

Liv.52 Therapy in Cases of Malnutrition, Infective Hepatitis, Infantile Cirrhosis and Anorexia (A Clinico-Pathological Study)

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Other workers in different parts of our country have tried Liv.52, and assessed its usefulness and value in various hepatic disorders; they have also studied the extent of hepatic damage in the above mentioned conditions and its reversibility, if any. We also wished to give Liv.52 a fair trial and record our observations.

Liv.52, a product of The Himalaya Drug Co. Pvt. Ltd., is stated to contain several indigenous drugs and compounds reputed to be useful in the treatment of liver affections.

Mathur⁷ has recorded a good clinical response in cirrhosis of children. Sule and Sathe¹⁷ observed marked clinical improvement and improvement in liver function tests by the use of Liv.52 in cases of severe hepatic damage. Patro⁹ also found it very useful in cases of hepatic damage. Sheth *et al.*,¹⁶ experimentally showed considerable protection against hepatic damage. Joglekar *et al.*,⁴ Patel and Sadre⁸ and Karandikar *et al.*⁶ also noted similar observations.

Sheth *et al.*¹⁶ studied its effect in cases of anorexia and found that 68% of the patients showed good response. Damle and Deshpande¹ also found good clinical response in patients who were not ordinarily gaining weight.

Paulose¹⁰ noted great clinical improvement in children suffering from infantile cirrhosis. Sheth¹⁴ observed "definite decrease in fibrosis as well as change in the architecture of the liver in some cases of infantile cirrhosis". Jaffari and Shyamraj³ observed good clinical response in cases of infective hepatitis.

Prasad and Tripathi¹¹ noted greatly increased appetite in patients suffering from malnutrition and infective hepatitis.

OUR PLAN OF STUDY

A total of 130 patients comprises the material for the study; 65 were of malnutrition, 42 of anorexia without malnutrition, 14 had infective hepatitis and only 9 were with cirrhosis. All patients were collected from the out-patient department of S.N. Hospital, Agra and from 3 peripheral centres.

A detailed history of every patient regarding past illness, milestones and immunization was taken. Their feeding habits and caloric intakes were noted. A thorough clinical examination of each patient was made.

LABORATORY INVESTIGATIONS

- (i) Urine for bile pigment and bile salts.
- (ii) Haemoglobin percentage
- (iii) Total and differential white blood cell counts.

- (iv) Total serum protein, albumin and globulin
- (v) Thymol turbidity, flocculation and zinc sulphate turbidity
- (vi) Serum bilirubin
- (vii) Van denberg reaction
- (viii) Icteric index
- (ix) Serum alkaline phosphatase
- (x) Liver biopsy
- (xi) Mantoux test (if needed)
- (xii) Skiagram of the chest.

Proved tubercular cases were excluded.

TREATMENT

Liv.52 was administered in the doses recommended viz., 5 to 10 drops three times a day to infants and 10 to 20 drops 3 times a day to older children. Supportive measures were also adopted as required. Steroids were not given to any child.

Regular follow-up of all patients was made and investigations were all repeated 3 to 4 weeks later while biopsy was repeated after 4 to 6 weeks.

1. *Malnutrition*: Sixty five patients suffering from malnutrition were thus studied. The main aetiological factor was underfeeding. Fifty four children has been improperly fed right from birth and their weaning was delayed. In 8 of them the feeding was defective after the age of one year, and in three the cause for malnutrition could not be ascertained.

The associated presenting features were: Low grade fever in 45 patients, loose motions in 36, loss of appetite in 42, increasing pallor in 21 and distention of the abdomen in 8 of the children. History of recurrent attacks of upper respiratory tract infection was available in 28 patients. Bronchopneumonia in 6, measles in 4 and pertussis in two.

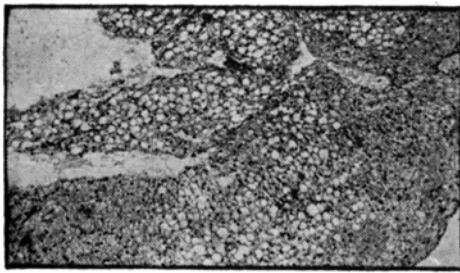
Table 1: Showing the age incidence

Age	Malnutrition	Cirrhosis	Infective hepatitis	Anorexia
Upto 1 year	25	Nil	Nil	18
1 to 2 years	11	5	3	24
2 to 5 years	20	3	6	–
5 to 10 years	8	1	4	–
10 years over	1	–	1	–
Total	65	9	14	42

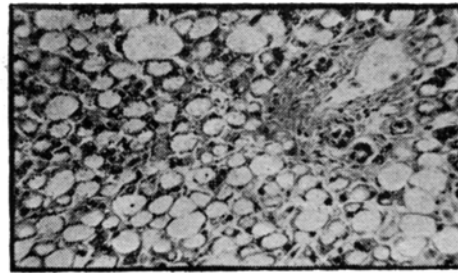
Developmental milestones were found delayed in 35 children. In 20 of them they were delayed after the first year of life. Forty four of the children belonged to the low socio-economic group on low income. Pallor was observed in 45 and lymphadenopathy in 32 of the patients.

Liver function tests were made on all patients. Hypoalbuminaemia was detected in 51 patients while total serum proteins were low in 42 patients. Other tests for liver function did not show any significant derangement.

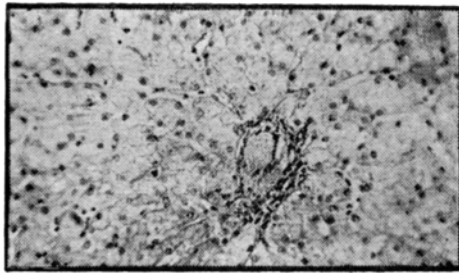
Liver biopsy was done on 48 patients and the liver tissue was inadequate in 5 for diagnosis. Histopathologically protein depletion was seen in 29 (see Photographs 3 and 4), fatty changes in 16 (see Photographs 1 and 2), parenchymatous swelling in 8; dilatation of sinusoids was reported in 15 patients (see Photograph 5). Infiltration of mononuclear cells of varying degrees was reported in 22 patients. Periportal fibrosis was noticed in 18 children.



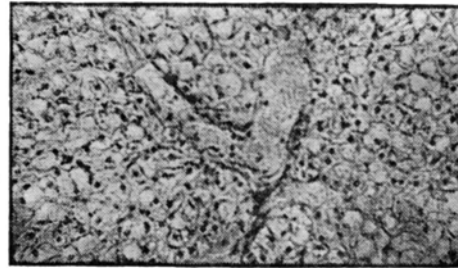
Liver Biopsy: showing marked fatty infiltration (H & E x 50)
PHOTOGRAPH: 1 (Slide 72-1309)



Liver Biopsy: showing fatty infiltration (H & E x 215)
PHOTOGRAPH: 2 (Slide 72-1309)

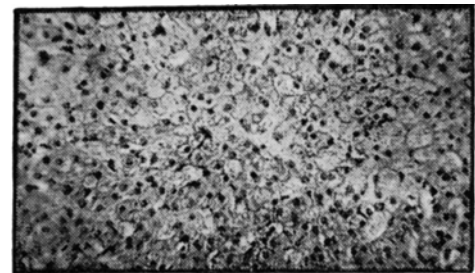


Liver Biopsy: showing mild protein depletion (H & E x 215)
PHOTOGRAPH: 3 (Slide 72-499)



Liver Biopsy: showing marked protein depletion (H & E x 215)
PHOTOGRAPH: 4 (Slide 72-1334)

Twenty nine patients could be followed-up, of whom 23 showed definite improvement in appetite and weightgain. Liver size diminished appreciably in 17. Rise in the total serum proteins was noticed in 21 children. The rise in albumin fraction was more than that in globulin. Thymol turbidity and Zinc sulphate turbidity tests showed improvement in 18 of the children.



Liver Biopsy: showing sinusoidal dilatation (H & E x 215)
PHOTOGRAPH: 5 (Slide 72-1335)

Repeat biopsy was possible on 19 patients. There was improvement in the histopathological picture as shown by a diminution in fatty infiltration in the case of 8 patients after 4 weeks. Hepatic cells varying in size and shape and from disorderly arrangement, returned to more regular arrangement in 5 patients, and cytoplasmic repletion was also noted in them.

Infective hepatitis: Fourteen children with infective hepatitis were studied. The common presenting features were: fever, marked loss of appetite, distention of the abdomen, yellowish discoloration of the skin and the passing of dark coloured urine. There was a past history of bronchopneumonia in 3 and of measles in 2. History of underfeeding was obtained in 5 children and weight-loss was noted in 2. In one case, another sib had suffered from jaundice in the recent past.

Table 2: Showing the presenting features in these patients

Symptoms	Malnutrition	Cirrhosis	Infective hepatitis	Anorexia	Total
Fever	45	7	14	—	66
Loss of appetite	42	9	14	42	107
Distention of the abdomen	8	9	9	—	26
Increasing pallor	21	4	—	—	25
Cough	28	3	1	—	32
Loose motions	36	1	—	—	37
Yellowish discoloration of the	—	6	12	—	18

skin					
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Jaundice in varying degrees was present in all the cases. It disappeared after one week's treatment in 6, and after 3 weeks in 7; but it took over 4 weeks to disappear in one patient. Liver size diminished appreciably in 10 patients. There was a tendency in the liver function tests returning to normal after 2 weeks in 5 patients and 3 weeks in 8 and after 4 weeks in one. There was improvement in appetite in all of them except one, 10 days after therapy. Rise in haemoglobin percentage was also noticed in 4 children.

Liver biopsy was done on 7 patients. Post-necrotic cirrhosis was seen in two, in one of whom the changes were those of early cirrhosis. In one, the liver histopathology was compatible with that of viral hepatitis (cholestatic type), and in another marked swelling of liver parenchyma, obliteration of sinusoids with fibroblastic activity were detected. Repeat biopsy was not possible in any of these patients.

Table 3: Showing the socio-economic status of the patients' families and the symptoms found in the patients

S.E. Status	Income per head	Malnutrition	Cirrhosis	Infective hepatitis	Anorexia	Total
Low	Less than Rs. 50/- p.m.	44	3	4	11	62
Middle	Rs. 50-to Rs. 100/- p.m.	15	5	7	17	44
High	More than Rs. 100/- p.m.	6	1	3	14	24

Table 4: Showing the various signs observed in the patients

Signs	Malnutrition	Cirrhosis	Infective hepatitis	Anorexia	Total
Pallor	21	6	–	6	33
Weight-loss	65	7	4	11	87
Jaundice	–	8	14	–	22
Lymphadenopathy	16	5	2	9	32
Oedema	5	2	–	–	7
Anaemia	28	4	1	16	49

Cirrhosis: Nine children with cirrhosis aged between 9 months and 3 years (8 males and one female) were studied. Weakness, distention of abdomen, fever, cough and puffiness over the face were the presenting features. Loss of appetite was generally present. Family history of tuberculosis was detected in 3 children. A history of under-feeding was noted in 6. Development milestones were delayed in 4. History of cirrhosis was obtained in another sib in the case of 2 children.

Jaundice of moderate to severe degree was present in all the patients. Consciousness had been altered in one, while another was brought in deep coma. The liver was 2.5 to 3.5 cm enlarged in 4, 5-6 cm in three and 8 cm in one. In one other child, it was 11 cm below the subcostal margin. The consistency was firm. The general condition remained the same after 3 weeks of treatment in 5 except that the liver regressed in size by 0.5 cm. In two other there was slight improvement in appetite and the liver regressed by 1 cm. However, there was no appreciable biochemical improvement in the liver function tests.

Liver biopsy was made on 7 patients but repeat biopsy was possible only in two. In one of them it was done twice subsequently. In four patients post-necrotic cirrhosis was diagnosed histopathologically while in two diffuse hepatic cirrhosis was reported. In one child, a swelling of the liver parenchyma, scanty periportal fibrosis with infiltration of mononuclear cells were reported. In this patient repeat biopsy showed evidence of periportal fibrosis with increased infiltration of mononuclear cells. The third repeat biopsy on the same patient showed increased fibrosis. In the second patient also, fibrosis had increased in the repeat biopsy. Six children who were in the advanced stages expired.

Anorexia: In this series 42 patients were studied. Only those who were free from infection and infestations were included in the trial. Their main complaints were "reluctance for food", "loss of appetite", "has to be forced for feeding", "disinclination for feeds" etc.

Besides the routine investigations, skiagrams of the chest and stool examinations were done on all patients. Liv.52 was administered in the recommended doses. Weight was recorded before and after therapy. Enquiries regarding appetite were made.

Twenty normal children in the corresponding age groups served as control. The gain in weight was compared with those who received Liv.52 therapy.

Although there were considerable variations in the gain in weight in the Liv.52 and control groups, the mean weight-gain was comparatively higher in patients who received Liv.52 and their appetite had also noticeably improved after 10 to 15 days of therapy.

Discussion: Malnutrition: In cases of malnutrition improvement in liver function tests has been reported, after Liv.52 therapy, by many workers. They have also reported improvement in appetite and gain in weight in a significant number of cases. Similar observations were made by Sheth *et al.*, in 1963 and Damle and Deshpande in 1966. Kale, Kulkarni, Joglekar and Balwani in 1966 observed "Liv.52, an indigenous proprietary drug exerts a beneficial effect on growth...". Prasad and Tripathi (1969) and Dayal *et al* (1970) reported with similar observations. In the present study on 65 children the gain in weight and improvement were more or less constant features. After 3 to 4 weeks of Liv.52 therapy, these patients showed improvement in liver function tests. Histopathological changes also showed signs of regression. Fatty infiltration diminished and the disorderly arrangement of hepatic cells returned towards more regular arrangement. It is justifiable to conclude that Liv.52 helps in fighting malnutrition in children. Good diet and correct technique of feeding are other important factors.

Table VI (a): Showing the results of treatment in patients with Anorexia (Up to 1 year)		
No. of patients	Weight gain in gms after 15 days' treatment with Liv.52	
1	70	Range 70 to 350 gms Mean 152 gms
2	100	
2	110	
2	130	
4	150	
2	180	
2	210	
2	250	
1	350	
CONTROL CASES		
4	70	Range 70 to 265 gms Mean 146 gms
2	140	
2	185	
2	265	

Table VI (b): Anorexia Patients (Over 1 year; upto 2 years)		
No. of patients	Weight gain in gms after 15 days' treatment with Liv.52	
1	50	Range 50 to 250 gms Mean 99.5gms
1	10	
1	30	
7	50	
1	90	
3	100	
1	120	
4	150	
1	180	

1	200	
1	220	
2	250	
CONTROL CASES		
2	48	Range 481 to 16 gms Mean 90 gms
2	90	
2	96	
2	100	
2	116	

Sl.No.	Total No. of follow-up cases	Infective hepatitis (14)			Cirrhosis (7)			Malnutrition (29)			Anorexia (42)		
		Improvement	Deterioration	No change	Improvement	Deterioration	No change	Improvement	Deterioration	No change	Improvement	Deterioration	No change
1	General condition	14	–	–	2	5	–	24	2	3	40	–	2
2	Gain in weight	14	–	–	4	1	2	26	1	2	39	1	2
3	Appetite	11	–	3	1	5	1	27	–	2	41	–	1
4	Jaundice	14	–	–	2	5	–	–	–	–	–	–	–
5	Liver size	14	–	–	1	6	–	18	–	11	–	–	42
6	Liver consistency	14	–	–	–	6	1	4	–	25	–	–	42
7	Spleen	–	–	–	–	5	2	–	–	–	–	–	–
8	Total protein	9	–	5	2	4	1	20	6	3	–	–	–
9	Thymol turbidity	10	1	3	3	3	1	19	7	3	–	–	–
10	Thymol flocculation	10	–	4	3	4	–	20	6	3	–	–	–
11	ZnSO ₄ turbidity	11	1	2	2	4	1	18	9	2	–	–	–
12	Serum bilirubin	14	–	–	2	5	–	–	–	–	–	–	–
13	Van denberg test	14	–	–	2	5	–	–	–	–	–	–	–
14	Icteric index	14	–	–	2	4	1	–	–	–	–	–	–
15	Alkaline phosphatase	10	1	3	–	6	2	18	9	2	–	–	–

Infective hepatitis: Menon and Ravindran (1966) studied the value of Liv.52 in patients with infective hepatitis during an outbreak at Kottakal, Kerala State. They were of the opinion that "Liv.52 helps in quicker recuperation by the liver". Then Jaffari and Shamraj (1969) reported that Liv.52 clears jaundice earlier, improves the appetite and induces a sense of well-being Arora (1969) stated that Liv.52 ads "materially to the patient's comfort and accelerates recovery". In our present study, 12 patients were treated with Liv.52. The appetite in all but one of them improved appreciably. Jaundice regressed and the size of the liver got reduced. Liver function tests improved within 10 days of treatment. There was also a marked increase in the general sense of well-being.

Infantile cirrhosis: Mathur (1957) tried Liv.52 on eight children with cirrhosis "found it to be very effective without any toxic side effects and complications".

Sheth *et al.*, (1960) observed a protective action of Liv.52 on liver cells in experimental animals. Hepatic damage produced experimentally in rats by carbon tetrachloride, showed improvement after Liv.52 therapy. Patel and Sadre (1963); Karandikar *et al.*, (1963) reported similar observations. Vyas (1963) treated 70 patients with cirrhosis with Liv.52 and compared the results with 67 controls, and found "the addition of Liv.52 to conventional therapy increases the cure-rate from 1% to 21%." Sathe and Sule (1967) observed an increase in total proteins and return of liver function tests to normal. In 1968 Sheth *et al.*, again reported, "functional improvement to be noteworthy though histopathological changes did not revert completely to normal. Histopathological changes showed a definite decrease in fibrosis and a change in the architecture of the liver, indicating improvement in some cases".

In our present series of 9 cases, six expired and therefore only 3 were followed up. In one, there was regression of jaundice after 2 weeks but there was little improvement in size and consistency of the liver and liver function tests. In 2 other patients there was no clinical improvement, as there was no regression of jaundice and liver function tests also did not return towards normalcy. Histopathologically also progression of disease was confirmed.

Anorexia: Sheth *et al.*, (1963)¹⁶ studied 100 patients who had anorexia as a major presenting symptom, and reported that Liv.52 "contributed to a significant improvement in appetite in a large number of cases". Indira Bai *et al.*, (1971)² after a trial of Liv.52 on 100 children observed "with the improvement in appetite there was a marked feeling of well-being followed by gain in weight..." Saxena (1971) noted "improvement in appetite, a subjective feeling of well-being and gain in weight in 85.25% cases". She concluded that Liv.52 has a "definite and well established place in therapy of anorexia of varied aetiology..." Seshachari (1971)¹³ observed that "Liv.52 has a definite appetite stimulating effect in children... irrespective of the illness from which they were suffering."

In our own series of 42 we had infants only up to 2 years of age. Their presenting complaints were either reluctance or disinclination in accepting feeds. Besides this complaint they were otherwise normal, having no infection or infestation.

After 10 to 15 days of treatment they showed definite improvement and gained in weight quicker than the control group.

SUMMARY

One hundred and thirty cases were put on Liv.52 therapy in the present series. It comprised of 65 cases of malnutrition, 14 cases of infective hepatitis, 9 cases of infantile cirrhosis and 42 cases of anorexia. Liv.52 was given as an adjunct to the main line of treatment except in cases of anorexia where no other drug was given.

In cases of malnutrition there was definite improvement in appetite and weight gain was noted in 90% of cases who were followed up. Liver function tests and histopathology also showed improvement. In cases of anorexia appetite improved after 10-15 days of therapy.

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