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Liv.52 Therapy in Viral Hepatitis

Patel, G.T., *M.D.*, **Mruthyunjayanna, B.P.,** *M.D.*, **Seetharam, T.D.,** *M.B.,B.S.* and
Channe Gowda, A.C., *M.B.,B.S.,*
Medicine Unit, Victoria Hospital and Bangalore Medical College, Bangalore, India.

Viral hepatitis as observed in our country is frequently of prolonged duration with a predisposition to complications like post-hepatitis cirrhosis, chronic cholestasis, subacute necrosis and hepatic failure. Rarely the disease is fulminant and death ensues in the acute phase. Such cases are commonly those in whom a superimposed nutritional factor increases the susceptibility of the liver cells to necrosis due to direct deficiency in persons taking a poor diet lacking in animal protein, as it occurs commonly in Asia and Africa (Davidson, 1968).

The therapy of viral hepatitis assumes immense importance as death from this disease is much more common in India due to the poor standard of nutrition than it is in the West, though natural clinical cure may occur with or without residual liver cell damage. Hence the problem of therapy of viral hepatitis demands an ideal drug with the essential requisites of quicker recovery and convalescence without residual liver cell damage. In quest of such a drug we were prompted to undertake a study to evaluate the efficacy of Liv.52, an indigenous drug which has been widely used for more than a decade and has much published data heralding its beneficial effect in liver disorders.

REVIEW OF LITERATURE

A series of long-term experimental studies carried out by various workers substantiate the protective and regenerative action of Liv.52 on liver against a battery of hepatotoxins (Murkibhavi and Sheth, 1957; Sheth *et al,* 1960; Joglekar *et al.,* Patel *et al.,* Karandikar *et al.,* 1963; Qazi, 1965; Captain and Syed, 1966). Joglekar and Leevy (1970) confirmed this effect in albino rats by using the latest methods — Indocyanine Green clearance and Autoradiographic patterns. Srinivasan and Balwani (1968) noted the growth-promoting effect of Liv.52 in rats, mice and guinea pigs.

Clinically, Liv.52 has been tried extensively by various workers in cirrhosis of the liver and infective hepatitis. By using different parameters of liver function tests, these workers have consistently confirmed that Liv.52 accelerates the clinical and biochemical recovery, (Sule *et al,* 1956; 1957; Patrao, 1957; Sheth *et al,* 1960; Menon and Ravindran, 1966; Jaffari and Shyamaraj, 1969; Arora, 1969). Liv.52 has been found to be beneficial in infantile cirrhosis (Mathur, 1957; Vyas, 1960; 1963; Paulose, 1963; Sheth, 1968). Prasad *et al,* (1969; 1971) and Dayal *et al,* (1971) observed remarkable improvement in cases of viral hepatitis and malnutrition after Liv.52 therapy. Liv.52 has been found to be a good anabolic agent (Damle and Deshpande, 1966; Kale *et al,* 1966; Sheth, 1968; Mathur, 1969; Kulkarni and Joglekar, 1970). Mukerjee and Dasgupta (1971) observed that in viral hepatitis Liv.52 improved the bodyweight, reduced the period of illness and residual liver damage.

PHARMACOLOGY AND COMPOSITION

Liv.52 (Himalaya Drug Co. Private Ltd.) is a herbal proportion and is found to have anabolic, aperient, diuretic, stomachic effects with protective and regenerative action on liver. The drug is claimed to be non-toxic in doses upto ten times the therapeutic dose. Each tablet has processed extracts of various plants in varying proportions, namely:

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

MATERIAL AND METHODS

Fifty two cases of viral hepatitis (including three cases of post-transfusion hepatitis and one case of syringe hepatitis) were randomised into two groups, A and B. Of these, 25 cases receiving antibiotics and steroids acted as a control, Group A. The other 27 cases receiving only Liv.52 (two tablets thrice daily) were included in Group B for a schematic comparison with the control group.

Table I, shows the incidence and age and sex in the present study of 52 cases.

Table I: Age groups

11-20 years		21-30 years		31-40 years		41-50 years		51-60 years	
16		20		9		5		2	
M	F	M	F	M	F	M	F	M	F
10	6	13	7	6	3	4	1	1	1

Table II, shows the symptomatology of viral hepatitis observed in the 52 cases studied.

Table II

	Symptoms	Total no. of cases	Group A		Group B	Incidence
1.	Jaundice	All cases	(25	+	27)	100.0
2.	Loss of appetite	45	(24	+	21)	85.4
3.	Loss of weight	41	(25	+	16)	78.7
4.	Abdominal pain	20	(11	+	9)	38.4
5.	Constipation	17	(10	+	7)	32.6
6.	Nausea	13	(8	+	5)	25.0
7.	Vomiting	9	(6	+	3)	17.3
8.	Fever	8	(4	+	4)	15.4
9.	Malaise	8	(5	+	3)	15.4
10.	Pruritus	7	(3	+	4)	13.4
11.	Diarrhoea	5	(3	+	2)	9.6
12.	Cough	4	(2	+	2)	7.7
13.	Bleeding	3	(2	+	1)	5.8
14.	Hiccup	2	(1	+	1)	3.8
15.	Restlessness	2	(2	+	Nil)	3.8
16.	Comatose state	2	(2	+	Nil)	3.8
17.	Arthralgia	1	(Nil	+	1)	1.9

Detailed history taking and clinical examination in respect of each case was done. Liver function tests (including Serum bilirubin, SGPT, SGOT, Serum alkaline transaminase and thymol turbidity), ESR, weight recording and urine examination were carried out in each case and repeated after 14 days of treatment. Needle biopsy of the liver was done in some cases before and after the treatment.

OBSERVATION AND RESULTS

(a) *Jaundice*: All the patients had jaundice at the time of admission. In control group (A) four cases had deep jaundice of which two cases were restless and the other two cases were pre-comatose.

(b) *Loss of Appetite*: Appetite improved on an average of nine days in control group (A) and five days in group B.

(c) *Loss of weight*: In group A (control), marked loss of weight occurred in all the 25 cases with an average loss of 4.1 kg. as against 1.6 kg. in group B (Liv.52). In group B, loss of weight occurred in 16 out of 27 cases, in two cases bodyweight remained fairly constant and in 9 cases (33.3%) an average gain of 1.1 kg. was recorded.

(d) *Abdominal Pain*: Relief of pain was noticed after an average duration of 5 days in group A, as against 3 days in group B.

(e) *Nausea and Vomiting*: Nausea was relieved in an average duration of four days in group A as against three days in group B, and vomiting stopped within three days in group A as against two days in group B.

(f) *Constipation*: In control group (A), constipation was present in 10 out of 25 cases and needed mild laxatives or enemata. In group B, constipation was present in 7 out of 27 cases and bowel regularisation resulted within 4 days of Liv.52 therapy, without any recourse to laxatives or enemata.

(g) *Pruritus*: In group A, pruritus continued upto six days and required antihistaminics to alleviate itching. In group B, with Liv.52 therapy remarkable relief of itching resulted within two days.

Table III, shows average duration for improvement in symptomatology.

Table III: Average duration for improvement in Symptomatology

Symptoms	Group A	Group B
Loss of appetite	9 days	5 days
Abdominal pain	5 days	3 days
Nausea	4 days	3 days
Vomiting	3 days	2 days
Pruritus	*6 days	2 days
Constipation	**7 days	4 days

* After antihistaminic therapy.
** After mild laxative or enemata.

i) *Serum bilirubin*: After 14 days of treatment, serum bilirubin was below 5 mg% in 28 per cent of cases in control group (A) as against 74 per cent in Liv.52 series (B).

ii) *Serum transaminases*: After two weeks of therapy, the SGPT was below 100 units/ml in 24 per cent cases in control group (A) as compared to 55.6 per cent in Liv.52 series and the SGOT was below 50 units/ml in 44 per cent of cases in group A as against 77.8 per cent in group B.

BIOCHEMICAL

iii) *Serum alkaline phosphatase*: This is a more sensitive index of bile stasis than the serum bilirubin level. After 14 days of therapy, serum alkaline phosphatase levels reverted to normal in 32 per cent of cases in control group (A) as compared to 63 per cent in Liv.52 series (B).

iv) *Thymol turbidity*: Thymol turbidity reflects inflammatory activity rather than hepatocellular damage and continued elevation may be a reflection of portal zone infiltration. After therapy, the thymol turbidity level was below 15 units in 48 per cent of cases in control group (A) as compared to 8.15 per cent in Liv.52 series (B).

v) *Erythrocyte Sedimentation Rate*: The ESR is high in the pre-icteric phase, falls to normal with the development of jaundice, rises again as jaundice subsides and return to normal with complete recovery; a sustained high ESR indicates continuing hepatic inflammation *(Sherlock, 1968). After two weeks of therapy, ESR was below 15 mm/hour in 36 per cent of cases in control group (A) as against 77.8 per cent in Liv.52 series (B).

Tables IV and V show the comparative data of laboratory investigations in Group A and Group B, respectively. Values noted after admission are labelled as 1st and those after therapy of 14 days as 2nd. The data include the duration of jaundice at the time of admission, serum bilirubin, transaminase levels and serum alkaline phosphatase. Other liver function tests were also done.

Table IV: Control Series (Group A)

Case No.	No. of days of Jaundice prior to admission	Serum bilirubin		SGPT		SGOT		Serum Alk. Phosphatase K.A. Units/100 c.c.	
		1st	2nd	1st	2nd	1st	2nd	1st	2nd
1.	8	15.5	8.1	290	175	65	20	19.4	22.6
2.	12	21.0	18.0	185	110	70	25	21.1	18.4
3.	4	11.0	4.5	170	105	75	55	20.4	14.2
4.	6	16.1	12.0	250	170	70	30	17.3	11.5
5.	7	18.2	12.3	386	210	110	56	19.8	14.6
6.	10	9.0	3.4	150	105	90	65	24.5	7.2
7.	13	14.0	11.2	260	210	110	74	28.4	16.1
8.	4	13.0	4.8	170	40	80	30	29.8	11.3
9.	6	15.4	12.3	370	210	105	65	19.5	12.0
10.	8	9.2	4.7	112	35	65	22	30.2	17.4
11.	4	6.1	3.0	120	40	70	30	27.0	22.6
12.	8	6.4	4.1	135	70	80	55	17.0	14.0
13.	11	10.4	6.6	160	125	95	30	28.0	15.2
14.	3	13.8	10.2	210	160	135	60	31.2	27.3
15.	9	16.1	13.0	240	175	115	80	26.8	23.1
16.	5	11.2	4.8	180	105	80	42	14.2	4.4
17.	3	9.6	8.4	260	110	125	85	17.3	8.5
18.	4	12.6	10.2	290	185	120	65	12.8	16.6
19.	7	16.4	12.0	310	210	128	75	16.4	25.0
20.	8	8.5	6.0	136	64	65	34	12.0	17.1
21.	2	15.0	11.5	258	205	135	80	18.2	14.0
22.	9	7.4	4.5	132	75	85	40	19.1	6.3
23.	6	13.0	10.4	320	174	75	30	14.4	21.0
24.	10	15.2	13.6	245	190	105	75	14.0	23.3
25.	14	14.5	9.5	240	126	110	65	29.4	11.3

Table V: Liv.52 Series (Group B)

Case No.	No. of days of jaundice prior to admission	Serum Bilirubin in mg.%		SGPT Units/ml.		SGOT Units/ml.		Serum Alk. Phosphatase K.A. Units/100 c.c.	
		1st	2nd	1st	2nd	1st	2nd	1st	2nd
1.	9	12.1	4.4	175	70	90	40	16.4	13.0
2.	13	17.8	6.0	250	40	115	42	17.6	12.5
3.	4	11.0	3.5	180	32	90	25	15.2	8.0

4.	5	12.3	4.6	280	90	110	30	11.0	12.2
5.	6	15.2	6.0	290	130	100	44	26.0	14.8
6.	5	12.6	4.1	250	115	120	85	25.5	12.0
7.	8	12.5	3.6	170	48	92	24	12.6	9.0
8.	5	16.0	4.8	250	105	110	25	28.0	16.2
9.	8	18.0	8.2	290	120	125	45	19.3	10.5
10.	11	12.5	3.0	378	115	158	55	24.9	13.0
11.	7	13.6	2.8	250	132	128	22	22.4	11.0
12.	14	21.0	4.8	398	125	90	32	28.2	17.8
13.	3	12.0	3.2	230	40	138	54	16.6	12.2
14.	10	13.2	5.8	155	130	80	35	17.2	12.1
15.	8	5.3	1.7	170	44	95	20	26.0	14.5
16	9	12.6	7.4	250	152	75	34	12.0	14.9
17.	7	8.4	2.8	190	72	84	20	21.2	15.0
18.	6	6.8	3.1	80	65	75	12	18.6	11.0
19.	5	5.8	3.2	68	53	60	22	17.3	12.8
20.	4	11.2	3.8	180	75	80	36	15.0	7.2
21.	10	21.4	11.8	290	150	124	70	31.0	16.8
22.	7	12.8	4.1	310	142	118	56	20.6	11.5
23.	10	20.9	16.4	440	92	170	40	17.0	5.8
24.	14	7.8	3.2	145	38	96	22	23.0	12.7
25.	11	11.3	2.9	336	90	108	40	16.8	13.9
26.	8	7.2	1.8	180	64	85	26	19.3	15.0
27.	3	10.4	4.6	350	144	98	64	18.8	16.5

Table VI shows comparative data of thymol turbidity and ESR in the two Groups A and B, on admission and after 14 days of therapy.

Table VI: Comparative Data of Thymol Turbidity and ESR in the Groups "A" and "B" — Before and after therapy

		Thymol Turbidity Units						ESR Westergren, mm/hour					
	No. of patients	0-5	5-10	10-15	15-20	20-30	Over 30	0-5	5-10	10-15	15-20	20-30	Over 30
Group A	On admission	—	4	7	5	6	3	2	1	5	6	9	2
	After therapy	3	5	4	7	2	4	2	4	3	7	6	3
Group B	On admission	—	3	4	10	8	2	1	2	4	8	10	2
	After therapy	3	11	8	2	1	2	4	10	7	3	1	2

Table VII shows comparative evaluation of biochemical improvement after therapy.

Table VII: Comparative Evaluation of Biochemical Improvement after Therapy.

Values after two weeks of therapy		Group A (25 cases)		Group B (27 cases)	
		No. of cases	Percentage %	No. of cases	Percentage %
1.	Serum bilirubin (below 5 mg.%)	7	28	20	74.0
2.	SGPT (below 100 units/ml.)	6	24	15	55.6
3.	SGOT (below 50 units/ml.)	11	44	21	77.8
4.	Serum alkaline phosphatase (between 3-13 K.A. units)	8	32	17	63.0
5.	Thymol turbidity (below 15 units)	12	48	22	81.5
6.	ESR (Westergren, below 15 mm/hour)	9	36	21	77.8

DISCUSSION

In Liv.52 treated cases, improvement in symptomatology was remarkable as compared to the control group. After Liv.52 therapy, patients had a subjective sense of well-being and appetite improved in all these cases. Relief from nausea, vomiting, abdominal pain constipation and pruritus was rapid. The laxative effect of Liv.52 is a desirable action as it tends to lessen the pre-disposition to comatose state. None had any restlessness or precoma in Liv.52 series. In control series, two cases were restless and two cases were precomatose.

During this illness, the adult patient loses about 10 lb. in weight (Sherlock, 1968). Marked loss of weight occurred in all the cases of control group with an average loss of 4.1 kg. as against 1.6 kg. in Liv.52 series. In Liv.52 series, in two cases bodyweight remained fairly constant and in nine cases (33.3 per cent) average gain in weight of 1.1 kg. was recorded. This is an advantage in treating viral hepatitis and can be attributed to the anabolic effect of Liv.52 (Damle and Deshpande, 1966; Kale *et al,* 1966; Mathur, 1969; Kulkarni and Joglekar, 1970;; Mukerjee and Dasgupta, 1971; Dayal *et al,* 1971).

The serum bilirubin dropped below 5 mg% in 74 per cent of cases in Liv.52 series as compared to 28 per cent in control series. Hyperbilirubinaemia as an index of severity of jaundice remarkably regressed in Liv.52 treated cases. Serum alkaline phosphatase, which is a more sensitive index of bile stasis than the serum bilirubin level, remarkably reverted to normal in 63 per cent of cases in Liv.52 series as against 32 per cent in control series.

These observations affirm the efficacy of Liv.52 in clearing up the intrahepatic cholestasis, possibly by reducing the intrahepatic oedema and cellular infiltration in portal tracts. The protective and regenerative action of Liv.52 on liver (which has been confirmed by various experimental, clinical, biochemical and histopathological studies) may also help to relieve the cholestasis. Serial liver biopsy was possible in a limited number of cases in our series and the histological study revealed that the initial acute hepatic cell necrosis was restored to the normal reticulin framework of the liver lobule after Liv.52 therapy.

Serial transaminase estimations showed considerable fall after Liv.52 therapy. SGPT was below 100 units/ml in 24 per cent of cases in control series as against 55.6 per cent in Liv.52 series and SGOT was below 50 units/ml in 44 per cent of cases in control series as compared to 77.8 per cent Liv.52 series.

As extremely sensitive indices, the transaminase levels reflect the extent of hepatic injury and continued elevation suggests that the disease is not yet resolved. Taken in conjunction with the improvement in symptomatology, serum bilirubin, alkaline phosphatase and hepatic histology, the rapid return of transaminase levels to normalcy after Liv.52 therapy strongly supports the protective and regenerative action of Liv.52 in viral hepatitis and affirms the observations made earlier.

After therapy, thymol turbidity was below 15 units in 48 per cent of cases in the control series, as compared to 81.5 per cent in Liv.52 series, indicating the efficacy of Liv.52 in reducing inflammation and also residual hepatic damage. Rapid fall of turbidity levels in Liv.52 series also reflects that complications (like chronic cholestasis and post-hepatic cirrhosis, in which the turbidity levels remain very high) are less likely after Liv.52 therapy. ESR values are also parallel with the turbidity levels. ESR was below 15 mm/hour (Westergren) in 36 per cent cases of control series as against 77.8 per cent in Liv.52 series. The rapid return of ESR to normalcy confirms the

observations already made that Liv.52 reduces inflammation, promotes a rapid and uneventful recovery, thereby preventing residual hepatic damage. Our observations affirm those of Mukerjee and Dasgupta (1971) who studied cases of viral hepatitis after Liv.52 therapy by Bromsulphthalein test and liver biopsy, arriving at a similar conclusion.

SUMMARY

A study to evaluate the efficacy of Liv.52 in viral hepatitis was undertaken. In all 52 cases were studied — 25 cases served as control and 27 cases received Liv.52.

Clinical, biochemical (based on serum bilirubin, SGPT, SGOT, alkaline phosphatase, thymol turbidity and ESR values) and histological recovery was rapid and uneventful in Liv.52 - treated cases as compared to the control series.

We feel that Liv.52 richly deserves to be used as a routine treatment in all cases of viral hepatitis — particularly in our country, as death from this disease is much more common (because of poor standard of nutrition which increases the susceptibility of liver cells to necrosis) than it is in the Western countries.

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