases of hepatic cirrhosis having moderate to marked steatorrhoea but this also could not explain the genesis of fat malabsorption in cases of hepatic cirrhosis.

The present study done so far, thus, clearly demonstrates the significant beneficial effect of Liv.52 on liver functions and steatorrhoea of hepatic cirrhosis. How it reverses the steatorrhoea of liver cirrhosis, can only be theorised. The improvement in steatorrhoea in these cases of hepatic cirrhosis after Liv.52 is likely due to the anabolic and regenerating effect of Liv.52 on the hepatic cells and it also stimulates the secretion of bile salts from these cells, thereby increasing the concentration of conjugated bile salts in the intestinal lumen which are deficient in these cases of cirrhosis (Badley *et al.* 1970) and thus more lipid micelle are formed and the absorption of fats improves.

CONCLUSION

Liv.52 has got a marked beneficial effect in the early cases of hepatic cirrhosis. It is useful in the cases of hepatic cirrhosis having steatorrhoea as it causes an increased absorption of fats by increased lipid micelle formation and thus diminishes the daily faecal fat excretion and cures it.

SUMMARY

Twenty cases of hepatic cirrhosis with steatorrhoea were taken for the present study. Twelve cases were kept on Liv.52 therapy and 8 cases on supportive therapy for one month each. Liv.52 caused marked improvement in liver function tests in the early cases of cirrhosis and there was reduction in the total daily fat excretion in 83.3% of the cases and complete reversal of steatorrhoea in 66.6% of these cases.

Liv.52 is, thus, a strong therapeutic agent for improving the health and nutrition of the cases of cirrhosis of liver not only by improving the liver functions but also by curing the accompanying steatorrhoea.

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