

Study of Liv.52 Therapy in Cases of Indian Childhood Cirrhosis and Other Liver Disorders

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The aim of the present study is to assess the effectiveness of Liv.52 therapy in cases of Indian Childhood Cirrhosis (I.C.C.) and other liver disorders, e.g. infective hepatitis, subacute hepatitis, portal vein thrombosis and hepatomegaly due to tuberculosis and other unknown causes. There were two Australia Antigen positive cases.

Australia Antigen has been found to be associated with increasing frequency in patients suffering from serum hepatitis (Type B hepatitis) and in cases of Indian Childhood Cirrhosis by Chandra *et al.*, 1971. Australia Antigen was first detected in 1965 by Blumberg and his colleagues. In two patients of haemophilia who had received multiple transfusions, they found that there was an antibody which reacted with an antigen in a single serum in their panel and this came from an Australian aborigine. This is found in about 80 per cent of sera tested within 12 days of symptoms of type B hepatitis. It is usually found for 3 to 4 weeks in patients transfused with blood containing Australia Antigen (Goche *et al.*).

MATERIAL AND METHODS

During the period of fourteen months from 1st January 1976 to 28th February 1977, 66 cases between 0 to 12 years of age attending S.N. Children's Hospital were taken up for study. The children were from all strata of society, although most of them belonged to the middle class.

In all cases detailed history of the presenting symptoms was taken. Past history regarding blood transfusion, umbilical sepsis and repeated injections was also taken. Every case was thoroughly examined and if any behaviour change was present, it was also noted.

All the cases were subjected to the following investigations: Routine haematological tests for TLC, DLC, Hb%, ESR, urine examination for albumin, bile salts and bile pigments; liver function tests for total serum protein and albumin/globulin ratio, serum bilirubin, Van den Bergh reaction, SGOT and SGPT; detection of Australia Antigen by immunoelectrophoresis and liver biopsy.

OBSERVATIONS

In the present study, 66 cases were classified as follows:

I	Indian Childhood Cirrhosis	25
II	Infective hepatitis	24
III	Subacute hepatitis	04
IV	Tuberculosis with hepatomegaly	07
V	Juvenile cirrhosis	01
VI	Portal vein thrombosis	01
VII	Hepatomegaly of unknown aetiology	<u>04</u>
	Total	<u>66</u>

I. Indian Childhood Cirrhosis

The present study included 25 cases of Indian Childhood Cirrhosis (ICC). Out of them 14 patients were males and 11 cases were females. The age group was between 10 months to 4 years of age.

Presentation

Majority of the patients presented with low grade fever, increasing weakness, lethargy and irritability for one to four months. In some children there was history of diarrhoea alternating with constipation and gradually increasing distension of abdomen. In 18 patients jaundice appeared later, it was mild to severe in degree. On examination, majority of them had jaundice, hepatomegaly of moderate (3 to 5 cm.) to marked (5 to 8 cm.) degree. The liver was firm to hard in consistency with well-defined margins, and granular or nodular on palpation. Six cases also had mild to moderate splenomegaly. Six cases presented in comatose stage with marked jaundice, ascites etc.

Investigations

Haemogram was normal in majority of them. Urine examination revealed bile salts and bile pigments. Liver function tests showed:

Serum bilirubin raised (0.8 to 11.2 mg%),

Van den Bergh reaction positive,

Total serum protein ranging from 5.6 to 8.0 g%,

Albumin/globulin ratio was reversed in majority of the patients.

Only one case was positive for Australia Antigen. She was admitted in a state of hepatic coma with history of fever, irritability and increasing weakness, distension of the abdomen for the last two months. The jaundice had appeared only 15 days earlier. The patient expired in the hospital in spite of the best possible care.

Liver biopsy – Only two cases were proved by biopsy.

Treatment

All the cases were put on Liv.52 drops 2 tsf. Three to four times a day along with B-complex, high protein and high carbohydrate diet (protein was restricted in comatose patients) and other supportive measures were taken.

Results

Six cases who were admitted at a late stage with coma expired in spite of all possible treatment. In rest of the patients, response to Liv.52 was good. It was noticed that these patients regained their appetite; the fever and irritability were also relieved in about one to two months' time. Biochemically the course of the disease was found to be arrested.

Discussion

Only one case in our study of 25 cases of ICC was positive for Australia Antigen (HAA). The incidence was 4 per cent. P.S. Datta, 1973 was not able to find any positive case in his study of 17 cases. Similarly, Sundaravalli *et al.*, 1971 also failed to detect HAA in any of their cases with classical features of Indian Childhood Cirrhosis. However, Aggarwal, S.S., Lahiri *et al.*, 1972 reported that 47 per cent of patients of Indian Childhood Cirrhosis were positive for HAA.

Wright *et al.*, and Shulman, 1970 have suggested that the variation in the frequency of HAA positively depended upon the stage of the disease at which the serum was taken and also on the technical procedure used. High frequencies were seen when the samples were taken during the early stage and when more sensitive techniques were used.

In 19 cases out of 25, the response to Liv.52 was good. These patients regained their appetite; the fever and irritability were relieved in 1-2 months. Biochemically the course of the disease was found to be arrested. However, six other patients in comatose condition expired.

II. Infective Hepatitis

In the present study, out of 24 cases of infective hepatitis, 13 were males and 11 were females. They were between 7 months to 7 years of age. The presenting symptoms were fever, malaise, anorexia, nausea and vomiting of the duration of one week to one month. Jaundice and deep coloured urine appeared later. Majority of them had hepatomegaly of mild (2 cm to 3 cm) to moderate (3 cm to 5 cm) degree. There was no case with splenomegaly or ascites. Four of them presented with hepatic coma.

Investigations

Serum bilirubin was raised in all the cases ranging from 3 to 18 mg per cent and, Van den Bergh reaction was positive directly. Serum protein was within normal range (between 6.8 to 8.0), albumin/globulin ratio was not reversed. SGOT was raised in all the cases (22 to 140 units) and SGPT was also found to be markedly raised (36 to 200 units). Urine was positive for bile salts in all the cases. Two cases were subjected to biopsy and the diagnosis confirmed.

Australia Antigen test showed negative in all the cases.

Treatment

All the cases were put on Lvi.52 drops in the dose of 1 tsf., three to four times a day for children below 2 years of age and 2 tsf., three to four times a day in children above 2 years of age. Along with B-complex syrup, a high-carbohydrate diet, low in fat and protein content was also given. In two cases of coma, a steroid was also used along with the above treatment.

Results

In general, it was observed that cases presenting with acute onset showed dramatic clinical response within 3 to 4 days, with restoration of appetite, diminution of icterus and return to normal behaviour. Biochemical values normalised within 14 days' time but raised SGOT and SGPT values took further two weeks to come to normal.

Similarly, patients with sub-acute onset, having associated symptoms, showed clinical improvement within a week's time. The biochemical values normalised between 4 to 6 weeks' time after commencement of Liv.52 therapy.

Out of 4 patients in comatose stage, 2 patients recovered within 4 weeks' time clinically and biochemically within 4 to 6 weeks' time. In two cases steroid had to be administered along with Liv.52 and other supportive measures, but they could not be saved.

Discussion

Out of 24 cases of infective hepatitis, 4 cases presented with coma. There was no case positive for Australia Antigen (Hepatitis Associated Antigen, HAA). Blumberg *et al.* (1967) reported HAA in 13 per cent of cases of viral hepatitis. Since then several workers have reported HAA in 15 to 47 per cent of cases of viral hepatitis (Okochi *et al.* 1968; Hirschman *et al.* 1968).

After the commencement of therapy with Liv.52, the clinical response in the form of return of normal appetite, feeling of well being and diminution in icterus was noticed as early as 3 to 4 days and biochemical recovery within 2 weeks' time. In a similar study by V. Ramalingam and V. Balagopal Raju, 1971, they had reported a fall in serum bilirubin below 2.5 and SGOT and SGPT below 40 units within 2 weeks' time. S. Gupta *et al.* 1972 had reported return to normal values of

serum bilirubin and SGOT and SGPT within 10 to 14 days. C.R. Sule, 1968, had reported clinical improvement in 2 to 5 days' time and return of liver function values to normal within 10 to 19 days.

III. Subacute Hepatitis

In the present study, 4 cases of sub-acute hepatitis were studied. They presented with long history of fever off and on (one case presented with H/O fever off and on for the last 10 years), loss of appetite and malaise and jaundice for 2 to 4 weeks. Examination revealed hepatomegaly in all the cases and hepatosplenomegaly in one case.

Investigations

Serum bilirubin was raised (2.8 to 6.6 mg%),
Van den Bergh reaction was positive,
Albumin/globulin ratio was reversed in all the cases,
Total serum protein was normal,
SGOT was raised (20 to 56 units),
SGPT was raised (27 to 37 units),
Urine examination was positive for bile salts and bile pigments.

All the cases were negative for Australia Antigen.

Treatment and Results

All the patients were put on Liv.52 drops and B-complex syrup. The response was good; they regained their lost weight, and appetite improved within 2 to 3 months' time. On follow-up they showed that the disease process was arrested in 6 months to one year's time.

Discussion

Among four cases of subacute hepatitis, there was no case positive for Australia Antigen. Sama *et al.*, 1973 reported the incidence to be as high as 59 per cent. Other workers have reported the incidence from 26 to 87 per cent (Blumberg, 1967; Wright *et al.*, 1971; Canlla *et al.*, 1972).

After commencement of therapy, the patients showed clinical improvement within 2 to 3 months and significant biochemical improvement was noted within 6 months to one year's time. M. Dasgupta, *et al.*, 1971 have reported good clinical response with improvement in liver function test done at the interval of one and a half to two years, suggesting arrest in the progress of chronic active hepatitis towards cirrhosis.

IV. Tuberculosis with Hepatomegaly

In the present study, seven cases presented with tuberculosis-associated hepatomegaly. They had complained of fever, loss of appetite, failure to thrive and irritability. On examination, there was no jaundice, three of them had hepato-splenomegaly and the rest had only hepatomegaly.

Investigations

Liver Function Tests including SGOT and SGPT were within normal limits.

Chest X-ray showed evidence of Tuberculosis. There was no case positive for Australia Antigen.

Treatment and Results

All the cases were put on antitubercular treatment and Liv.52. They responded very well and hepatomegaly either disappeared or diminished within 2 to 3 months' time.

Discussion

Regression in the size of liver and clinical improvement was noted within 2 to 3 months' time. It is very difficult to comment whether the response was due to Liv.52 alone or as a result of combined therapy. Inderjeet Singh, *et al.*, 1974 reported hepatic involvement in 63 to 100 per cent of patients with tubercular infection. There was no case positive for HAA.

V. Juvenile Cirrhosis

There was only one case of Juvenile cirrhosis which presented with a history of jaundice 2½ years back, fever, malaise and loss of appetite for 15 days.

On examination, there was no jaundice. Hepato-splenomegaly was evident. The liver was 8 cm in size, firm in consistency with well defined margins. The spleen was about 4 cm in size and was firm.

Investigations

Liver Function Tests:

Serum bilirubin	1.0 mg%
Van den Bergh reaction	Negative
Albumin/globulin	5.5/3.1
SGOT	11 units
SGPT	44 units
Urine examination	Normal
Australia Antigen	Negative

Treatment and Results

The patient was put on Liv.52 drops 2 tsf four times a day and showed good clinical response. His appetite improved and he started gaining weight and had a feeling of well being.

VI. Portal Vein Thrombosis

One child 7 years old was admitted as a case of portal vein thrombosis with history of fever, malaise and vomiting for two days. There was past history of melaena and haematemesis 2 months earlier.

On examinations:

No jaundice was detected.

The liver was 7 cm, firm, nontender with margins well defined, and

The spleen, 1 finger, firm.

Investigations

Liver Function Tests:

Serum bilirubin	1.2 mg%
Total serum protein	7.5 g%
Albumin/globulin	4.4/3.1
SGOT	18 units
SGPT	24 units
Urine examination	Normal
Australia Antigen	Positive

Treatment and Results

He was put on Liv.52 and B-complex. He was discharged after one week with good response. However, he did not turn up for further follow-up.

VII. Hepatomegaly of Unknown Aetiology

In the present study, four cases presented with hepatomegaly with varying complaints like fever off and on, excessive appetite, distension of abdomen, dysentery etc. On examination, the liver was moderately enlarged (5 to 8 cm.).

Investigations

Liver Function Tests were within normal limits.

SGOT and SGPT were within normal limits.

Australia Antigen test was negative in all cases.

Treatment and Results

They were all put on Liv.52 therapy. The response was very good. The hepatomegaly disappeared or markedly diminished within one or two months.

CONCLUSIONS

1. Sixty six cases of liver disorders were assessed for the effectiveness of Liv.52 therapy and incidentally the effect of Liv.52 on Australia Antigen positive cases, of which there were two in the present group.
2. Indian Childhood Cirrhosis occurred in 25 cases, one of them being positive for Australia Antigen. Six advanced cases in comatose condition failed to respond to therapy and did not survive. In the remaining 19 cases the response to Liv.52 was good. The course of the disease was arrested, as Liv.52 helped to check further necrosis and promote regeneration.
3. The next largest group comprised of 24 cases of infective hepatitis, including 4 comatose cases. Of the latter, 2 died despite recourse to steroids. Of the rest, acute cases showed dramatic clinical response to Liv.52 within 3-4 days and biochemical improvement in 2-4 weeks. Sub-acute cases, however, needed a little longer time for recovery. Liv.52 deserves to be used as routine treatment for infective hepatitis, in view of the exceptionally good response.
4. Four cases of sub-acute hepatitis improved within 2-3 months on Liv.52. Although recovery was slow, Liv.52 seemed to arrest the disease process.
5. Seven cases of tuberculosis with hepatomegaly or hepato-splenomegaly responded very well when Liv.52 was used as an adjuvant to routine antitubercular drugs.
6. The lone case of juvenile cirrhosis showed good clinical response to Liv.52.
7. One case of portal vein thrombosis proved to be Australia Antigen positive. One week's therapy with Liv.52 sufficed to obtain good response and the case was discharged.
8. Four cases with hepatomegaly of unknown aetiology showed very good response to Liv.52.
9. Although the patients in this study presented with variable manifestations of liver derangement, Liv.52 therapy succeeded in achieving early restoration of liver function, improvement in appetite, weight gain and general well-being.
10. No toxic effects were encountered with Liv.52 even though therapy had to be necessary prolonged in certain conditions.