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Treatment of viral hepatitis by an indigenous drug – Liv.52

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Since World War II the diagnosis of infectious hepatitis in adults has been made from various parts of the globe with increasing frequency. The course of the disease varies in duration and severity. Being viral in origin its treatment is not laid down in specific terms but the same becomes imperative when it affects an appreciable percentage of the population in a country like India every year. Unlike western countries the disease as recorded in India is more often a prolonged affair with a likelihood of complications, including hepatic failure and post-hepatic cirrhosis, developing. As such, though most of the patients might usually get clinical cures with relief of symptoms the prevention of hepatic failure and assessment of residual hepatic cell damage must guide the clinician in his choice of therapy.

A scientific approach to the problem of therapy of infectious hepatitis in adults thus assumes importance and the criteria of success should be rapid recovery and convalescence without residual liver cell damage. An attempt has been made in the present instance to carry out treatment of infectious hepatitis with an indigenous drug combination in an adult group of cases attending a general hospital.

The drug, 'Liv.52' (The Himalaya Drug Co.), is a herbal preparation and is claimed to have diuretic, aperient, stomachic, anabolic and choleretic effects. Each tablet contains processed extracts of several plants in varying proportions, viz.:

Capparis spinosa	23%
Cichorium intybus	23%
Solanum nigrum	12%
Cassia occidentalis	6%
Terminalia arjuna	12%
Achillea millefolium	6%
Mandur bhasma	12%
Tamarix gallica	6%

Experimental studies have been reported for substantiating the therapeutic properties of the combined formula in respect of protection of liver cells from permanent damage by various noxious agents (Northover, 1960; Joglekar *et al.*, 1963; Patel *et al.*, 1963; Karandikar *et al.*, 1963; Murkhibhavi and Sheth, 1957 and Captain *et al.*, 1966).

It has also been tried clinically in cirrhosis of the liver and viral hepatitis and reasonable success claimed (Mathur, 1957; Patrao, 1957; Sheth *et al*. 1960; Sule *et al.*, 1956, 1957, 1968; Vyas, 1963; Menon and Ravindran, 1966; Arora, 1969; Joglekar and Leevy, 1970).

In view of these observations it was decided to study the effects of 'Liv.52', and compare the same with those of a placebo and of combined 'Liv.52' and steroid therapy.

MATERIAL AND METHODS

Twenty five cases were selected for this study. After clinical diagnosis liver function tests were determined in each of them. Needle biopsy of the liver was done, when required, before and after the treatment.

The patients were followed-up either in the hospital indoors or in the O.P.D. and the progress was noted on the basis of jaundice, hepatomegaly, anorexia, colour of urine, etc. At the same time biochemical investigations were repeated at intervals.

The clinical assessment of recovery of the patient was not based on the single criterion of disappearance of jaundice but the persistence or otherwise of hepatomegaly and the return of liver function tests to normal values were also taken into account.

After the therapy was over, the overall residual liver damage in each case was assessed by means of B.S.P. (Bromsulphthalein) tests (45 mts. value). This Bromsulphthalein test was carried out by following the method of Mateer *et al.* (1942) with a dose of 5 mgm. Of the dye per kg. of the body weight. Our laboratory normal value varied from 0-5% retention at the end of 45 mts. Values above 5% were indicative of liver cell damage and more than 25% indicative of advanced degree of liver cell damage. The results thus obtained are presented below.

RESULTS

Of the 25 cases, 13 received treatment only with 'Liv.52' tablets (2 tablets thrice daily); 4 were treated with placebos (2 tablets thrice daily) only and the rest (8 cases) were treated with 'Liv.52' and steroid combined. The overall results of each of these groups are given as follows:

Group I — Treated with 'Liv.52' alone: Out of 13 cases treated, 9 were entirely from the O.P.D. The average period of therapy was 6 weeks in this group, but two were followed-up to a maximum period of 14 weeks.

The residual liver damage, when assessed by B.S.P. test at the end of therapy, was found to be within normal limits showing thereby excellent degree of response with the drug. Table I shows the details of the therapy and its results.

Table I: Cases treated with 'Liv.52' (alone)

Sl. No.	Name, age/sex	Period of treatment (weeks)	Place of treatment	Clinical diagnosis	B.S.P. 45 mts. result at the end of therapy	Body weight changes	Liver biopsy	Results
1.	P.D. 21/F/H	12	Hosp. & O.P.D.	Pregnancy with viral hepatitis	2.8%	Gained by 4 kgs.	Done I-Picture of icteric hepatitis with cholestasis II-Normal liver (See Figs. 1 & 2)	Good
2.	S.R. 20/M/H	6	O.P.D.	Viral hepatitis	1.2%	Loss by 2 kgs.	Not done	Good
3.	P.K.D. 25/M/H	6	O.P.D.	"	1.8%	Loss by 1 kg.	"	Good
4.	P.K. 10/M/H	14	O.P.D.	"	0.6%	Loss by 1 kg.	"	Good
5.	A.K. 13/M/H	14	O.P.D.	"	0.8%	Gained by 3 kgs	"	Good
6.	N.R. 18/M/H	6	O.P.D.	"	0.4%	Loss by 2 kgs	"	Good
7.	B.R. 18/M/H	6	O.P.D.	"	3.8%	Constant	"	Good
8.	T.S.	11	Hosp. &	"	—	Loss by	"	Good

	12/M/H		O.P.D.			3 kgs		
9.	R.B. 18/F/H	5	Hosp. & O.P.D.	"	1%	Loss by 1 kg.	"	Good
10.	L.P.B. 32/M/H	6	O.P.D.	"	1.6%	Loss by 5 kgs	"	Good
11.	P.S. 25/M/H	6	O.P.D.	"	2.4%	Loss by 3 kgs	"	Good
12.	K.C.M. 30/M/H	6	O.P.D.	"	2.6%	Gained by 2 kgs	"	Good
13.	D.C.	8	Hosp. & O.P.D.	"	0.4%	Loss by 4 kgs.	Done I–Picture of icteric hepatitis II–Areas of focal necrosis persisting, otherwise normal	

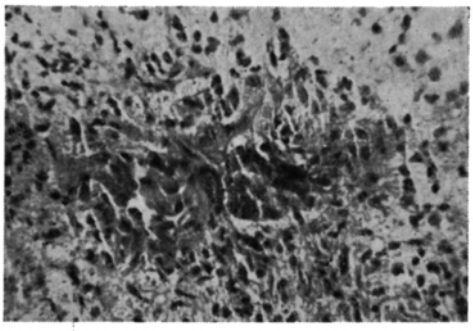

Fig. 1: P.D.
Picture of icteric hepatitis with intrahepatic cholestasis (High power view).

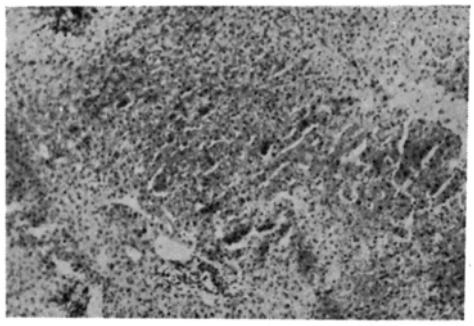

Fig. 2: P.D.
(12 weeks after therapy with Liv.52)
Complete healing with picture of normal liver and regeneration

Liver biopsy was performed in two cases (Nos. 1 and 13). Both showed the picture of acute icteric hepatitis with cholestasis. At the end of treatment the cholestasis was absent in both of them and slight focal necrosis was present in one. There was no evidence of any architectural damage or portal tract scarring after the treatment.

It will appear from Table I that besides other points patients treated with 'Liv.52' alone had minimum weight loss and in certain cases there was actually gain in body weight.

Group II – Treated with placebo: Only 4 cases were treated in this group. Two of them took a long time to recover – 11 and 15 weeks respectively – and the other two took 6 and 7 weeks respectively. The loss in body weight was much more comparison with the group treated with 'Liv.52' alone. Residual liver damage when assessed at the end of therapy with B.S.P. test was found to be present in all, and abnormal values indicating persistence of mild degree of liver cell injury were noted in three of them. The detailed results are shown in Table II.

In 2 cases (Nos. 1 and 3) liver biopsy was performed before and after the treatment. At the beginning of the treatment, both the histological pictures were suggestive of acute icteric hepatitis, but at the end of therapy, normal liver pattern was found in one while in the other (No. 3) there was evidence of early portal scarring.

Table II: Cases treated with placebo only								
Sl. No.	Name, age/sex	Period of treatment (weeks)	Place of treatment	Clinical diagnosis	B.S.P. 45 mts. result at the end of therapy	Body weight changes	Liver biopsy	Result
1.	P.B.D. 21/F/H	7	Hosp. & O.P.D.	Viral hepatitis	5.7%	Loss by 3 kgs.	I–Picture of icteric hepatitis II–Normal liver	Good
2.	B.N.S. 30/M/H	6	O.P.D.	"	3.8%	Loss by 4 kgs.	Not done	Good
3.	M.D. 30/F/H	15	Hosp. & O.P.D.	"	6.2%	Loss by 3 kgs.	I–Picture of icteric hepatitis II–Areas of portal scarring (See Figs. 3 & 4)	Delayed response
4.	K.C.R. 26/M/H	11	O.P.D.	"	6.0%	Loss by 8 kgs.	Not done	Delayed response

Thus the over-all response was unsatisfactory in Group II and even after clinical cure B.S.P. evidence of persistent liver damage and development of early portal scarring in one of the liver slides points out that these patients might go on to the phase of chronic hepatitis, and later on to hepatic cirrhosis, though they have apparently made a clinical recovery.

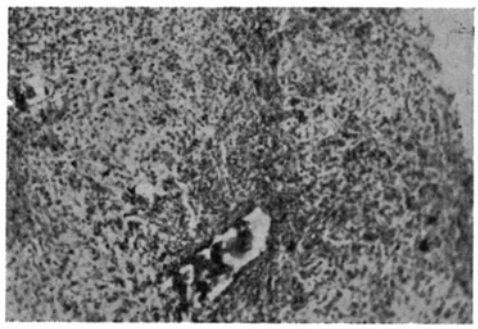

Fig. 3: M.D.
Picture of icteric hepatitis (Placebo)

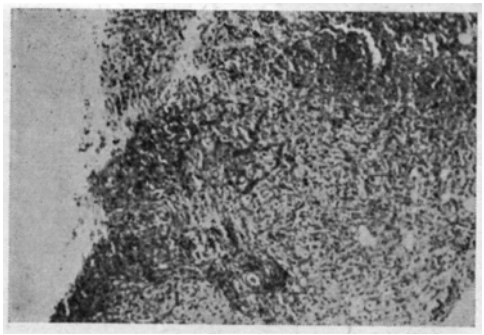

Fig. 4: M.D.
15 weeks after placebo therapy showing portal scarring (Placebo)

Group III – Cases treated with steroid and 'Liv.52': Eight cases were included in this group and good response was obtained in most of them within 4 to 5 weeks. Weight gain was a common feature except in two. There was persistent hepatomegaly even after disappearance of jaundice in two cases, one of whom took 16 weeks and the other about 22 weeks for recovery. Detailed observations are given in Table III.

Table III: Cases treated with 'Liv.52' and steroid combined								
Sl. No.	Name, age/sex	Period of therapy (weeks)	Place of treatment	Clinical diagnosis	B.S.P. 45 mts. result at the end of therapy	Body weight changes	Liver biopsy	Result
1.	P.S. 23/M/ H	16	Hosp. & O.P.D.	Viral hepatitis with pre-coma	0.6%	Gained by 2 kgs.	I–Picture of icteric hepatitis II–Normal liver	Good
2.	S.D. 25/F/H	5	Hosp.	Pregnancy (24 weeks), viral hepatitis with oedema & early hepatic failure	3.8%	Gained by 2 kgs.	I–Picture of icteric hepatitis with cholestasis II–Normal liver	Good
3.	H.L.M. 35/M/ H	4	Hosp.	Viral hepatitis with deep jaundice	4%	Gained by 2 kgs	I–Picture of icteric hepatitis II–Normal liver Leucocytic infection of parenchyma persisting	Good
4.	N.C.J. 20/M/ H	5	Hosp. & O.P.D.	Viral hepatitis with deep jaundice	2%	Gained by 1 kg.	Not done	Good
5.	K.B. 12/M/ H	4	Hosp. & O.P.D.	Viral hepatitis with deep jaundice	3%	Gained by 1 kg.	I–Picture of icteric hepatitis II–Normal liver except areas of focal necrosis	Good
6.	S.D. 16/M/ H	7	O.P.D.	Viral hepatitis with deep jaundice	4.2%	Constant	Not done	Delayed Response
7.	A.P. 42/M/ H	9	Hosp. & O.P.D.	Serum hepatitis with cholestasis hepatitis	1.8%	Gained by 4 kgs.	Not done	Good
8.	B.D. 27/F/H	22	O.P.D.	Viral hepatitis (moderately severe case)	8%	Loss by 4 kgs	Not done	Delayed response

Liver biopsy was done in 4 cases before and after treatment. Sections showed picture icteric hepatitis which returned to normal at the end of treatment.

Besides weight gain, the B.S.P. results were also within normal limits at the end of therapy, except in one case where the B.S.P. value was 8% and the patient had the longest period of suffering. In this case hepatomegaly also persisted for a long time even after the disappearance of jaundice.

A summary of the observations has been made in Table IV stressing the main points of comparison of results, of treatment of viral hepatitis with 'Liv.52' alone, placebo and 'Liv.52' and steroid combined.

DISCUSSION

It will appear from the foregoing observations that response to drug therapy against placebo is encouraging in the treatment of viral hepatitis. The period of recovery is shorter in cases treated by either 'Liv.52' alone or 'Liv.52' and steroid combined (6 and 4 weeks respectively), whereas with a placebo it is much longer (9 weeks). Though the combined 'Liv.52' and steroid therapy was restricted to the severe and moderately severe types of cases, specially those showing features of

pre-coma or coma, the total time taken for recovery was almost the same as in those treated with 'Liv.52 alone.

Body weight is usually lost in this illness and an adult patient may lose about 10 lbs. (Sherlock, 1968). But cases treated with 'Liv.52' did not show gross loss in weight, on the other hand, body weight was constant or even increased in some cases as in those treated with 'Liv.52' combined with steroid. This is another advantage in treating cases of viral hepatitis with 'Liv.52' because the drug had been found to be a good anabolic agent (Damle and Deshpande, 1966; Kale *et al.,* 1966; Kulkarni and Joglekar, 1970). Patients treated with placebo alone actually showed more loss in body weight.

Natural clinical cure is common in this disease and has, therefore, led to the general unwillingness of physicians to institute scientific methods for evaluating therapy in human subjects. Moreover, clinical cure is generally thought to be a guarantee of recovery from the disease without any trace of residual liver cell damage. This point, however, can only be verified clinically by estimation of B.S.P. values when jaundice and subjective symptoms have disappeared. This procedure has been recommended for proper evaluation of therapy in this disease by Chalmers (1962) and Sherlock (1968). By adopting their procedure we found that patients treated with 'Liv.52' alone or with 'Liv.52' combined with steroid showed normal B.S.P. values, that is, there was no residual liver cell damage at the end of therapy. This was not so in cases treated with placebo only, where abnormal B.S.P. excretion values were demonstrated. Thus the previous experimental and clinical observations on prevention of hepatic cell damage by 'Liv.52' have been confirmed in our study. This beneficial effect is also proved histologically in the present study. Though liver biopsy was not done in all cases, histological evidence of acute hepatic cell necrosis when detected at the beginning of therapy was followed by restoration of normal hepatic structure at the end.

On the other hand, in cases treated only with placebo, the histological picture of acute icteric hepatitis with areas of hepatic cell necrosis at the beginning, have ended in portal scarring and fibroblastic proliferation with early formation of septae and mild degree of liver cell damage, suggesting thereby a phase of chronic hepatitis. These findings are correlated to B.S.P. studies. The phase of chronic hepatitis might lead to a chronic vague illness and ultimately develop into a full-fledged picture of hepatic cirrhosis.

The role of steroid is controversial, even in recent years, in the management of viral hepatitis and is mostly reserved for severely ill patients. Its anti-inflammatory, anabolic and other properties possibly contribute to the therapeutic success. 'Liv.52' when combined with steroid has shown the best results in our series. The duration of illness was shortest and there was no evidence of residual cell damage, as judged from B.S.P. values at the end of therapy and hepatic histology also returned to normal. It is probable that the anabolic effect of 'Liv.52' and its role in prevention of hepatic cells damage might have acted synergistically with the effects of steroid to produce continued good results as shown in our study. As such, 'Liv.52' may be given in combination with steroids in severe cases of viral hepatitis. In mild and moderately severe cases 'Liv.52' alone may help the patients to have a rapid and uneventful recovery. Our observations confirm those of Arora (1969) who has studied 676 cases of viral hepatitis recently and has arrived at a similar conclusion.

SUMMARY

A study of the effects of treatment of infectious hepatitis with an indigenous drug 'Liv.52' has been done and clinical recovery was finally assessed by B.S.P. excretion tests and in some cases by liver biopsy at the end of therapy in a group of cases. The therapeutic results have been compared with those of a placebo and a combination of the drug with steroid.

Use of the drug in mild and moderately severe cases of infective hepatitis is recommended in order to prevent prolonged course of illness and residual liver cell damage.

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