HEPATO-PROTECTIVE ROLE OF INDIGENOUS DRUG LIV-52 IN LEPROMATOUS LEPROSY I

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ABSTRACT — The present study incorporates a study of 42 cases of lepromatous leprosy for hepatic involvement and role of indigenous herbal preparation in protecting the liver in leprosy. Liver was enlarged in 32 cases which was tender in 8 patients. Alteration in liver function irrespective of extent and duration of the illness (3 months to 10 years with mean duration of illness = 2 years 5 months) was mainly seen as uniform elevation of serum proteins (6.2-9.2 gms%, mean = 7.5 gms%) with hypoalbuminaemia (2.0-4.4 gms%, mean = 2.9 gms%). Highest level of serum bilirubin of 1.6 mg% was detected in 6 cases, emphasising the presence of leprous hepatitis. Raised level of serum transaminases (SGOT = 65.2 IU, SGPT = 78.7 IU) were proportionate to the liver and muscle involvement. Presence of characteristic granulomata in the liver around the central vein, periportal area and even distribution at various locations in the liver lobules were the most significant changes in 12 out of 15 liver tissues. Acid fast **M. leprae** were demonstrated in 12 patients. The present work emphasises the detection of hepatic involvement in the early stage of the disease and hepato-protective role of indigenous drug Liv-52 in lepromatous leprosy which usually lead to dreaded mutilated complications in the body.

Key words: Lepromatous leprosy. Liver. Herbs.

1 INTRODUCTION

Leprosy is a chronic progressive granulomatous infection which affects various systems of the body of which hepato-biliary system is the most commonly affected[9, 12, 13, 18]. The hepatic involvement is seen in early stages of the disease. The specific granulomatous changes in liver and deranged liver functions are mainly seen in lepromatous leprosy [10,12,13] . Whenever a derangement in liver function is recognised it is generally late, which deprives the sufferer from proper treatment and quicker recovery. The aim of treatment is to check and stop the further damage to the perishing liver, to reduce the accumulating fibrous tissue and to encourage mitosis for new cell formation. In Indian Medicinal Sciences, Ayurveda and Siddha, human body is the replica of the five mighty elements in which liver

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plays the major role in life. Emphasis has been laid to protect the liver from various ailments[1]. Various herbs were described for the hepatic restorative and protective effects[1,2,15]. The present study was undertaken to present the liver in lepromatous leprosy and to evaluate hepatic restorative and protective effect of an indigenous herbal preparation Liv-52.

2 MATERIAL AND METHODS

Forty two patients of lepromatous leprosy were included in this study, who were diagnosed on clinical, histological and bacteriological grounds[5,12,13]. All patients were thoroughly scrutinized to exclude any other overt cause which is known to produce derangement in liver function and such cases were not included in this study.

Biochemical liver function tests were performed by standard techniques before and after 6 and 12 weeks of therapy. These included serum proteins, albumin, globulin, bilirubin, thymol turbidity, serum transaminases, L. D . H. , alkaline phosphatase and prothrombin time. Percutaneous liver biopsy was performed under aseptic technique wherever possible. Hematoxyline and eosine stained sections were examined. Acid fast bacilli were demonstrated by Fite Faraco's modified technique[17].

Patients were grouped into two groups: Group I: Control, group of 20 cases treated with Dapsone etc., but without Liv-52. Group II: Clinical trial group of 22 cases getting Liv-52 two tablets three times a day for at least 12 weeks along with antileprotic drugs.

Follow up was made for first two months every week then monthly for the 12 months. The clinical assessment of recovery of patients regarding protective role of Liv-52 was judged by the clinical improvement, biochemical tests and histo-pathological changes in the liver[12,16,19].

3 OBSERVATIONS

Forty two cases of lepromatous leprosy were grouped into two groups Group I (20 cases) and Group II (22 cases) for studying therapeutic response of the drug. Their ages varied from 8 to 62 years with the mean age of 30.2 years and male to female ratio of 3.4:1 (Table 1). The duration of illness varied from 3 months to 10 years and the mean duration of illness was 2 years 5 months. Hepatomegaly was noted in 32 patients which was tender in 8 of them.

3.1 *Biochemical Changes.* Liver functions were deranged in proportion to the liver involvement (Table 2). Hepatic damage and dysfunction was manifested as raised serum levels of transaminases, L L. D .H . and alkaline phosphatase. There is uniform elevation of serum proteins with lowered level of serum albumin leading to reversal of albumin globulin ratio. This alteration was irrespective of the extent and duration of the disease.

3.2 *Histological changes in the liver.* The liver architecture was preserved in all of them without any parenchymal changes. Characteristic granulomata (12 out of 15 cases) of different sizes were seen, which were extensive and diffuse in 8 cases and localised in 4 cases. Granulomata were chiefly located in the periportal areas (Fig. 1), which were sharply circumscribed, spherical accumulation of histiocytes, foam cells and lymphocytes with a somewhat clear sorrouding zone. Granulomata were loaded with acid fast bacilli (12 cases). Foam cells were arranged in groups (Fig. 2). Apart

TABLE 1 — Age and sex distribution

Age groups	Group I		Group II		Total	Incidence
	Male	Female	Male	Female		
0 — 20 years	1	—	1	1	3	7.1%
21 — 30 years	5	1	2	2	10	23.8%
31 — 40 years	7	—	8	2	17	40.4%
41 — 50 years	4	1	4	1	10	23.8%
Above 50 years	—	1	1	—	2	4.9%
Total	17	3	16	6	42	100%
Sex ratio =	5.6 : 1		2.6 : 1		3.4 : 1	
Age range =	13 — 62 yrs.		8 — 58 yrs.		8 — 62 yrs.	
Mean age =	29.6 years		30.8 years		30.2 years	
Duration of illness =	3 mths.-10 yrs.		4 mths.-10.5 yrs.			
Mean duration =	2 yrs.3 mths.		2 yrs.6 mths.		2 yrs.5 mths.	

TABLE 2 — Liver function tests in two groups

Tests		Group I (20 cases)	Group II (22 cases)
1 Serum bilirubin (mg%)	range	0.31-0.98	0.42-1.2
	mean	0.56	0.82
2 Thymol turbidity (units)	range	12-20	16-22
	mean	16.8	19.2
3 Serum proteins (gms%)	range	6.2-8.2	6.8-9.2
	mean	6.87	7.24
4 Serum albumin (gms%)	range	2.4-4.0	2.0-4.4
	mean	3.02	2.84
5 Serum globulin (gms%)	range	3.9-5.8	3.5-6.2
	mean	4.21	4.62
6 S.G.O.T. (I.U.)	range	42-84	58-82
	mean	64.2	66.2
7 S.G.P.T. (I.U.)	range	58-92	49-94
	mean	74.8	82.6
8 Alk.phosphatase (K.A.U.)	range	18-38	20-42
	mean	26.2	32.8
9 L.D.H. (Units)	range	520-640	480-620
	mean	568.2	552.8

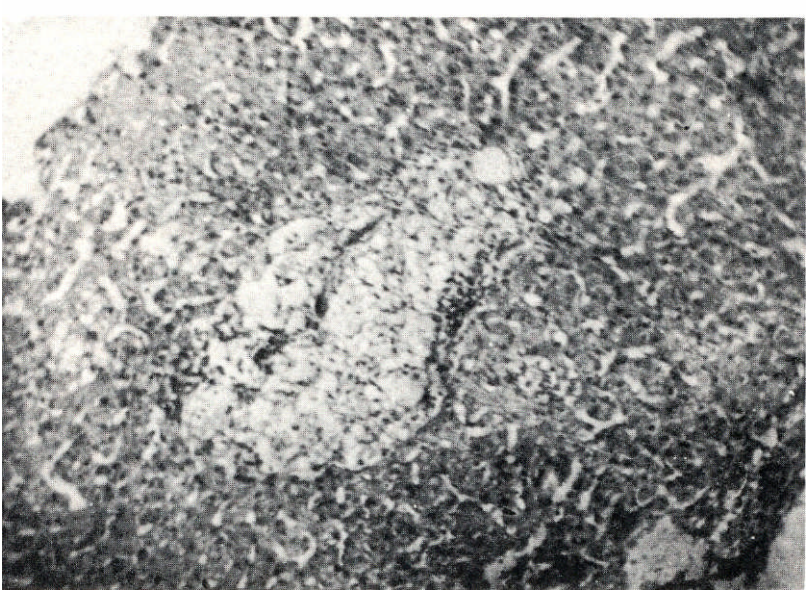

FIGURE 1 — Liver in lepromatous leprosy showing localised microgranulomata. H & E x 100.

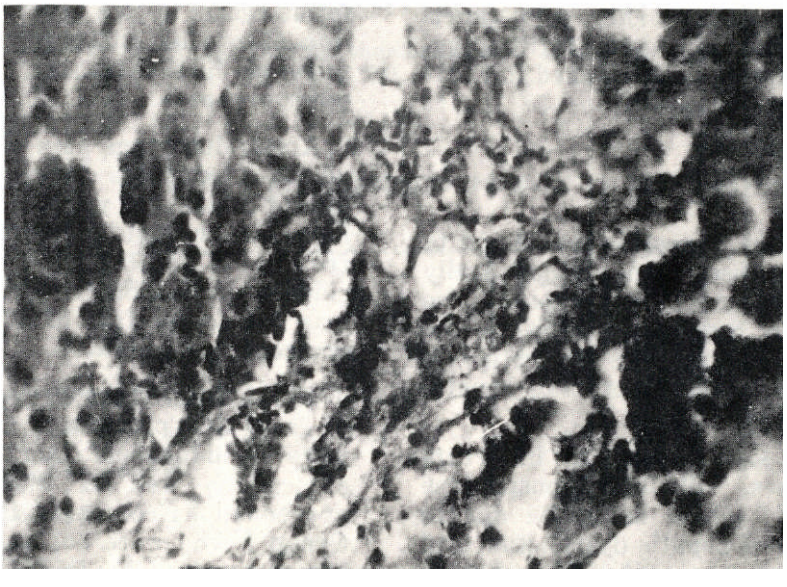

FIGURE 2 — Microgranulomata under high power magnification showing acid fast bacilli also.

from these there was proliferation of Kupffer's cells and sinusoidal dilatation in 4 cases (Fig. 3). In one case of Group I there was evidence of amyloid tissue who had the extensive disease for the last 10 years. Progression of hepatic lesion to fibrosis was seen in 8 cases (Table 3).

3.3 *Therapeutic Response.* The average period of therapy pertaining to hepatic dysfunction was 12 weeks in Group II cases but were followed to a maximum period of 12 months and Liv-52 was repeated as and when indicated (5 cases). The findings are summarised in Table 4 and Table 5. The mean fall of enzymatic levels after scheduled therapy was better and quick in Group II cases as compared to Group I. Serum albumin was raised from 2.84 gms% to 4.6 gms% in Group II cases. This rise in serum albumin was significant as compared to Group I cases.

Histology of the liver showed decreased stellate fibrosis in Group II cases along with earlier and quick clearance of lymphocytic infiltration. Liver cell necrosis was checked in clinical trial group cases.

4 DISCUSSION

Lepromatous leprosy is considered to be a systemic disease and pathologically it is a reticuloendothelial disease. The alteration in hepatic function in the present series of cases is the testimony of involvement and affection of hepato-biliary system.

There is significant rise in serum transaminases, alkaline phosphatase and L.D.H. which might be due to combination of hepatic dysfunction and muscular involvement[7,12,13], whereas Mohanty & Murty[11] stressed mainly on muscular involvement. Gupta *et al* [9] and Lodha *et al* [10] reported normal values. There is uniform rise serum proteins with hypoalbuminaemia (serum albumin=2.0-4. 4 gms%) which was irrespective of extent and duration of the disease. This is the result of derranged hepatocyte function and hyperplasia of reticuloendothelial cells[7,10,12,13].

The typical histological lesions of the liver have been reported by various workers[4,13,14,21]. Two types of lesions have been encountered i.e., granulomata specific of leprosy and non-specific collection of mononuclear cells, both types of lesions progressed to portal scarring in due course of time which might be due to drug, nutritional factors or end result of the disease itself. The predominance of histiocytes containing multiple *M. leprae* and lipoid material was the important feature of its being a disease of reticulo-endothe lial system. The presence of *M. leprae* all along the sinusoids evidently showed that the spread of infection occurs through blood stream and the body tissue reacts to this insult by proliferation of reticulo-endothelial cells in the form of histiocytes in the liver and other organs[21].

Amyloidosis was seen in one patient who had extensive disease for the prolonged period (10 years). Its incidence has been variously reported ranging from 5.9% to 50%[22]. The higher incidence of it from Western Countries was due to the fact of dietary and/or environmental factors.

It is observed in the present series of cases that patients of Group II who were on indigenous drug, had speedier clinical as well as biochemical improvement as compared to patients of Group I who were not on Liv-52. The period required for improvement is cut short in Group II cases and thereby helping in overcoming the morbidity of the disease. It has been reported

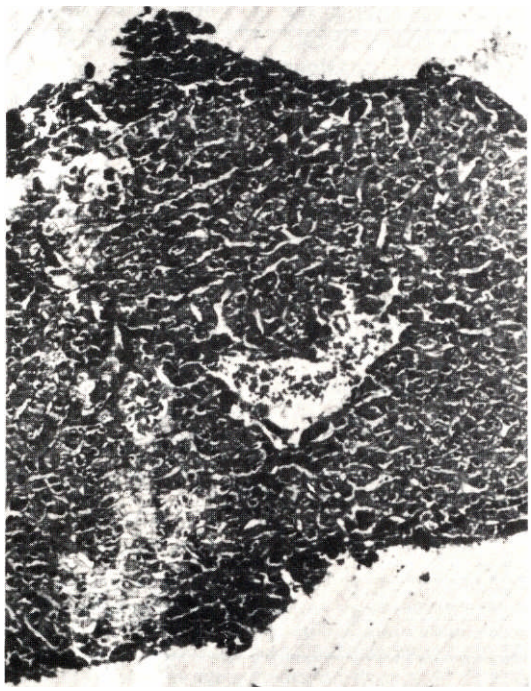

FIGURE 3 — Liver in lepromatous leprosy showing multiple granuloma with sinusoidal dilatation and Kupffer's cells. H & E x 100.

TABLE 3 — Histo-pathological changes of the liver

Histo-pathological changes	Group I (6 cases)	Group II (9 cases)
1 Specific granulomata = diffuse and extensive	3	5
2 Progress of hepatic lesion to fibrosis	3	5
3 Specific localised granulomata	2	2
4 Non-specific changes	—	1
5 Normal histology	1	1
6 Demonstration of Acid Fast Bacilli	5	7
7 Amyloid deposition	1	—

TABLE 4 — Biochemical evaluation of protective role of Liv-52

Biochemical tests	Group I (20 cases)			Group II (22 cases)		
	Duration of treatment in weeks					
	0	6	12	0	6	12
S.G.O.T. < 40 IU	4	8	11	5	12	18
	20%	40%	55%	22.7%	54.5%	81.8%
S.G.P.T. < 40 IU	3	6	10	4	9	20
	15%	30%	50%	18.1%	40.5%	90.9%
Alk.phosphatase < 14 KAU	5	9	10	6	12	19
	25%	45%	50%	27.6%	54.5%	86.4%
Thymol turbidity < 5 Units	10	10	14	8	16	20
	50%	50%	70%	36.2%	72.6%	90.9%
L.D.H. < 350 Units	4	8	8	4	9	18
	20%	40%	40%	18.1%	40.5%	81.8%
Serum albumin > 2.5 gms%	3	5	9	4	10	18
	15%	25%	45%	18.1%	45.4%	81.8%

TABLE 5 — Biochemical estimations before and after treatment

Biochemical tests		Group I (20 cases)		Group II (22 cases)	
		Duration of treatment in weeks			
		0	12	0	12
S.G.O.T. (IU)	range	42-84	44-64	58-82	32-58
	mean	64.2	58.6	66.2	39.8
S.G.P.T. (IU)	range	58-92	41-68	49-94	28-72
	mean	74.8	59.8	82.6	32.8
Alk.phosphatase (KAU)	range	18-38	12-24	20-42	9-26
	mean	26.2	19.6	32.8	13.8
L.D.H. (IU)	range	520-640	480-610	480-620	250-380
	mean	568.2	512.6	552.8	278.6
Serum albumin (gms%)	range	2.4-4.0	3.0-4.1	2.0-4.4	3.8-5.4
	mean	3.02	3.24	2.84	4.60
Thymol turbidity (Units)	range	12-20	8-18	16-22	4-10
	mean	16.8	12.4	19.2	6.02

that many indigenous plants have beneficial effects on liver disease and act as hepato-protective[2,13,15,19]. Liv-52 is a preparation from indigenous herbs of Himalaya Drug Co., which accelerates the clinical as well as biochemical recovery[20]. It stimulates mitotic activity[15] of the hepatic cells and thus stimulates the regeneration of liver cells which will correct all secondary abnormalities consequent to liver parenchymal necrosis and degeneration. Liv-52 presumably improves the function of hepatocytes and promotes the regeneration of the necrosed cells, thereby improving the protein synthesis. It diminishes the activity of serum transaminases and arrests the cell necrosis and inflammation. It is observed histologically in Group I cases the persistence .of necrotic changes, granulomata formation progressing to stellate fibrosis, which is not seen in Group II cases. Therefore it can be said that Liv-52 restores normal liver functions earlier and in shorter duration, improves appetite, gives sense of well being, anti-inflammatory and effectively contributes to healthy repair and regeneration of liver cells which proves its hepato-protective role.

Acknowledgement

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RESUMO — O presente trabalho se refere a um estudo de 42 casos de hanseníase virchowiana com comprometimento hepático e ao efeito de uma preparação de ervas nativas na proteção do fígado. O fígado estava aumentado em 32 casos e sensível em 8 pacientes. Alterações das funções hepáticas, independentes da extensão e da duração da doença (3 meses a 10 anos, com duração média de doença = 2 anos e 5 meses), foram principalmente observadas pela elevação uniforme das proteínas séricas (6,9 — 9,2 g%, média - 7,5 g%) com hipoalbulinemia (2,0 — 4,4 g%, média — 2,9 g%). O nível mais elevado de bilirrubina no soro (1,6 mg%) foi observado em 6 casos, evidenciando a presença de hepatite hansênica. Os altos níveis de transaminase sérica (SGOT = 65,2 UI, SGPT = 78,7 UI) foram proporcionais ao comprometimento hepático e muscular. A presença de granulomas característicos no fígado ao redor da veia central, na área periportal e mesmo distribuídos por vários locais dos lóbulos hepáticos foi a modificação mais significativa em 12 dos 15 tecidos hepáticos estudados. **M. leprae,** álcool-ácido-resisten-tes, foram observados em 12 pacientes. O presente trabalho evidencia o comprometimento hepático nos estadios precoces da doença e o efeito hepato-protetor da droga nativa Liv-52 na hanseníase virchowiana, a qual geralmente leva a temidas mutilações e complicações. **Tradução do Editor.**

Palavras chave: Hanseníase virchowiana. Fígado. Ervas.

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