[*Ind. Med. J*. (1977): 5, 69]

Observations on the treatment of infective Hepatitis with an indigenous drug Liv.52

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SUMMARY

A controlled study in 50 cases of infective hepatitis was carried out with an indigenous drug Liv.52 and conventional therapy like B-complex and corticosteroids. The cases were divided into two groups of 25 cases each, those treated with Liv.52 being the test group while the other 25 on B-complex and corticosteroids alone served as control. The evaluation of therapy in each group was done from the clinical standpoint as well as by liver function tests like serum bilirubin, serum alkaline phosphatase, thymol turbidity, S.G.P.T. and S.G.O.T. and histological studies, initially, after 4 weeks and 8 weeks of treatment respectively. The overall result showed that the addition of Liv.52 is much more effective than B-complex and corticosteroids administered alone. Liv.52 brings about early clinical improvement as well as promotes rapid and highly significant biochemical as well as histological improvement in infective hepatitis cases. Attempts have been made to explain the multi-faceted improvements on the basis of the multi-pronged action of Liv.52.

Infective hepatitis accounts for nearly 90% of all jaundice cases in our country. The mode of infection is oro-faecal. It thrives in congested and insanitary conditions so rampant in our country. Besides, nutritional deficiencies increase the susceptibility of liver cells to necrosis. The resulting complications of hepatic failure and coma or the post-hepatic cirrhosis with its ultimate fatality, appear quite frequently in our country and constitute a major therapeutic challenge. No such drug has been found to have a specific curative action in this disease process. It has become necessary, therefore, to use drugs having poly-directional actions such as B-complex and corticosteroids.

Liv.52 is an indigenous product having many Ayurvedic constituents. Each tablet of Liv.52 contains: Capparis spinosa, Cichorium intybus, Solanum nigrum, Terminalia arjuna, Cassia occidentalis, Achillea millefolium, Tamarix gallica and Mandur bhasma.

Many actions such as anabolic, choleretic, stomachic, diuretic and aperient have been attributed to Liv.52. (Sule *et al,* 1956; Murkibhavi and Sheth, 1957; Karandikar *et al,* 1963; Captain and Syed, 1966; Joglekar and Leevy, 1970). Liv.52 has undergone extensive clinical trials in liver disorders like infective hepatitis and cirrhosis of the liver, and encouraging results have been claimed (Mathur, 1957). Experimental studies carried out on mice (Joglekar *et al.* 1963) and dogs (Murkibhavi *et al.* 1957) and in rats (Karandikar *et al.* 1963), have shown its efficacy in acute hepatic toxicity, thereby, suggesting its protective action on the hepatic parenchyma. The drug has also been claimed to stimulate cellular growth in the presence of hepatotoxins and necrosing substances (Prasad, G.C., 1974).

The present study was undertaken to evaluate the efficacy of Liv.52 in infective hepatitis, in the light of these highly encouraging claims by various authors.

MATERIAL AND METHODS

A total of 50 patients of infective hepatitis of varying age groups admitted to the medical wards of Darbhanga Medical College Hospital were selected for study. These cases were divided into two groups of 25 each. One group was put on Liv.52, six tablets in divided doses along with B-complex and corticosteroids daily while the other group was treated with B-complex and corticosteroids alone and served as control. The cases, on admission, underwent thorough clinical examination and routine laboratory investigations like total and differential count of white blood cells, stool examination, urine examination. Specialist investigations like serum bilirubin, serum alkaline phosphatase, thymol turbidity, S.G.P.T. and S.G.O.T. estimations were also performed initially in order to assess derangement in liver functions. These were repeated after 4 weeks and 8 weeks of treatment to determine the degree of improvements in both the groups.

Ten cases in each group were subjected to histopathological studies initially and then after 4 weeks and after 8 weeks of treatment. The efficacy of the treatment was judged by the amelioration in subjective symptoms and objective signs as well as the degree of improvement in various liver function tests as also in the histopathology.

OBSERVATIONS AND RESULTS

Of the 50 cases, 34 were males and 16 were females of ages ranging from 15 to 65 years. The majority (40%) were in the age group of 26 to 35 years (Table I). Of the various manifestations, jaundice and dark-coloured urine were present in all the cases, while other symptoms like anorexia, nausea, vomiting, constipation, abdominal pain, diarrhoea, pruritus, bleeding, fever, etc. were found in varying degrees (Table II and III).

Table I: Showing age and sex of patients with infective hepatitis

Sl. No.	Age group	No. of cases				Total No. of cases
		Male		Female		
		Control	Liv.52	Control	Liv.52	
1.	15-25	4	3	2	2	11
2.	26-35	9	5	2	4	20
3.	36-45	4	2	1	3	10
4.	46-55	1	2	1	1	5
5.	56-65	2	2	—	—	4

Table II: Showing degree of jaundice in infective hepatitis

Sl. No.	Jaundice	Total No. of cases	Control	Liv.52
1.	Mild	23	14	9
2.	Moderate	18	8	10
3.	Severe	9	3	6

Table III: Showing comparative improvements in symptomatology in the Control and Liv.52 groups

Sl. No.	Symptoms	Control		Liv.52	
		Initial	After	Initial	After
1.	Jaundice	25	12	25	4
2.	Loss of appetite	22	9	23	6
3.	Loss of weight	22	15	20	6
4.	Abdominal pain	19	6	16	3
5.	Nausea	9	5	11	3
6.	Vomiting	5	6	3	3
7.	Constipation	16	4	12	3
8.	Epigastric discomfort	23	10	25	2
9.	Fever	5	5	3	3
10.	Malaise	6	6	4	2
11.	Pruritus	6	7	3	4
12.	Bleeding	0	0	1	0
13.	Yellow-coloured urine	25	20	25	23

14.	Restlessness	2	10	2	0
15.	Precoma	0	0	1	0
16.	Diarrhoea	4	4	2	2

Of the physical signs the most conspicuous was tender hepatomegaly varying from a just-palpable liver to massively enlarged liver in both the control and Liv.52 groups (Table IV). Palpable spleen, ascites, and oedema were also found in varying percentages (Table IV).

Table IV: Showing physical signs—initial and at the end of treatment

	Control		Liv.52	
	Initial	End	Initial	End
Tender liver	25	12	25	4
Liver palpable enlargement	7	8	5	6
Liver moderate enlargement	12	6	15	6
Liver marked enlargement	5	3	3	1
Liver massive enlargement	1	1	2	1
Oedema of the legs	1	1	4	1
Ascites	2	1	1	0
Palpable spleen	12	8	10	3

In the Liv.52 group, symptoms abated much earlier–in ½ to 2/3 the time required in the control group (Fig. 1). The pre-treatment level of E.S.R. in the control and test series showed high values ranging from 11 to 25 mm per hour in 80% and 84% of cases respectively. After treatment they were found persisting in 72% in the control as against 52% in the Liv.52 group. 48% cases returned to normal in the Liv.52 group as against only 28% in the control group.

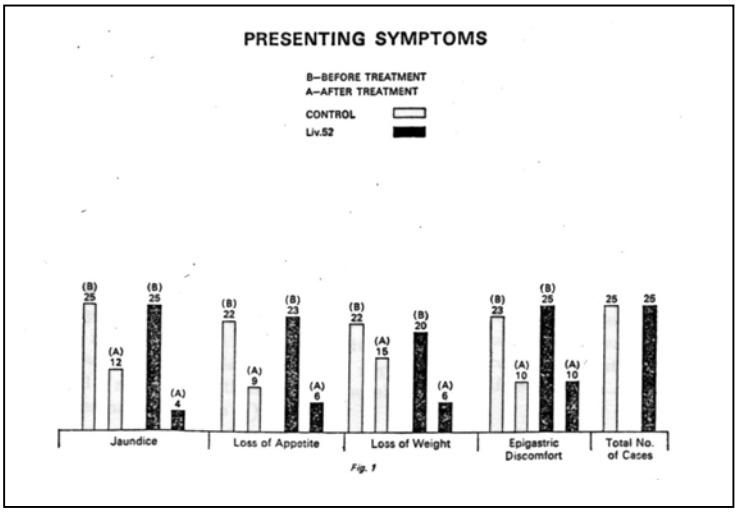


Fig. 1

LIVER FUNCTION TESTS

Serum bilirubin: The range of serum bilirubin in the control group was 5 to 18 mg% initially (Average—12.06 mg%). In the Liv.52 group it ranged from 5 to 22 mg% (Average—12.8 mg%). The average values in control and Liv.52 groups after 4 weeks of treatment were 8.87 mg% and 4.96 mg% respectively. The values further declined to 4.81 mg% and 1.8 mg% respectively after 8 weeks of treatment. (Table V).

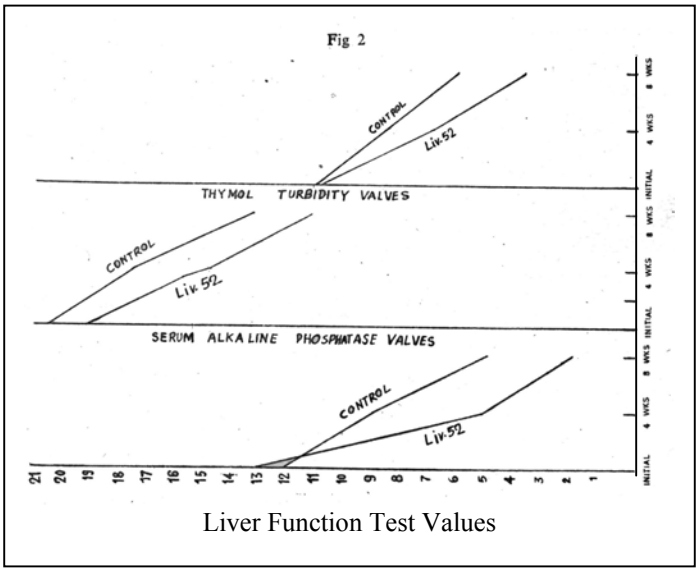
Table V: Showing comparative improvements in biochemical parameters in control and Liv.52 groups

	Bilirubin		S.G.P.T.		S.G.O.T.	
	Initial	8 weeks	Initial	8 weeks	Initial	8 weeks
Control	12.06	4.81	210.8	60.6	97.8	25.8
N = 25	± 0.7	± 0.6	± 10.1	± 5.6	± 5.8	± 2.8
Liv.52 treated	12.8	1.8	219.6	38.4	99.94	14.00
N = 25	± 0.74	± 0.04	± 10.6	± 2.6	± 6.2	0.9
p	N.S.	< 0.01	N.S.	< 0.01	N.S.	< 0.01

Table V shows serum bilirubin, S.G.P.T. and S.G.O.T. (mean ± SE) in control and Liv.52 treated groups before and 8 weeks after admission. There was no significant difference in the two groups initially but at the end of 8 weeks the Liv.52 treated group had significantly lower levels.

The percentage reduction in the control and Liv.52 groups after 4 weeks were 36% and 61% respectively and 66% and 86% after 8 weeks. The sub-icteric values of bilirubin was seen in only 36% of controls as against 84% in the Liv.52 group after 8 weeks of treatment. (Fig.2).

Serum Alkaline Phosphatase: The initial levels ranged from 12 to 28 K.A. units (Average 20.27 K.A. units) in the control group and 12 to 26 K.A. units (Average value 19.12 K.A. units) in the Liv.52 group. The average values after 4 weeks and 8 weeks of treatment in the control group were 17.34 K.A. units and 13.31 K.A. units respectively representing a reduction of 14% and 34% over the initial level. The values in the Liv.52 group after 4 weeks and 8 weeks of treatment were 14.72 K.A. units and 11.08 K.A. units respectively representing reductions of 23% and 42% over the initial values (Fig.2).



Liver Function Test Values

Thymol Turbidity: The initial values in the control and Liv.52 groups were 5 to 15 units with an average of 11.0 and 10.8 units in the control and Liv.52 groups respectively. The average values after 4 and 8 weeks of treatment in the control group were 8.4 units and 6 units as against 6.8 units and 3.64 units respectively in the Liv.52 group (Fig. 2). The percentage decline after 4 and 8 weeks of treatment in the control group was 24% and 29% as against 37% and 66% in the Liv.52 group.

S.G.P.T.: The average initial values in the control and Liv.52 groups were 210.8 and 219.6 units respectively which declined to 131.4 units and 104.2 units respectively after 4 weeks of treatment, while after 8 weeks of treatment they were observed respectively to be 60.6 units and 38.4 units (Table V). The decline of values over the initial after 4 and 8 weeks of treatment in the control group were to the tune of 38% and 71% as against 53% and 82% in the Liv.52 group (Table V).

S.G.O.T.: The initial average values of S.G.O.T. in the control and Liv.52 groups were 97.8 units and 99.94 units. In the control group, the value declined to 48.2 units as against 40.8 units in the Liv.52 group after 4 weeks of treatment, while the average values after 8 weeks of treatment in the control and Liv.52 groups were observed to be 25.8 units and 14 units respectively (Table V).

Histopathology: Initial histopathological picture in both control and Liv.52 groups showed varying degrees of cell necrosis and infiltration with inflammatory cells in the periportal areas. Persistence of the diseases was found in 4 cases of the control with varying degrees of fibrosis in 2 cases after 8 weeks of treatment. No histopathological evidence of the disease was found in the Liv.52 group after 8 weeks.

DISCUSSION

The results of this study indicate speedier clinical improvements in the Liv.52-treated cases, than in those on conventional therapy with B-complex and corticosteroids. The period required for relief of symptoms and signs is cut short to almost half in the Liv.52 group as compared to the control group of cases. This itself is an obvious advantage in overcoming the morbidity of the disease.

As regards the liver function tests, a uniform improvement has been noted in both the groups under study, but in the Liv.52 treated cases the improvement appears to be much more rapid and complete as judged from the comparative data after 4 to 8 weeks of treatment (Fig. 2). Complete return to normal in the various liver function tests like serum alkaline phosphatase, thymol turbidity, S.G.P.T. and S.G.O.T. values in the Liv.52 group was observed in 21, 19, 16 and 25 cases respectively as against 16, 9, 7 and 20 cases in the control group. Even the serum bilirubin level was seen to return to sub-icteric level in 21 cases in the Liv.52 group as against only 9 cases in the Control group after a full eight weeks of treatment. This signifies a much more comprehensive ameliorating effect of Liv.52 over the B-complex and corticosteroids regimen in the infective hepatitis cases.

The beneficial effect of Liv.52 is attributed to its multipronged actions. The anabolic effect of the drug is discernible in the improvement of general well-being and appetite and in the relief of nausea, vomiting and malaise. The control of abdominal pain and hepatic tenderness is presumably the result of the anti-inflammatory effect of the drug. Similar effects have been reported by Jaffari, 1969. Constipation, in infective hepatitis, is partly the result of an inadequate intake of food due to anorexia. It is also partly due to the deficiency of bile salts which are the known stimulants of peristalsis. The relief of constipation, therefore, appears partly the result of choleretic action of Liv.52 and partly of the increased food intake in response to improved appetite.

Icterus, in infective hepatitis, presumably results from the intrahepatic obstruction of biliary canaliculi. The obstruction is the direct consequence of cellular inflammation. The fall in serum bilirubin in Liv.52 treated cases, appears to be an index of diminishing intrahepatic obstruction consequent to the amelioration in inflammatory processes. Diminishing serum alkaline phosphatase level provides further proof of the effectiveness of Liv.52.

The flocculation test like thymol turbidity is an index of the disturbed hepatic synthesis of serum proteins by the disease process. A diminution in the thymol turbidity value confirms the corrective action of Liv.52.

Liv.52 presumably improves the function of hepatocytes and promotes regeneration of the necrosed cells, thereby improving the protein synthesis. Another indication of cellular regeneration with Liv.52 is the progressive diminution in the activity of the serum enzymes like S.G.P.T. and S.G.O.T.

The diminution in enzyme activity consequent to Liv.52 therapy is an indication of arrest of cell necrosis as well as inflammation. The present findings confirm earlier observations by Vimala Ramalingam *et al.* 1971, and Prasad, G.C., 1974. Admittedly, they need histological corroboration on an extensive scale which has not been possible in the present study. Histological study in a few cases. However, showed no evidence of the disease after the full course of Liv.52 treatment. The biopsy results in the control group on the other hand showed a persistence of necrotic changes of fibrosis in two cases.

So, in the final analysis, Liv.52 appears to have a definite edge over conventional therapy like B-complex and corticosteroids in infective hepatitis and the authors are in agreement with Vimala Ramalingam *et al.* 1971 that "Liv.52 restores liver functions to normal earlier than prednisone, clears jaundice, improves appetite, causes a sense of well being and has an anti-inflammatory effect and it effectively contributes to healthy repair and regeneration of liver cells".

ACKNOWLEDGEMENT
We are much obliged to the Superintendent, D.M.C.H. for allowing us to conduct this work and permitting it to be published.

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