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Part II

Studies on Liv.52 in hepatic disorders

Part II: Indian Childhood Cirrhosis and Miscellaneous Conditions — 97 Cases

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In Part I of their Paper the Authors reported on 58 Cases of Viral Hepatitis. Of these 32 cases were treated with Liv.52 and supportive therapy while 26 cases served as controls and received only supportive therapy. These 58 cases were in Group I of their study. Findings in the remaining 97 cases are presented in Part II of the Paper.

GROUP II

Indian Childhood Cirrhosis — 41 cases

This group consisted of 41 cases of Indian childhood cirrhosis. The diagnosis of these cases was made on the basis of criteria laid down by the Liver Disease Sub-Committee Report of I.C.M.R. (1955) as under:

Stage I: A firm liver with a rather sharp edge with or without palpable spleen and mild constitutional symptoms.

Stage II: Progressive deterioration, hepatosplenomegaly, distended abdomen, slight icterus, slight oedema and ascites may be present. Child is irritable and loses weight.

Stage III: Marked deterioration with signs and symptoms of hepatocellular failure like hepatosplenomegaly, oedema, ascites, jaundice, haematemesis and/or malena.

Only the early cases of Stage I and Stage II of Indian Childhood Cirrhosis were included in the present study. Stage III cases were not included in the present study. Thirty two cases were in Stage I and 9 in Stage II. In every case, detailed present history, past history, family and dietetic factors were noted and liver function tests were done. These cases were divided into two sub-groups:

Sub-Group A: Liv.52 with minerals and vitamins – 21 cases.
Sub-Group B: Given only minerals and vitamins – 20 cases.

Table V

Signs and Symptoms		Total No. of Infantile Cirrhosis = 41	
		No. with positive Signs & Symptoms	Percentage
1.	Fever	21	51.22
2.	Anorexia	30	73.17
3.	Vomiting	3	7.31
4.	Diarrhoea	28	68.29
5.	Constipation	10	24.39
6.	Abdominal distension	35	85.36
7.	Jaundice	3	7.31
8.	Irritability	32	78.04

9.	Oedema		Nil	—
10.	Underweight		34	82.92
11.	Anaemia		15	36.58
12.	Lymphadenopathy		4	9.75
13.	Liver size –	Up to 3 cm	28	68.29
		3 to 5 cm	13	31.70
14.	Spleen –	Up to 3 cm	34	82.92
		3 to 5 cm	7	17.07

Table VI: Improvement of clinical features in cases of infantile cirrhosis receiving Liv.52 as compared to controls

Signs and Symptoms		Improvement in % of cases with Liv.52		Improvement in % of cases of controls	
1.	Irritability (32)	75%	(15/20)	33%	(4/12)
2.	Anorexia (30)	90%	(16/18)	16.6%	(2.12)
3.	Enlarged liver (41)	80%	(16/20)	55%	(11/20)
One patient left against medical advice.					

OBSERVATIONS AND RESULTS

In Group II — Infantile cirrhosis of liver – 41 cases

The majority of cases were between 1 to 3 years: 34 males and 7 females. Positive family history of infantile cirrhosis was obtained in 14 cases only (34.12%).

The Liv.52 treated group showed much better clinical response than the control group in both signs and symptoms and the progress of the clinical course.

Cases which received Liv.52 showed improvement in general health and well-being along with gain in weight in 17 out of 21 cases (81).

Seventy five per cent of cases showed early improvement of irritability compared with 33% in the control group.

Ninety per cent showed improvement in appetite compared to 16.6% in the control group.

Cases in the Liv.52 group showed regression in liver size in about 80% of cases (16 out of 20 cases) along with clinical remission (Table VII). There was improvement in liver function tests though they could not be done in every case (Tables VIII and IX).

Table VII: Clinical course in infantile cirrhosis treated with Liv.52 as compared to controls

Groups	Total No. of cases	Left against medical advice	Deaths	Progression to III stage	Clinical remission
Therapeutic group (Liv.52)	21	1	1	3	16
Control group	20	Nil	1	8	11

Table VIII: Liver Function Tests in cases of Indian Childhood Cirrhosis receiving Liv.52 (21 patients)

Time	Serum protein in gm%					Serum bilirubin in mg%						Thymol turbidity	
	Up to 4	4 – 5	5 – 6	6 – 7	Above 7	Less than 2	2 – 5	5 – 10	3 – 13	14–30	31–50	1 – 4	4 – 8
Initially	5*	7	6	2	1	19	2	–	5	10	6	15	6
After 2 weeks	1	9	7	2	1	10	–	1•	6	12	2	15	5
After 4 weeks	–	3	11	1	–	15	–	–	7	8	–	12	3
After 8 weeks	–	4	7	2		10	3	–	6	7	–	9	4
After 12 weeks	–	2	8	–		7	3	–	5	4	1	7	3
After 14 weeks	2	1	3	4		7	2	1	6	3	1	7	3
After 18 weeks	3	–	1	6		7	–	3	7	2	1	7	3
* One patient left against medical advice after 10 days • One patient died													
Others recovered and repeat was not necessary													

Table IX: L.F.T. in infantile cirrhosis with no treatment (20 patients)													
Time	Serum protein in gm%					Serum bilirubin in mg%						Thymol turbidity	
	Up to 4	4 – 5	5 – 6	6 – 7	Above 7	Less than 2	2 – 5	5 – 10	3 – 13	14–30	31–50	1 – 4	4 – 8
Initially	5	8	3	2	2	10	1	–	4	10	6	16	4
After 2 weeks	4	9	4	2	1	17	2	1	3	13	4	17	3
After 4 weeks	2	8	3	2	–	14	1	–	2	11	2	13	2
After 8 weeks	2	8	3	–	–	10	3	–	–	10	3	8	5
After 12 weeks	1	7	2	–	–	7	3	–	–	8	2	5	5
After 14 weeks	6	3	–	1	–	5	3	2	2	6	2	2	8
After 18 weeks	8	–	1	–	1	4	2	4	2	2	6	2	8

In the Liv.52 group 20% cases progressed to stage III compared to 45% in the control.

Liver biopsy showed cellular damage of variable degree, hyaline inclusions in hepatocyte, fibrosis with disruption of lobular architecture, mainly monocytic infiltration, no fatty change, minimal parenchymal regeneration. No repeat biopsy could be done. Though the cases treated with Liv.52 showed clinical and laboratory improvement during the period of observation, it would be difficult to forecast the ultimate outcome in this disease.

GROUP III

Miscellaneous Group

This group consisted of 56 cases (a) 35 of malnutrition (b) 18 of anaemia and (c) 3 of infections.

Thirty five malnutrition cases were divided into cases of kwashiorkor and marasmus. Most of the cases of kwashiorkor showed stunted growth, mental changes like apathy, irritability and oedema, anorexia, other gastrointestinal symptoms, skin and hair changes, enlarged liver and low serum proteins. Most of the marasmus cases showed marked loss of weight, gastrointestinal symptoms, loss of subcutaneous fat and wrinkling of skin, enlarged liver, probably secondary to recurrent non-specific infections. In all these cases liver function tests and serum protein studies were carried out and the diagnosis of kwashiorkor was supported by liver biopsy.

Eighteen anaemia cases presented with pallor and poor dietetic history, chronic, recurrent diarrhoeas, along with history of worms. Routine stool and blood examination and reticulocyte count were done. These cases were of iron deficiency anaemia.

There were three cases of primary tuberculosis confirmed on clinical laboratory and radiological studies.

These 56 cases of the miscellaneous group were divided into two sub-groups:
Sub-Group III A: On Liv.52 plus specific therapy — 31 cases.
Sub-Group III B: Control, on only specific therapy — 25 cases.

OBSERVATIONS AND RESULTS

In Group III — Miscellaneous group – 56 cases

This group included cases of hepatomegaly of diverse aetiology, like malnutrition, anaemia, primary tuberculosis. The cases on Liv.52 definitely showed a quicker response in the form of earlier improvement of appetite and irritability rapid regression of liver size, rise in haemoglobin percentage, rapid gain in weight, shortened hospital stay, return of liver function tests to normal (Table XI and XII). Liver biopsies in kwashiorkor cases showed fatty infiltration. Repeat biopsy could not be done.

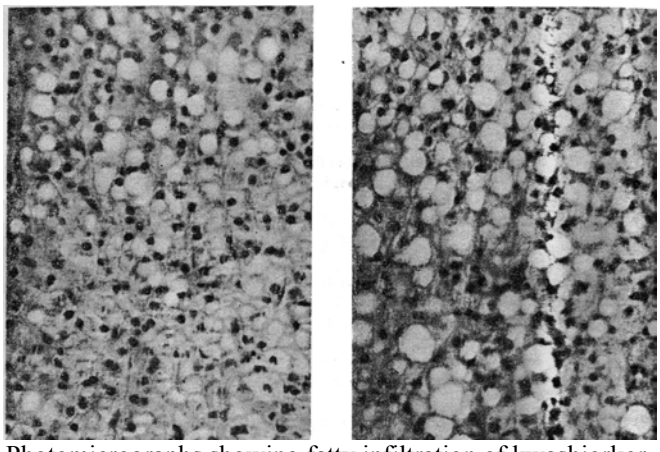
Table X: Total no. of miscellaneous cases = 56				
	Signs and Symptoms		Number with positive signs and symptoms	Percentage
1.	Fever		34	60.71
2.	Anorexia		46	82.14
3.	Vomiting		5	8.93
4.	Diarrhoea		43	76.78
5.	Constipation		2	3.75
6.	Abdominal distension		45	80.35
7.	Jaundice		Nil	—
8.	Irritability		26	42.85
9.	Oedema		21	37.5
10.	Underweight		56	100
11.	Anaemia		56	100
12.	Lymphadenopathy		36	64.3
13.	Liver size—	Up to 3 cm	44	78.57
		3 to 5 cm	12	21.43
14.	Spleen—	Up to 3 cm	6	10.7
		3 to 5 cm	–	–

Table XI: Improvement in clinical features with Liv.52 in the miscellaneous group, as compared to controls					
	Clinical Features	Improvement in Days with Liv.52		Improvement in Days in Controls	
		Near Average	Range	Near Average	Range
1.	Anorexia	5	2-12	10	3-16
2.	Anaemia	6	5-9	9	6-12
3.	Irritability	7	5-9	13	7-20
4.	Enlarged Liver	10	6-16	14	7-18

Table XII: L.F.T. in non-specific cases with Liv.52 treatment (31 cases*)													
Time	Serum protein in gm%					Serum bilirubin in mg%						Thymol turbidity	
	Up to 4	4 – 5	5 – 6	6 – 7	over 7	Upto 2	2 – 5	5 – 10	3 – 13	14–30	31–50	1 – 4	4 – 8
Initially	11	15	4	–	–	30	–	–	14	12	4	25	5
After 2 weeks	3	16	7	1	–	27	–	–	23	4	–	25	2
After 4 weeks	–	3	14	3	2	22	–	–	20	2	–	22	–
* In one case no L.F.T. was done													

Table XIII: L.F.T. in non-specific group without Liv.52 treatment (25 cases*)													
Time	Serum protein in gm%					Serum bilirubin in mg%						Thymol turbidity	
	Up to 4	4 – 5	5 – 6	6 – 7	over 7	Upto 2	2 – 5	5 – 10	3 – 13	14–30	31–50	1 – 4	4 – 8
Initially	10	11	2	–	–	23	–	–	10	11	2	21	2
After 2 weeks	6	15	2	–	–	23	–	–	12	10	1	22	1
After 4 weeks	1	12	3	2	1	18	–	–	12	6	–	18	–
* L.F.T. could not be done in 2 cases.													

In this study an attempt is made to study the effects of Liv.52 in three groups of cases (a) viral hepatitis (b) Infantile cirrhosis of liver, Stages I and II, I.C.M.R. and (c) miscellaneous group. This study also shows the behaviour and functional response of liver cells in a number of conditions affecting young children. It is a well-known observation that young liver cells have a particularly high susceptibility to noxious substances and are thereby liable to be damaged readily. It is also true that the liver is one organ in the body that has a



Photomicrographs showing fatty infiltration of kwashiorkor.

remarkable capacity for regeneration. What are the precise factors which tend to strike a balance between the functional efficiency and its deterioration, is difficult to say since liver function tests and even at times liver biopsy slides may fail to give a clear picture of the state of liver cells. Under these handicaps the task of precise evaluation of the effectiveness of a particular drug becomes all the more difficult. Nevertheless, using as scientific an approach as possible, certain tentative conclusions have emerged from the foregoing study which are briefly summarised as below:

SUMMARY

1. In early stages of Indian Childhood Cirrhosis a certain degree of improvement in symptoms and some improvement in liver function tests was observed compared to the control group without Liv.52. This was during the period of study. The ultimate outcome of these cases cannot be predicted.
2. In the miscellaneous group with hepatomegaly there was improvement in symptoms, decrease in liver size and improvement in liver function tests.

I Three groups of cases:
58 of viral hepatitis,
41 of early stages I & II infantile cirrhosis of the liver,
56 miscellaneous group,
were studied for the effect of Liv.52. In each group control cases were studied simultaneously.

(i) Liv.52 was very effective in infective hepatitis,
(ii) Liv.52 helped in early cases of infantile cirrhosis of liver,
(iii) In the miscellaneous group Liv.52 led to regression of liver size, symptomatic relief and weight gain,
(iv) There were no toxic effects.