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Treatment of Hepatopathy in Children with a Combination of *Capparis Spinosa* and Other Indian Indigenous Drugs

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INTRODUCTION

Hepatopathy, commonly encountered in our paediatric practice, may be just a benign one or an indication of an underlying serious pathological process. One such malignant hepatopathy is the Cirrhosis of the liver. Any enlarged liver with some degree of firmness should be looked upon with suspicion, especially when such enlargement is associated with gastrointestinal symptoms, low fever, inability to thrive and increasing pallor. Cirrhosis of the liver is still a baffling problem from the therapeutic point of view. It is now increasingly realised that only in early stages the disease can be arrested and cured with suitable treatment. In advanced cases the chances of recovery are very thin or almost nil.

The usually employed drugs in the treatment of Cirrhosis are proteins, aminoacids, monosaccharides, vitamins, liver preparations, Vit. B_{12}, lipotropic agents etc., which protect the liver tissue from further damage and help in its regeneration. During 1956-57 we treated 50 cases of Cirrhosis of the liver, diagnosed clinically, with a combination of Indian indigenous drugs in all cases and the above mentioned conventional therapy in some cases. Our results of that preliminary study were very encouraging. Nine cases were cured, 24 cases were relieved, in 12 cases there was no response and 5 cases expired. Thus 66% of cases recorded therapeutic benefit. Encouraged by these results we continued this study further and this time we tried to confirm the diagnosis in all cases by liver biopsy studies.

MATERIAL AND METHODS

Twenty three cases of hepatopathics were studied clinically and histopathologically and treated mainly with a combination of Indian indigenous drugs, called "Liv.52", to note any beneficial effects. The various constituents and their proportion of weight in grains in each tablet of Liv.52 are:

Exts.	*Capparis spinosa*	1.00
	Cichorium intybus	1.00
	Solanum nigrum	0.50
	Cassia occidentalis	0.25
	Terminalia arjuna	0.50
	Achillea milleflium	0.25
	Tamarix gallica	0.25
	Mandur bhasma	0.50

The action of different constituents, according to Ayurveda, are as follows:

Capparis spinosa is a hepatic stimulant and is effectively used for functional efficiency of liver and spleen. It has also a diuretic and an aperient action. *Cichorium intybus* is a hepatic stimulant and enhances the action of *Capparis spinosa. Solanum nigrum* is a hydragogue and is used in reducing anasarca and ascites of hepatic origin. It has a marked diuretic action. *Cassia occidentalis* is a tonic,

diuretic, stomachic and choleretic in action. *Terminalia arjuna* is a cardiac tonic and is also used in the treatment of liver disorders and dropsy. *Achillea milleflum* has a tonic and carminative action. *Tamarix gallica* is a digestive and a hepatic stimulant. *Mandur bhasma* is prepared from ferric oxide triturised in juices of many hepatic stimulants and cholagogues. It has a tonic and a haematinic effect. During the process of manufacture, according to manufacturers, there is a definite interaction of the various ingredients all of which have both individual and synergistic action on the liver.

The drug was given orally in a dose of 4-6 tablets in two or three divided doses. Injections of a Liver Extract preparation, 2 c.c. I.M. daily, were given in 22 cases (The preparation used was Inj. UNI B_{12} with Folic, 1 cc., of which contains Vit. B_{12} 25 mcgm, Folic acid 5 mgm, Nicotinamdie 100 mgm, Choline citrate 25 mgm, and Liver extract from 10 gms of Liver.) A liquid lipotropic preparation was given in the dose of 1 teaspoonful (4 c.c.) t.d.s. in addition to 10 cases. (The preparation used was Univite with Choline 30 c.c., of which contains Choline citrate 4 gm, Acetyl methionine 0.75 gm, Inositol 0.25 gm, Vit. B_{12} 30 mcgm, Folic acid 7.5 mgm, Thiamine Hydrochloride 12.5 mgm, Riboflavin 7.5 mgm, Ascorbic acid 0.25 gm, Nicotinic acid 75 mgm, Pantothenol 5 mgm, Calciferol 2500 I.U. and Proteolysed Liver Extract equivalent to 28 gms of fresh liver). In 6 cases with marked reduction in haemoglobin percentage, iron was given, in 3 cases orally and in others I.V. No other drugs were given. No extra proteins or special diets were prescribed and only routine hospital diet was given. It must be said that this routine type of diet with added milk was far better than the home diet of most of the children. Salt restriction was imposed in cases with oedema.

Twenty cases were males and 3 were females. The ages of the patients were:

3 months	1 case
1 year	3 cases
1-2 years	5 cases
2-3 years	5 cases
3-4 years	2 cases
7-12 years	7 cases.

The nutritional status was poor in 21 cases and fair in 2 cases. The duration of the disease before the institution of therapy, as assessed from the history of the patients, was 7 days in one case, 25-30 days in 3 cases, 45 days in 2 cases, 60-90 days in 9 cases and 100-120 days in 8 cases. Thus the majority of cases were admitted in advanced stages of the disease. Twenty cases were of Cirrhosis of the liver, 2 cases were of Subacute Infective Hepatitis and one case was of Acute Infective Hepatitis. Four cases were in early, 8 cases were in intermediate and 11 cases were in late stage of the disease.

Liver biopsy was done in each case before the start and after the termination of treatment, except in cases that expired, in whom only one pretreatment biopsy was done. Inj. Vit. K, 10 mgm, I.M., was given to all cases 24 hours before biopsy.

For comparison we cite here a group of 69 cases treated previously, from 1953-56, with the routinely employed drugs. This group, therefore, does not constitute a simultaneous control. In this group of 69 cases, 11 were in early, 21 were in intermediate and 35 were in late stage of Cirrhosis of liver and 2 cases were of Acute Infective Hepatitis.

RESULTS

The evaluation of the efficacy of treatment was judged clinically and histopathologically. From the clinical standpoint, stress was laid on improvement in general condition; reduction in size and

alteration in the consistency of liver; reduction in intensity of oedema, ascites and icterus and reduction in the prominence of abdominal distension and superficial abdominal veins.

Out of 23 cases treated with Liv.52,

7 cases were completely cured	(30.43%)
6 cases had marked relief 1 case had moderate relief 1 case had slight relief	(34.78%)
4 cases had no relief	(17.39%)
4 cases expired	(17.39%)

By complete cure we mean total absence of any signs and symptoms of the disease and by relief we mean amelioration in signs and symptoms and reduction in size of liver and spleen. The results in 69 cases treated without addition of Liv.52 were:

1 case was cured	(1.44%)
13 cases were relieved	(18.88%)
40 cases had no relief	(57.97%)
15 cases expired	(21.73%)

Details of 23 cases treated with Liv.52: Of the 7 cases (3, 14, 16, 17, 19, 20, 21) completely cured, 4 were in early and 2 in intermediate stage of Cirrhosis and 1 case (3) was of Acute Infective Hepatitis. The livers of 6 cases of Cirrhosis had slight to moderate enlargement and firmness. In case 3 the jaundice gradually disappeared by the 10th day and liver gradually reduced in size till it became 'not palpable' on the 56th day of treatment. In case 14, liver showed slight reduction in size on the 10th day and then onwards gradually reduced and became 'not palpable' on 45th day. The abdominal distension, which used to start in the evening and persist through the major part of the night, ceased to occur on the 18th day of treatment. In case 16 reduction in size of the liver and abdominal distension was first noticed on the 6th day of the treatment. Thereafter the distension was only prominent after the meals. This also ceased on the 13th day. Liver gradually reduced and lost its firmness till it became 'not palpable' on 38th day. Case 17 was of Cardiac Cirrhosis. This girl was admitted for Congestive Cardiac Failure from Rheumatic Carditis. After all the signs of C.C.F. had disappeared, her liver remained moderately enlarged and firm and it took 40 days of treatment to become 'not palpable'. In case 19 reduction in oedema and ascites was first apparent on the 7th day of treatment. On the 1wth day icterus also lessened in intensity. On the 17th day only a trace of oedema, ascites and icterus was left. On 27th day there was no icterus and liver was 'not palpable'. In case 20 liver showed slight reduction in size and abdominal distension and the superficial veins were less prominent on the 7th day of treatment. On 20th day there was marked reduction in size of liver and abdominal distension. Gradually the liver became 'not palpable' on the 45th day. In case 21 the reduction in size of liver and abdominal distension was apparent on the 5th day of treatment. By 21st day there was no abdominal distension and liver had much reduced in size. Gradually the liver became 'not palpable' on 56th day.

Of the 6 cases (2, 4, 7, 8, 10, 22), who had marked relief, 2 were in early, 3 in intermediate and 1 in late stage of the disease. In case 2, a period of one month elapsed before any reduction in the size of liver was noted. But from thereon the liver gradually reduced in size and consistency. In case 4 small reduction in size of right lobe was noted on the 5th day and of left lobe on the 15th day. Abdominal distension was much less on 21st day and ascites cleared up on the 27th day. On 52nd day there was no abdominal distension at all and liver had markedly reduced in size and had become softer. In case 7 small reduction in size of the liver was first noted on the 11th day and oedema had lessened by the 8th day. Ascites became less by the 17th day. On 23rd day liver had markedly reduced in size, oedema had disappeared completely and abdominal distension and the

superficial veins were only slightly prominent. Case 8 had associated Diabetes Mellitus. Slight reduction in size was first noted on the 11th day. On 25th day marked reduction in size of the liver and abdominal distension was noticed. Abdominal distension became more pronounced after feeds only. On 35th day only the edges of the liver lobes were palpable and abdominal distension even after feeds was not much noticeable. In case 10 the general condition improved by the 5th day; slight reduction in size of liver was noted on the 7th day. On 13th day liver was further reduced in size and was less firm and abdominal distension was less prominent. Thereafter the progress was very gradual as the child had two attacks of diarrhoea. In case 22 oedema becomes less and liver had a small reduction in size on the 11th day. On 14th day oedema further lessened and ascites was also less. On 20th day liver size showed further reduction and abdominal distension was markedly less. On 26th day the right lobe of the liver became 'not palpable', oedema and ascites completely disappeared and the left lobe of the liver was only slightly palpable. Except one case (2) the livers of these cases were not so grossly enlarged and firm. Case 2, of late stage of Cirrhosis, was treated for 136 days and was taken away from the hospital markedly relieved.

Case 23, who had moderate relief, was admitted in a late stage of Cirrhosis, resulting from an attack of Infective Hepatitis. His liver was 3 fingers enlarged below the costal margin and was very firm, almost hard. He had moderate ascites and oedema. On 8th day of treatment ascites and oedema abated. On 10th day there was no oedema and liver showed a small reduction in size. Then onwards the progress became very slow. Ascites disappeared on 68th day. On 75th day liver was half the original size with moderate firmness.

Case 13, who obtained slight relief, was admitted with severe anaemia, massive ascites and moderate general anasarca. The liver was moderately firm with right lobe ½ and left lobe 3 and spleen 2 fingers enlarged. He was given I.V. iron daily for 12 days and paracentesis abdominis was performed twice. His anaemia improved and the rate of refilling of ascites after the second tapping was much slower than before. Unfortunately he left the hospital after only 34 days stay with a slight reduction in size of the left lobe of the liver.

The 4 cases (5, 6, 11, 18) who had no relief at all, were admitted in late stage of Cirrhosis. Case 5 had grossly enlarged and firm liver which rapidly shrank in size with increase in jaundice and oedema. Case 6 and 18 had moderately enlarged but very firm, almost hard, livers. In case 6 the jaundice and hepatic foetor rapidly increased. Case 18 showed a slight reduction in the size of liver on the 7th day and a further reduction on the 11th day. On 13th day the child had moderate epistaxis and an attack of diarrhoea and next day liver and spleen increased in size. On 21st day diarrhoea relapsed and persisted, general condition became worse, oedema and icterus increased and ultimately the child was taken away from the hospital in a comatose condition. Case 11 had epistaxis on the 5th day. On 8th day liver increased in size and temperature shot up. On 19th day there was slight reduction in size of the liver. On 28th day oedema and ascites had slightly diminished. On 30th day the child had massive epistaxis and from thereon the condition deteriorated. These 4 cases could not be followed up after their discharge from the hospital and we presume that all had expired.

The 4 cases (1, 9, 12, 15) that expired were all admitted in late stage of the disease. Case 1 was of rapidly progressive disease resulting from an attack of Acute Infective Hepatitis. Foetor hepaticus increased on 3rd day; restlessness and oliguria developed on 4th day; diarrhoea started on 5th day and on 7th day icterus increased, abdominal distension became marked and drowsiness set in. Diarrhoea did not respond to any treatment till the day of expiry. Case 9 had grossly enlarged and firm liver and expired on the 67th day of the treatment with progressive shrinking of liver and enlargement of spleen. Case 12 was a rapidly deteriorating case of Subacute Infective Hepatitis. Case 15 had a moderately enlarged but very firm, almost hard, liver and showed no clinical improvement in the

first two weeks. On 17th day icterus and hepatic foetor developed; on 23rd day oedema and ascites appeared and the deterioration could not be checked.

DISCUSSION

We are aware that it is not easy to correctly assess the results of our study; still however, comparing our results in 69 cases treated without Liv.52 and in 23 cases with Liv.52 we venture to say that Liv.52 has a definite place in the treatment of these liver disorders and exerts a substantial beneficial effect. *Sule* and *Sathe* tried the drug in 25 adult cases of ascites of various etiology. Fourteen of their cases were of Cirrhosis of the liver, 6 of whom showed marked relief and 2 had fair improvement. They observed that the drug has a definite action in reducing oedema and ascites and improving hepatic function. The drug also showed a definite improvement in the liver function tests. *Patrao* treated 6 adults cases of advanced Cirrhosis with this drug and 3 of them improved remarkably well. *Mathur* tried Liv.52 in 8 cases of Cirrhosis in children aged 1-5 yeas and all cases except one responded very well. *Murki Bhavi* and *Sheth* tried the drug orally in 26 cases of jaundice in dogs, 14 of whom died within 72 hours of admission and 12 cases recovered completely. In comparison to 100% mortality in dogs suffering from jaundice during the last three years, they found this improvement fairly promising.

It can be argued that the same kind of results as we have obtained, especially in cases of Infective Hepatitis and early Cirrhosis, could also be achieved by the routine conventional treatment without the assistance of this indigenous preparation. But comparing our results with the two types of treatment, we could say that addition of Liv.52 gave better results, even in intermediate and advanced stages of Cirrhosis.

Inspite of substandard nutritional status in our cases, we deliberately did not give any extra proteins. Only a balanced diet was given. Still, however, we were able to cure 7 cases and gave slight to moderate relief in 8 other cases. Thus massive protein supplements may not be necessary in the treatment of these liver diseases.

Two cases of Subacute Infective Hepatitis and two cases of Cirrhosis resulting from a previous attack of Infective Hepatitis suggest the possibility that one of the major causes of Cirrhosis of the liver in our children is a virus infection. The chances of missing a very mild attack of Viral Hepatitis are many and coupled with the notorious poor observance of the parents we may remain in the dark about the actual incidence of Viral Hepatitis. Moreover, anicteric attacks of Viral Hepatitis are also known to occur and these may also lead to subsequent Cirrhosis.

Lipotropics were employed in 10 cases (2 of Subacute Infective Hepatitsi, 4 of late, 2 of intermediate and 2 of early stage of Cirrhosis). Three of these cases expired, 1 had no relief, 3 had marked relief, 1 had moderate relief and 2 were cured. Lipotropics were particularly helpful in case 2 of late Cirrhosis, where their later addition in the treatment definitely helped to reduce the size of the liver. Their use with Liv.52 is thus very helpful in some cases.

All the 8 cases, who were relieved, would have been cured completely if they had continued the treatment still further. Grossly enlarged and firm livers are still not amenable to treatment and prognosis in most of these cases was not in any way altered by Liv.52.

In the 7 cases that were cured, the beneficial effects of the treatment were evident very early in the course of treatment and it was a smooth sailing towards recovery, although a long time elapsed before the liver became 'not palpable'. The good effects of the treatment in the group of 8 cases that got 'relief' were also evident early in the course of treatment, except in 2 cases. It seems that once the recovery starts the process persists. In 4 cases that had 'no relief', 2 deteriorated rapidly. The third case (case 18) had slight initial improvement but an attack of epistaxis and diarrhoea tilted the

balance and the condition gradually worsened. The fourth case (case 11) also showed slight improvement after an initial setback but after an attack of massive epistaxis on the 38th day the condition showed no improvement. The 4 cases that expired showed no benefit at any time during the course of treatment. It seems that attacks of diarrhoea or haemorrhage adversely affect the prognosis in these cases. In one case (case 10) attacks of diarrhoea retarded the process of recovery.

The duration of treatment is a long drawn out affair in majority of cases. It was relatively shorter in early cases. The left lobe of the liver always took a longer time to reduce in size or become 'not palpable'.

In one (case 7) of intermediate stage of Cirrhosis the use of Liv.52 alone produced marked relief and reduced the liver to half its original size in 34 days. Hence it may be suggested that Liv.52 has a lipotropic and liver tissue regenerative actions.

Early diagnosis and treatment of the Cirrhosis of the liver is of prime importance and likelihood of recovery is excellent with the treatment we have tried out. Liv.52 used along with Inj. Liver Extract in all cases and lipotropics in suitable cases, is an efficacious, nontoxic and a well tolerated drug in the treatment of cirrhosis of the liver and Acute or Subacute Infective Hepatitis.

Table showing details of cases

Case No.	Age/Sex	Cause of Hepatopathy	Duration before treatment in days	Initial palpability Liver/Spleen (Fingers)	Final palpability Liver/Spleen (Fingers)	Liv.52 Tablets		Other drugs	Nutritional status	Results
						Daily dose	Duration in days			
1	2	3	4	5	6	7	8	9	10	11
1	1½ Y/M	Late cirrhosis	60	4 both 2 Firm++	Rt. 4 2 Ltd. 5	4	12	Inj. Uni B_{12} Folic	Poor	Expired
2	8Y/M	– do –	120	Rt. 2 2 Lt. 4½ Firm ++ 2	Rt. Nil Nil Lt. 1½	4	136	Inj. Uni B_{12} Folic Iron Univite + Choline	Poor	Marked Relief
3	10Y/M	Acute infective Hepatitis	7	Both 2 Nil Firm + Tender	Both Nil –	4	56	Inj. B_{12} Folic	Poor	Cured
4	7Y/M	Intermediate stage cirrhosis	120	Rt. 1 Nil Lt. 3½ Firm++	Rt. Only – edge Ltd. 1½	4	90	Inj. Uni B_{12} Folic Iron Univite + Choline	Poor	Marked Relief
5	2½Y/M	Late cirrhosis	60	Rt. 5 3 Lt. 4 Firm ++	Rt. 2½ 3 Lt. 3½	4	13	Inj. Uni B_{12} Folic	Poor	No clinical relief but size of liver and spleen reduced
6	1Y/M	Late cirrhosis	120	Both 3 2 Firm +++	Same Same	6	7	– do –	Poor	No relief
7	3Y/M	Intermediate stage cirrhosis	120	Rt. 2 Nil Ltd. 3 Firm +	Rt. 1 – Lt. 1½	4	34	Iron	Poor	Marked relief
8	12Y/M	Intermediate cirrhosis	60	Rt. 2 Nil Lt. 2½ Firm +	Both only - Edge palp	4	33	Inj. Uni B_{12} Folic and Iron	Poor	Marked relief

9	2Y/M	Late cirrhosis	45	Rt. 3 1 Lt. 6 Firm ++	Rt. 1½ 3½ Lt. 3	6	67	Inj. Uni B_{12} Folic Univite + Choline	Poor	Expired
10	3M/M	Subacute Infective Hepatitis	25	Rt. 2 2 Lt. 1 Firm +	Rt. 1½ 1 Lt. Edge palp	4	60	Inj. Uni B_{12} Folic Univite + Choline	Poor	Marked relief
11	4Y/M	Late cirrhosis	90	Rt. 5½ 3½ Lt. 5½ Firm +++	Both 5½ 5	6	50	– do –	Poor	No relief
12	3 Y/M	Subacute Infective Hepatitis	30	Both 2 1 Firm ++	Same Same	6	6	– do –	Poor	Expired
13	12Y/M	Intermediate cirrhosis	3	Rt. 1½ 2 Lt. 3 Firm ++	Rt. ½ 2 Lt. 2½	6	34	Inj. Uni B_{12} Folic Iron	Poor	Slight Relief
14	2Y/M	Intermediate cirrhosis	45	Rt. 2 1 Lt. 3 Firm +	Nil Nil	4	45	Inj. Uni B_{12} Folic	Fair	Cured
15	1Y/F	Late cirrhosis	90	Both 8 2½ Firm +++	Both 2½ 2	4	38	Inj. Uni B_{12} Folic Univite + Choline	Fair	Expired
16	2½Y/M	Early cirrhosis	75	Rt. 1½ 1 Lt. 2½ Firm +	Nil Nil	4	38	– do –	Fair	Cured
17	10Y/F	Cardiac cirrhosis (Intermediate stage)	120	Both 3 1 Firm ++	Nil Nil	4	40	Inj. Uni B_{12} Folic Iron	Poor	Cured
18	2Y/M	Late cirrhosis	90	Both 3 2 Firm +++	Both 2 3	6	42	Inj. Uni B_{12} Folic Iron	Poor	No relief
19	4Y/F	Early cirrhosis (From Infective Hepatitis)	105	Both 1 Nil Firm +	Nil Nil	6	27	Inj. Uni B_{12} Folic	Poor	Cured
20	1Y/M	Early cirrhosis	60	Rt. 3 1½ Lt. 2 Firm ++	Nil Nil	4	45	– do –	Poor	Cured
21	2Y/M	– do –	70	Rt. 2 2 Lt. 3 Firm +	Nil Nil	4	66	Inj. Uni. B_{12} Folic Univite + Choline	Poor	Poor cured
22	2½Y/M	– do –	30	Both 2½ Nil Firm +	Rt. Nil Nil Lt. 1	4	30	Inj. Uni B12 Folic Iron	Poor	Marked
23	8Y/M	Late cirrhosis (From infective hepatitis)	120	Both 3 2 Firm +++	Both 1½ Nil	6	75	Inj. Uni B_{12} Folic Univite + Choline	Poor	Moderate

SUMMARY

Liv.52, a combination of Indian Indigenous drugs, was used as the main weapon in 23 cases of Hepatopathy, along with I.M. Inj. of a Liver Extract preparation in 22 cases and a lopotropic

preparation in 10 cases. Twenty cases were of Cirrhosis of the Liver, 2 cases were of Subacute Infective Hepatitis and one case was of Acute Infective Hepatitis. The diagnosis and results of treatment were confirmed by liver biopsies. Seven cases were cured, 8 cases were relieved, 4 cases had no relief and 4 cases expired. All the cases that had no relief or expired were admitted in late stage of the disease, with either grossly enlarged or very firm livers. The results of treatment show that Liv.52 has a useful and definite place in the treatment of Viral Hepatitis and Cirrhosis of the liver. The drug is cheap, non-toxic and well tolerated.

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