[***Probe*** (1972): (XI), 2, 93-99]

Therapy of Infectious Hepatitis and Other Liver Disorders

Prof. Gupta, S., *F.R.C.P., M.R.C.P., D.C.H.,*
Head of the Department of Paediatrics, Gastroenterology Unit,
Maulana Azad Medical College, New Delhi-1.
Khatri, R.L., *D.C.H.,* Resident Medical Officer, Paediatrics.
Srivastava, G., *M.D.,* Paediatrician.

INTRODUCTION

Hepatic disorders in infancy and childhood continue to pose problems in regard to their management. Even though the aetiological factors are many and some of them ill-understood today, the manifestation is the same - that of hepatic insufficiency. Since liver performs many functions of the body - some understood well, some not so well and others not at all—a drug that would help in keeping the liver functioning would go a long way in solving the problem of treating hepatic disorders.

Liv.52 is an indigenous drug which has shown in the recent past to have some protective action against hepatotoxic substances like carbon-tetrachloride. It stimulates the cellular growth in the liver in the presence of hepatotoxic or necrotic substances and also promotes the metabolic functions of the liver (Joglekar, *et al.,* 1963 and Karandikar, *et al.,* 1963).

Liv.52 contains extracts of Capparis spinosa, Cichorium intybus, Solanum nigrum, cassia occidentalis, Terminalia arjuna, Achillea millefolium and Tamarix gallica, prepared in the juice and decoctions of various hepatic stimulants.

The drug has been used clinically in different hepatic disorders for the last ten years with beneficial effect (Sule, *et al.,* 1957; 1968). It has been tried in cases suffering from diffuse hepatic fibrosis, portal hypertension (Mathur, 1957), acute hepatic toxicity (Patel, *et al.,* 1963) and acute infectious hepatitis (Arora, 1969; Deshpande, *et al.,* 1971). Since Liv.52 has been reported to be useful in the above-mentioned conditions the present study was undertaken to study the efficacy of this drug in various hepatic disorders affecting infants and children.

MATERIAL AND METHODS

The drug Liv.52 was tried on cases with the following diagnosis:
(1) Infectious hepatitis and subacute hepatitis
(2) Post-necrotic cirrhosis
(3) Cirrhosis liver and
(4) Malnutrition with hepatomegaly.

The criteria of diagnosis were based on the established clinical manifestations and biochemical data of these diseases and liver biopsy, wherever possible. In all 85 cases were taken up for study. Out of a total of 85 cases, 55 cases were studied with the drug and 30 served as control. Controls were selected as far as possible from the same age group and with similar clinical manifestations. A detailed history and physical examination were recorded in each case in a prepared proforma.

The following investigations were done in each case:
(a) Urine examination for bile salts and pigments and urobilinogen in addition to the routine examination;
(b) Haemogram;
(c) Liver function tests;

(d) Liver biopsy, wherever possible;
(e) Radiological examination wherever thought necessary and
(f) Any other investigation indicated.

All the cases attended the paediatric service of the Irwin Hospital, New Delhi and were subsequently followed up at the Liver Clinic of the Department.

Irrespective of the clinical diagnosis all patients, except in the infectious hepatitis group, were put on the following regimen:

Upto	Liv.52 or	Twice a day
2 years	1 tablet or 10 drops	Three times a day
2-5 years	1 tablet	Three times a day
Above 5 years	1 tablet	Four times a day

In infectious hepatitis patients, 50 percent or even higher doses were used depending on the severity of the disease.

Each patient was followed up regularly in the liver clinic of the Department of Paediatrics at intervals of 15 days/one month. History of main symptoms and physical examination was recorded at every visit.

Distribution of cases	Drug treated	Control	Total
Infectious hepatitis	27	9	36
Post-necrotic cirrhosis	7	1	8
Indian childhood cirrhosis	5	4	9
Malnutrition	16	16	32
Total	55	30	85

INFECTIOUS HEPATITIS - 36 CASES

Infectious hepatitis is a systemic disease caused by a virus or viruses. It is characterised by evidence of liver injury and constitutional and gastrointestinal signs and symptoms. it occurs predominantly in childhood, sporadically in epidemics. Jaundice, the most distinctive symptom, does not always occur in a minority of patients.

The main pathologic changes are in the liver which have been observed both by liver biopsies at the various stages of the disease and at necropsy. The size of the liver may be larger than normal and in subacute and fulminating cases may be reduced. The clinical picture shows great variation. The disease may be inapparent or evanescent and in children its course is generally mild. The course of the disease may be separated into pre-icteric and icteric, although frequently jaundice may be the presenting symptom. The onset may be sudden or gradual with anorexia, fever, headache, irritability, lassitude and sometimes nausea, vomiting and abdominal pain. Mental depression and bradycardia are commonly observed symptoms in adults which are uncommon in children. The liver is enlarged and tender, the stools may be clay-coloured but this is not a constant finding. The icteric phase persists from a few days to as long as a month or even longer, the average duration being about eight to eleven days in children in contrast to three to four weeks in adults. As jaundice fades, the appetite returns and the patient gradually feels better.

There is no specific test to predict the patient's response to the infection with this agent. Liver function tests and routine blood examination are helpful. The rise in serum bilirubin usually precedes jaundice and bile may be detected in the urine before the level of serum bilirubin rises. Serum transminase assay is one of the useful non-specific tests available for the diagnosis of infectious hepatitis. Clinical and epidemiological grounds aided by laboratory tests help in the diagnosis of

hepatitis in the absence of specific urologic tests. There is no specific treatment and symptomatic therapy consists of bed rest and adequate diet. The diet is best regulated by the patient's appetite.

Thirty six patients of infectious hepatitis varying in age from infancy to twelve years were studied out of which twenty seven were treated with the drug and the rest served as control as shown in Table I.

Table I: Age in years - 36 cases			
Age in years	No. of cases on Liv.52	Control	Total
Birth to 2 years	5	2	7
3 - 5 years	12	4	16
6 - 9 years	6	2	8
10 - 12 years	4	1	5
Total	27	9	36

Table II			
	On Liv.52	Control	Total
Fever	23	5	28
Jaundice	27	8	35
Anorexia	22	8	30
Nausea and/or vomiting	15	5	20
Pain in abdomen	12	4	16
Distention of abdomen	12	4	16
Pallor	14	5	19
Yellow urine	27	8	35
Clay-coloured stool	9	3	12
Oedema	2	1	3
Bleeding tendency	1	—	1

Table III: Size of Liver - 36 cases			
Palpable in mid-clavicular line in cm.	No. of cases	Control	Total
Upto 2 cm	5	2	7
3-5 cm	18	6	24
6-10 cm	4	1	5

Symptomatology as observed in 36 cases is shown in the accompanying tablet.

The jaundice was mild, moderate or severe in degree, reached its peak within 12 to 16 days and gradually receded in the majority of cases.

The liver was palpable in all cases but the size and the degree of tenderness varied in different cases. Spleen was palpable in 17 cases.

Liver function tests were performed in all cases. These included total serum protein estimation, albumin/globulin ratio studies, serum bilirubin estimation, serum alkaline phosphatase studies, serum transaminase assessment and prothrombin time. Liver biopsy studies were done in ten cases in the early and receding phases of the disease.

OBSERVATIONS

Liv.52 was tried with the hope that it would cut short the acute phase or lessen the severity of the disease and prevent post-hepatitis complaints. No other drugs were administered to the drug treated group. Observations show that fever, anorexia, vomiting and jaundice improved considerably on Liv.52 therapy than in cases in the control group. Appetite improved in 72 percent of cases and this improvement continued for a prolonged period. A much higher percentage of children, 72 percent, were symptom-free earlier and the liver size and tenderness, returned to nearer normal.

Careful observations clearly demonstrate that Liv.52 therapy improves appetite, reduces the intensity and duration of jaundice and markedly cuts short the course of the attack and probably reduces the incidence of subacute hepatitis by protecting the liver.

Laboratory studies also show that total serum protein readings were not effectively affected; the albumin/globulin ratio reverting to normal limits: Serum bilirubin levels which were raised in the earlier stages returned to nearer normal earlier, thus showing regression in clinical jaundice. Serum alkaline phosphatase and prothrombin time values were not affected effectively in the treated cases. SGOT and SGPT levels which were initially higher returned to normal within 10 to 14 days. Liver biopsy studies were done in 10 cases. Seven of these were treated with Liv.52. Biopsies clearly showed receding phase of infectious hepatitis in the group treated with Liv.52 tablets.

This therapeutic study of the clinical course of the disease, the changes in the liver function tests and the histopathological studies of the affected liver clearly indicate a remarkable degree of earlier improvement in the cases treated with Liv.52. The clinical, laboratory and histopathological response was significant in the treated group as it cut short the duration and course and severity of the attack and showed remarkable improvement toward normal values. Increased appetite was noted in a large number of cases on trial in this series. No toxic effects were observed in any of the treated cases.

POST-NECROTIC CIRRHOSIS - 8 CASES

Of the seven cases of post-necrotic cirrhosis included in the Liv.52-treated series there was symptomatic improvement in fever, jaundice, anaemia and oedema. The liver size showed reduction in two cases, while in one the size increased. Two cases of post-necrotic cirrhosis showed marked improvement symptomatically although there was minimum change in hepatosplenomegaly. In two of the cases the liver histopathology revealed normal structure after a follow-up of one year. Since the control series has only one case, no comparison is possible, but it is probable that with prolonged treatment there may be reversal of post-necrotic changes in the liver to the normal or near-normal pattern. Detailed studies on this condition with microphotographs are being reported separately.

INDIAN CHILDHOOD CIRRHOSIS—9 CASES

All the cases of Indian childhood cirrhosis were of moderate degree and did not show significant alteration of liver functions. However, following therapy, although the response in our cases of Indian childhood cirrhosis was unsatisfactory—and the patients showed deterioration clinically as well as biochemically—yet the duration in which the deterioration took place in these cases was more than that in the case of the control series.

MALNUTRITION - 32 CASES

Out of 32 cases of malnutrition with hepatomegaly, the cases in the trial series had an early weight gain with improvement in appetite. There was a reduction in the size of the liver in these cases. The mean values of total proteins and serum albumin showed a rise over pre-treatment values.

DISCUSSION

Liv.52, an indigenous drug combination has been reported by various laboratory and clinical workers to be of value in hepatic disorders. Pharmacological studies by Joglekar, *et al* (1963), Karandikar, *et al* (1963), Joglekar and Balwani (1967), Patel and Sadre (1963), Sheth, *et al* (1960), Joglekar and Leevy (1970) have repeatedly proved by various parameters the protective and regenerative action of Liv.52 against experimentally induced hepatic damage.

In their clinical studies and assessment, Dayal *et al* (1970), Deshpande, *et al* (1971), Prasad and Tripathy (1969), Prasad and Prasad (1971), Arora (1968), Mukerjee and Dasgupta (1970), Sule *et al* (1968) all have in different planned studied reported extremely favourable results in cases of infectious hepatitis and malnutrition; though most workers feel that in established cases of Indian childhood cirrhosis, no substance is known at present to be capable of converting interstitial tissue into cellular tissue; and, all that Liv.52 does is to prolong life for some time after which the disease marches to its fatal end.

In the present study, in 36 cases of infectious hepatitis and 32 cases of malnutrition the clinical, laboratory and histopathological response was significant as Liv.52 therapy cut short the severity, duration and the course of the disease. Liver function tests and biochemical findings tended to revert to normal earlier in the Liv.52 treated cases. Anorexia responded very favourably as there was significant improvement in appetite in the Liv.52-treated cases.

In our cases of Indian childhood cirrhosis Liv.52 delayed to some extent the progress of the disease to its inevitable end.

There was very remarkable response in our cases of post-necrotic cirrhosis. Two of the cases showed interesting changes in the histopathological picture. Probably the drug prevents further damage and necrosis in post-necrotic hepatitis and may be helpful in cases of post-necrotic cirrhosis.

Taking hepatic disorders as a whole (except established cases of Indian Childhood Cirrhosis) in the Liv.52 group there is earlier improvement in the symptoms like fever, amorexia, vomiting, jaundice, distension of abdomen. The physical signs like jaundice, anorexia, hepatomegaly regress faster.

Taking hepatic disorders as a whole there is improvement in the symptoms like fever, anorexia, vomiting, jaundice, distension of abdomen, in the cases included in the trial. The physical signs like jaundice, anaemia, hepatomegaly, distension of abdomen in these two groups of cases improved remarkably.

SUMMARY

Controlled studies on 85 cases of various hepatic disorders were carried out at the Liver Clinic, Irwin Hospital, New Delhi. There were 36 cases of infectious hepatitis, eight of post-necrotic cirrhosis, nine of Indian childhood cirrhosis and 32 of malnutrition.

In cases of infectious hepatitis, the clinical laboratory and histopathological response was significant. It cut short the duration, course and severity of the attack and showed regression of disease with remarkable improvement of appetite and toxic symptoms.

The clinical, biochemical and histopathological changes in the group with malnutrition were significant and the patients improved and gained in weight.

In cases of post-necrotic cirrhosis there was remarkable improvement with impressive results.

In nine cases of Indian childhood cirrhosis, there was some symptomatic relief, though no significant alteration of liver function or pathology.

No toxic or untoward side effects were observed in any of the cases studied.

ACKNOWLEDGEMENTS

We acknowledge the help and co-operation rendered to us by the Departments of Pathology and Biochemistry, M.A.M. College.

We are thankful to Himalaya Drug Co., for providing the facilities for research and the drug.

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