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Studies with Liv.52 therapy in Infective Hepatitis

Sule, C.R., *M.D.*, **Pai, V.R.,** *M.D.*, **Damania, R.F.,** *M.D.,* and **Miss. Joshi, V.S.,** *M.B.,B.S.*
Medicine Unit, Sassoon General Hospitals, and B.J. Medical College, Poona, India.

INTRODUCTION

Liv.52, an indigenous product has been widely used clinically in various hepatic disorders for the last eight years. The drug has been tried in cases of diffuse hepatic fibrosis and portal hypertension (Mathur, 1957). Also a number of experimental studies have been carried out in mice (Joglekar *et al*, 1963) and dogs (Murkibhavi *et al,* 1963) and rats (Karandikar *et al,* 1963). These suggest the protective action of Liv.52 against hepatotoxicity. Patel *et al* (1963) showed its efficacy in acute hepatic toxicity.

The present studies were undertaken to evaluate the efficacy of Liv.52 (product of the Himalaya Drug Co.) in acute infective hepatitis, and to find out the clinical and biochemical changes in infective hepatitis of varying severity, with Liv.52.

Liv.52 contains Capparis spinosa 64.8 mg,, Cichorium intybus 64.8 mg., Solanum nigrum 32.4 mg., Cassia occidentalis 16.2 mg., Terminalia arjuna 32.4 mg., Achillea millefolium 16.2 mg., Tamarix gallica 16.2 mg. and Mandur bhasma 32.4 mg.

MATERIAL AND METHODS

The present work was done over a period of three years from 1964-66. In all 150 cases were studied. Of these, 25 cases were from other wards and were treated by our colleagues with antibacterial antibiotics and steroids. This group, Group I, acted as a control.

Our series of 125 cases was treated with Liv.52, two tablets t.d.s. From these 125 cases treated with Liv.52, we selected for the purpose of schematic comparison with the control group, 25 cases of infective hepatitis of identical severity and duration as the control group. This was Group II. Group III consisted of all 125 cases treated with Liv.52. The cases were treated as and when seen. A few cases which were treated with Liv.52 had to receive in addition, steroids and antibiotics. These have been excluded from the series.

Primarily the cases were clinically investigated. In all cases liver function tests were carried out. These included estimations of serum bilirubin, SGPT, SGOT and serum alkaline phosphatase. These tests were carried out on the 5th day and repeated on the 12th and 19th days.

RESULTS

Table No.1, showing the incidence of age and sex in the present trial. (The number of female patients was small because of restricted female admissions).

Table 1

	Age Groups									
No. of cases	11-20 yrs		21-30 yrs		31-40 yrs		41-50 yrs		51-60 yrs	
	50		52		31		12		4	
	M	F	M	F	M	F	M	F	M	F
150	45	5	43	9	29	2	11	2	4	—

Table No. 2 shows the symptomatology of acute infective hepatitis noticed in the 150 cases studied.

Table 2						
Symptoms		Total No. of cases	(25 Group I	+	125) Group II & III	Incidence %
1.	Jaundice	90	(21	+	69)	60
2.	Loss of weight	60	(8	+	52)	40
3.	Abdominal pain	58	(8	+	50)	38.7
4.	Severe constipation	56	(6	+	50)	37.3
5.	Fever	40	(3	+	37)	26.7
6.	Nausea	37	(6	+	31)	24.6
7.	Vomiting	24	(3	+	21)	16
8.	Diarrhoea	16	(4	+	12)	10.7
9.	Fever with rigors	12	(1	+	11)	8
10.	Malaise	12	(3	+	9)	8
11.	Pruritus	8	(2	+	6)	5.3
12.	Bleeding	6	(3	+	3)	4
13.	Hiccup	5	(2	+	3)	3.3
14.	Restlessness	4	(Nil	+	4)	2.7
15.	Comatose state	4	(Nil	+	4)	2.7
16.	Cough	4	(Nil	+	4)	2.7

JAUNDICE

Incidence of jaundice at the time of admission was 60%, though it was apparent in all cases subsequently.

LOSS OF APPETITE

It was present in 40% of cases (60 cases). In the control group, Group I, the appetite improved on an average after 7 days, whereas it improved on an average in 4 days in Group II (the 25 Liv.52-treated cases). In Group III (125 Liv.52 - treated cases), it improved on an average in 5 days.

VOMITING

In the present series vomiting was present in 24 cases (16%). It took on an average 72 hours to check vomiting in the control group, Group I. the vomiting stopped on an average in 40 hours in Group III (125 Liv.52-treated cases).

NAUSEA

Nausea was seen in 24.6% (37 cases). In the control group, Group I, the nausea improved in 96 hours on an average, whereas it took only 72 hours in Group II of the Liv.52 trial series.

ABDOMINAL PAIN

Abdominal pain was present in 38.7% (58 cases). The data on the time taken to check it in the control series, Group I, was not available. In our series, Group III, the pain was relieved within a period of 72 hours.

FEVER

Fever was rather a confusing symptom in many cases. The incidence was 26.7%. Twelve cases had fever with rigors, whereas 40 cases had fever without rigors. There was no significant difference between the control and trial cases. The fever subsided on an average in 72 hours. The fever lasted for 7 days in two cases of severe infective hepatitis cases having signs of coma.

CONSTIPATION

Constipation was present in 37.3% (56 cases). The constipation required regular enemata or mild laxative therapy. The bowel regularization was achieved in an average period of five days with Liv.52 therapy (Group III).

DIARRHOEA

The pre-icteric symptom as diarrhoea was present in 10.7% (16 cases). Diarrhoea was controlled with Liv.52 within an average duration of 48 hours in Group III.

PRURITUS

Pruritus was a feature in 5.3% (8 cases). Marked relief of itching with Liv.52 was seen within 48 hours in Group III. None of he cases required any other medication for relief of itching.

Table 3: Control Series

Sl. No.	Duration of Jaundice	SGPT			SGOT			Serum bilirubin		
		1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
1	12 days	350	280	140	82	40	25	20	16.0	10.0
2	7 days	300	220	70	125	80	30	16	12.5	6.0
3	4 days	290	200	85	110	60	25	18	14.0	6.0
4	15 days	260	140	30	110	40	15	14	10.0	3.4
5	3 days	300	220	90	130	80	25	22	18.0	10.0
6	15 days	320	100	40	110	70	10	17	10.0	2.0
7	8 days	180	110	55	90	30	5	12	7.0	2.5
8	4 days	150	60	15	80	20	5	6	4.0	1.8
9	10 days	160	100	70	100	40	15	8	6.5	1.5
10	8 days	300	160	110	120	40	20	16	12.5	7.0
11	10 days	260	200	75	110	70	30	16	13.0	8.0
12	10 days	250	180	60	120	80	35	14	10.0	8.0
13	8 days	120	50	25	60	35	10	8	6.5	1.8
14	2 days	260	200	120	140	90	50	16	14.0	4.0
15	8 days	180	60	15	90	10	5	6	3.0	0.8
16	4 days	130	30	25	80	35	5	6	3.0	1.8
17	10 days	160	90	40	70	20	5	5	3.5	0.6
18	15 days	240	230	160	100	70	50	14	11.2	9.0
19	3 days	220	140	90	140	60	25	14	10.0	4.0
20	4 days	180	85	50	90	30	10	12	7.0	3.0
21	3 days	280	200	140	100	85	40	16	12.5	8.0
22	5 days	190	95	30	85	40	10	10	6.5	2.0
23	12 days	170	120	30	40	25	5	19	18.0	14.0
24	6 days	240	185	70	80	30	25	14	11.0	5.0
25	9 days	140	80	30	90	40	25	6	5.0	1.0

Table No. 3 shows the comparative data in the control series, i.e. Group I. The data include the serum bilirubin, SGPT and SGOT. In all these cases alkaline phosphatase was not estimated routinely as these cases were selected from the other hospital data.

Table 4: Liv.52 Series

Sl. No.	Duration of Jaundice at the time of admission	SGPT Units/ml.			SGOT Units/ml.			Serum bilirubin in mg%			Alkaline phosphatase		
		1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
1.	10 days	160	140	30	90	40	15	13.5	6.0	2.0	12.0	11.5	8.0
2.	10 days	300	120	40	140	40	15	12.0	4.0	2.0	23.9	18.0	14.0
3.	8 days	180	40	25	60	20	5	5.0	1.8	0.8	24.7	16.0	11.0
4.	10 days	245	160	70	50	30	15	12.0	8.0	3.0	10.9	14.0	12.0

5.	5 days	290	120	70	40	25	10	11.9	4.0	2.0	16.5	18.0	12.5
6.	8 days	200	70	30	60	15	10	8.0	3.0	1.6	22.6	16.0	10.0
7.	15 days	346	146	50	80	30	20	24.0	14.0	4.0	18.0	28.0	20.6
8.	8 days	180	40	20	100	25	5	12.0	3.3	0.6	12.6	6.0	10.0
9.	8 days	77	63	24	40	15	5	5.0	3.2	0.8	16.0	10.0	12.0
10.	4 days	185	85	30	80	30	10	10.0	4.0	0.6	12.0	8.0	14.0
11.	8 days	300	140	80	120	56	20	12.0	4.0	1.8	19.5	11.6	10.0
12.	10 days	300	150	60	130	80	30	25.0	12.0	4.0	12.0	16.0	14.0
13.	5 days	260	90	30	110	60	12	16.0	5.0	2.6	28.0	22.0	16.0
14.	10 days	250	110	40	190	40	10	16.0	6.0	2.0	26.8	22.6	14.0
15.	3 days	242	90	40	140	60	15	12.0	4.0	2.0	16.6	18.8	16.0
16.	6 days	280	130	40	110	50	20	14.4	6.0	2.0	25.5	22.0	16.0
17.	15 days	140	40	30	70	20	10	8.0	3.0	1.0	22.0	16.0	14.0
18.	12 days	240	100	30	100	40	10	10.0	3.0	1.0	16.2	14.0	13.5
19.	8 days	190	60	25	80	30	15	6.0	2.0	0.8	18.0	14.0	10.0
20.	8 days	300	120	70	140	40	25	22.4	10.0	4.5	21.2	16.0	12.0
21.	8 days	300	120	40	120	50	10	18.0	10.0	4.0	18.8	16.0	14.0
22.	7 days	260	130	30	110	40	10	16.0	10.0	2.0	32.0	22.0	16.0
23.	8 days	240	80	30	120	30	5	12.8	5.0	2.0	23.5	16.0	12.0
24.	2 days	220	160	40	90	60	15	10.0	6.0	2.0	18.0	17.0	13.0
25.	10 days	180	70	25	80	30	10	12.0	5.0	1.4	15.6	14.0	12.0

Table No. 4 shows comparative data of laboratory investigations in Group II receiving Liv.52 therapy. The data includes serum bilirubin, SGPT and SGOT and serum alkaline phosphatase. Other liver function tests were also done.

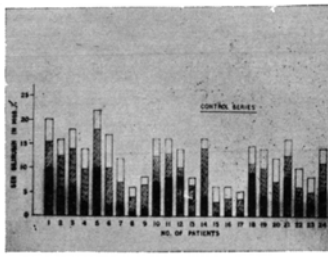
Table 5: Showing time taken to effect improvement in symptomatology

	Group I Control series (25 cases on antibiotics & steroids)	Group II for Schematic comparison (25 cases on Liv.52)	Group III (125 cases on Liv.52)
Loss of appetite	7 days	4 days	5 days
Vomiting	72 hours	40 hours	48 hours
Abdominal pain	(Data not available)		72 hours
Constipation	(Data not available)		5 days
Diarrhoea	(Data not available)		48 hours
Pruritus	(Data not available)		48 hours

In the control series, i.e. Group I, the serum bilirubin was below 2.5 mg% in 9 cases out of 25 (36%) by the 19th day. The serum bilirubin level at intervals in the treated group was significantly reduced (Graphs 1 and 2). by the 19th day the serum bilirubin level was below 2.5 mg% in 19 cases out of 25 (76%) in Group II. In Group III, i.e. the entire series treated with Liv.52, 98 cases (78.4%) had serum bilirubin below 2.5 mg by the 19th day.

In the control series in Group I there were 11 cases out of 25 (55%) where SGPT levels reverted to normal, i.e. below 40 units/ml. This clearly indicates that in this control group parenchymal damage was still active even on the 19th day (Graphs 3 and 4).

Graph No. 1: Control series
Serum Bilirubin in mgs%



In Group II (25 Liv.52-treated cases) the SGPT levels returned to normal, i.e. below 40 units/ml. in 19 out of 25 cases (76%) by the 19th day. In Group III (125 Liv.52-treated cases) the SGPT levels came to normal in 106 cases (84.8%) by the 19th day.

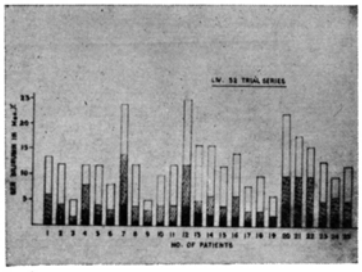
In the control series, Group I, the SGPT levels reverted to normal (15 units/ml.) by the 19th day in 12 cases out of 25 (48%), whereas the corresponding figures in Group II were 21 cases out of 25 (20%) – Graphs 5, 6 - and in Group III (125 cases treated on Liv.52), 98 patients (78.4%) had normal SGOT by the 19th day.

In our series of 125 cases (Group II and Group III) serum alkaline phosphatase was estimated regularly in only 56 cases.

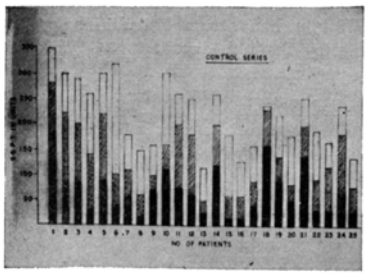
In Group II in 19 cases out of 25 (76%), the level of serum alkaline phosphatase level reverted to normal, i.e. 3-13 K.A. Units by the 19th day.

In Group III out of the 56 cases where the estimations were regularly done, 40 cases (71.5%) reverted to normal by the 19th day. The comparative data for the control series in Group I is not available as this group was selected from other wards.

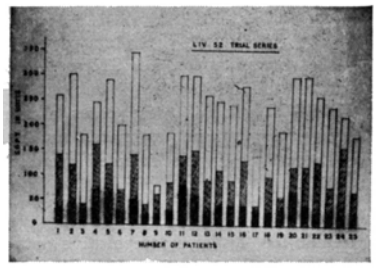
Graph No. 2: Liv.52 trial series
Serum Bilirubin in mgs%



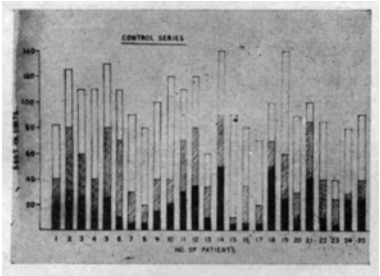
Graph No. 3: Control series
SGPT in Units



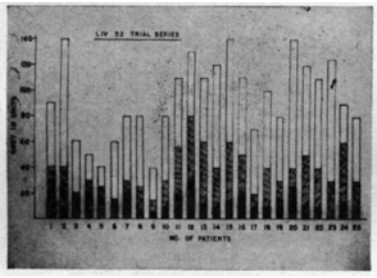
Graph No. 4: Liv.52 trial series
SGPT in Units



Graph No. 5: Control series
SGOT in Units



Graph No. 6: Liv.52 trial series
SGOT in Units



DISCUSSION

Till recently treatment has had little effect in altering the course of an ordinary case of acute infective hepatitis. Till today various drugs have been tried as therapeutic measures and various authors have claimed beneficial results with different drugs, (Sheila Sherlock, 1961).

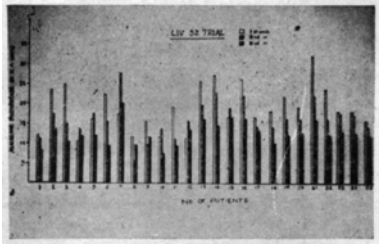
Liv.52, an indigenous proprietary medicine, was claimed to be a hepatic stimulant: Kirtikar and Basu (1933). Sheth *et al.* (1960), Joglekar *et al.* (1963), Karandikar *et al.* (1963), Patel *et al.*(1963), have shown protective effects of Liv.52 against hepatotoxic agents.

Sule and others (1956) showed clinical improvement in diffuse hepatic fibrosis with ascitis.

We were particularly impressed by the clinical improvement shown by Liv.52 in cases of infective hepatitis. Murkibhavi *et al* (1957) have shown the usefulness of the drug in cases of jaundice in dogs.

It appears that the clinical improvement noticed is probably due to the action of the individual components. Marked improvement was seen in relieving the symptoms of nausea, vomiting, loss of appetite and abdominal pain with diarrhoea and constipation. Appetite and a feeling of well-being particularly improved with Liv.52 therapy. Pruritus was significantly relieved.

Graph No. 7: Liv.52 trial alkaline phosphatase in K.A. units



The biochemical investigations of enzyme studies, i.e. SGPT and SGOT and alkaline phosphatase show considerable fall in the Liv.52 cases. The serum bilirubin, as an index of the severity of jaundice, had dropped significantly in the cases treated with Liv.52 (Graphs 1 and 2). In 76% the serum bilirubin dropped below 2.5 mg% as against only in 48% in the control series. This indicates that the cholestasis was greatly relieved, possibly due to reducing the interhepatic oedema and cellular infiltration. It is probable that the cellular regeneration was also rapid. This hypothesis is supported by histological observations done by Joglekar *et al* (1963). They have shown active regeneration with prevention of necrosis and progressive fibrosis.

The exact mechanism of the protective effect of Liv.52 remains still unexplained and requires further long-term study with individual components and various combinations of drugs in Liv.52.

Similarly, it would be interesting to note the long-term study of follow-up observations in Liv.52-treated cases of infective hepatitis, particularly to find out the incidence of post-hepatitis syndrome, sub-acute infective hepatitis. It is significant that none of the patients in this present series treated with Liv.52 has so far reported back with the above.

In the present series of 125 cases, 4 cases were in coma. They received Liv.52 therapy along with steroids, antibiotics and routine regimen. Two of these cases recovered.

None of the cases treated with Liv.52 showed any untoward toxic symptoms.

SUMMARY

A three-year study of 150 cases of infective hepatitis was undertaken. The clinical improvement in symptoms is discussed.

An attempt is made to show the comparative improvement in certain well-known liver function tests like serum bilirubin, enzyme, SGPT, SGOT and alkaline phosphatase.

ACKNOWLEDGEMENT

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