[*Hansenlogia Internationalis, Brazil* (1982): (7), 1, 36]

Hepato-protective Role of Indigenous Drug Liv.52 in Lepromatous Leprosy

Pranesh Nigam, Reader in Medicine, B.R.D. Medical College, Gorakhpur, India
Dayal, S.G., Lecturer in Dermato-venereology and Leprosy, Govt. Medical College, Jammu-Tawi, India,
Mukhija, R.D., Reader in Dermato-venereology and Leprosy, B.R.D. Medical College, Gorakhpur, India
Goyal, B.M., Reader in Tuberculosis and Chest Diseases, M.L.B. Medical College, Jhansi, India.
and
Joshi, L.D., Reader in Biochemistry**,** M.L.B. Medical College, Jhansi, U.P., India.

(* Paper presented at the 20th Annual Conference of Indian Society of Gastroenterology, Poona, Oct. 1979).

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.

INTRODUCTION

Leprosy is a chronic progressive granulomatous infection, which affects various systems of the body of which hepatobiliary 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 Medical Sciences, Ayurveda and Siddha, human body is the replica of the five mighty elements in which liver 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.

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 scrutinised 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, LDH, 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, 2 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 histopathological changes in the liver[12,16,19].

OBSERVATIONS

Forty two cases of lepromatous leprosy were divided into two groups:
Group I (20 cases) and Group II (22 cases) for studying the 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 3.6:1 (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.

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		3.6 : 1	
Age range =	13 - 62 years		8 - 58 years		8 - 62 years	
Mean age =	29.6 yeas		30.8 yeas		30.2 years	
Duration of illness =	3 months 10 years		4 months 10.5 years			
Mean duration =	2 years 3 months		2 years 6 months		2 years 5 months	

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 transminases, LDH and alkaline phosphatase. There is uniform elevation of serum proteins with lowered level of serum albumin leading to reversal of albumin globulin ration. This alteration was irrespective of the extent and duration of the disease.

Histological changes in the liver: The liver architecture was preserved in all of them without any paenchymal 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 (Figure 1), which were sharply circumscribed, with spherical accumulation of histiocytes, foam cells and lymphocytes with a somewhat clear, surrounding zone. Granulomata were loaded with acid fast bacilli (12 cases). Foam cells were arranged in groups (Figure 2). Apart from these there was proliferation of Kupffer's cells and sinusoidal dilatation in 4 cases (Figure 3). In one case of Group I there was evidence of

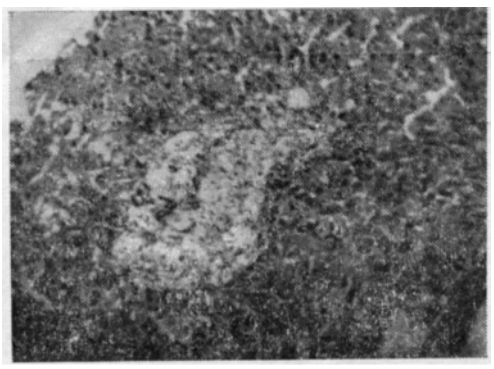

Fig. 1—Liver in lepromatous leprosy showing localised microgranulomata. H & E x 100.

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).

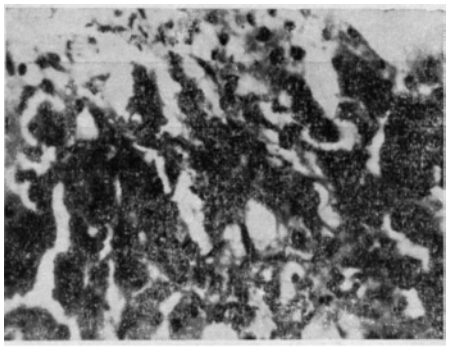

Fig. 2—Microgranulomata under high power magnification showing acid fast bacilli also.

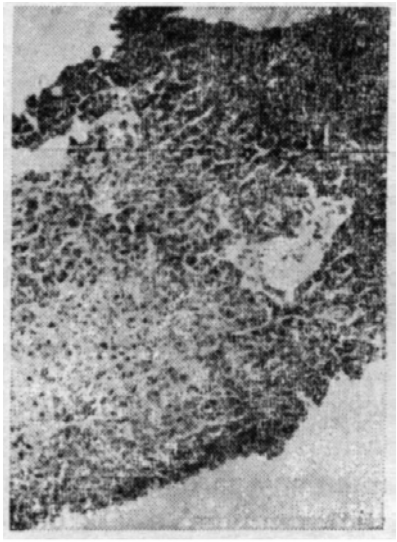

Fig. 3—Liver in lepromatous leprosy showing multiple granuloma with sinusoidal dilatation and Kupffer's cells. H & E x 100.

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.

Table 2: Liver function tests in two groups

Tests		Group I (20 cases)	Group II (22 cases)
Serum bilirubin (mg%)	Range	0.31-0.98	0.42-1.2
	Mean	0.56	0.82
Thymol turbidity (units)	Range	12-20	16-22
	Mean	16.8	19.2
Serum proteins (gms%)	Range	6.2 - 8.2	6.8 - 9.2
	Mean	6.87	7.24
Serum albumin (gms%)	Range	2.4 - 4.0	2.0 - 4.4
	Mean	3.02	2.84
Serum globulin (gms%)	Range	3.9 - 5.8	3.5 - 6.2
	Mean	4.21	4.62
SGOT (IU)	Range	42 - 84	58 - 82
	Mean	64.2	66.2
SGPT (IU)	Range	58 - 92	49 - 94
	Mean	74.8	82.6
Alkaline phosphatase (K.A.U.)	Range	18 - 38	20 - 42
	Mean	26.2	32.8
LDH (Units)	Range	520 - 640	480 - 620
	Mean	568.2	552.8

Table 3: Histopathological changes of the liver			
Sl.No.	Histopathological 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	Duration of treatment in weeks					
	Group I (20 cases)			Group II (22 cases)		
	0	6	12	0	6	12
SGOT <40 IU	4 20%	8 40%	11 55%	5 22.7%	12 54.5%	18 81.8%
SGPT <40 IU	3 15%	6 30%	10 50%	4 18.1%	9 40.5%	20 90.9%
Alkaline phosphate <14 KAU	5 25%	9 45%	10 50%	6 27.6%	12 54.5%	19 86.4%
Thymol turbidity <5 units	10 50%	10 50%	14 70%	8 36.2%	16 72.6%	20 90.9%
LDH <350 units	4 20%	8 40%	8 40%	4 18.1%	9 40.5%	18 81.8%
Serum albumin >2.5 gms%	3 15%	5 25%	9 45%	4 18.1%	10 45.4%	18 81.8%

Table 5: Biochemical estimations before and after treatment					
Biochemical tests		Duration of treatment in weeks			
		Group I (20 cases)		Group II (22 cases)	
		0	12	0	12
SGOT (IU)	Range	42-84	44-64	58-82	32-58
	Mean	64.2	58.6	66.2	39.8
SGPT (IU)	Range	58-92	41-68	49-94	28-72
	Mean	74.8	59.8	82.6	32.8
Alkaline phosphate (K.A.U.)	Range	18-38	12-24	20-42	9-26
	Mean	26.2	19.6	32.8	13.8
LDH (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

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 hepatobiliary system.

There is significant rise in serum transaminases, alkaline phosphatase and LDH, which might be due to combination of hepatic dysfunction and muscular involvement[7,12,13], whereas Mohanty and Murty[11] stressed mainly on muscular involvement. Gupta *et al*[9] and Lodha *et al*[10] reported normal values. There is uniform rise in 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 deranged 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 reticuloendothelial 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 histocytes 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 that many indigenous plants have beneficial effects on liver disease and act as hepato-protective[2,3,16,19]. Liv.52 is a preparation from indigenous herbs of The 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, is anti-inflammatory and effectively contributes to healthy repair and regeneration of liver cells which proves its hepato-protective role.

ACKNOWLEDGEMENT

We express our sincere gratitude to The Himalaya Drug Co., Shivsagar 'E', Dr. A.B. Road, Bombay-18 for the generous supply of Liv.52.

REFERENCES

1. Agnivesha, *Charak-Samhita,* 3rd ed., Bombay, Ed. Acharya, 1941, chap. 1, p. 8

2. Basu, B.D. and Kirtikar, K.R., *Indian Medical Plants,* 2nd ed., New Delhi, C.S.I.R., 1975.

3. Dave, D.S., Rajput, V.J. and Gupta, M.R., Clinico-biochemical study of infective hepatitis with special reference to Liv.52. *Probe* (1972): 11, 244.

4. Desikan, K.V. and Job, C.K., A review of postmortem findings in 37 cases of leprosy. *Int. J. Lepr.* (1968): 36(1), 32-44.

5. Dharmendra and Chatterjee, S.N., Diagnosis. In: Dharmendra, *Leprosy,* Bombay, Kothari Medical Publishing House, 1978. C. 1, sec. 3, pp. 245-282.

6. Dharmendra and Ramanujam, K., The lepromatous type. Dharmendra, *Leprosy*, Bombay, Kothari Medical Publishing House, 1978, v. 1, chap. 5, pp. 62-75.

7. Dhople, A.M. and Balakrishnan, S., Liver function tests in leprosy. *Ind. J. Med. Res.* (1968): 56, 1552-1558.

8. Gharpuray, S.M., Gharpuray, M.B., Kelkar, S.S., Liver function in leprosy. *Lepr. India* (1977): 49(2), 216-220.

9. Gutpa, M.C., Kumar, S. and Tyagi, S.P., Reappraisal of functional and structural changes in the liver in leprosy. *J. Assoc. Phys. Ind.* (1974): 22, 13-18.

10. Lodha, S.C., Bomb, B.S., Singh, S.V. and Sharma, N.L., A comparative study of liver function tests in various types of leprosy. *J. Assoc. Phys. Ind.* (1974): 22, 653-657.

11. Mohanty, H.C. and Murti, R.S., Serum transaminase in leprosy. *Lepr. India* (1973): 45(3), 163-166.

12. Nigam, P., Dayal, S.G., Goyal, B.M., Nimkhedakar, K.V., Joshi, L.D. and Samuel, K.C., Leprous hepatitis: clinico-pathological study and therapeutic efficacy of Liv.52. *Lepr. India* (1978): 50(2), 185-195.

13. Nigam, P., Mukhija, R.D. and Goyal, B.M., Study of histo-functional complex of liver in leprosy. *Ind. J. Dermatol. Venereol. Leprol.* (1976): 45(5), 217-222.

14. Powell, C.S. and Swan, L.L., Leprosypathological changes observed in 50 consecutive cases. *Am. J. Pathol.* (1955): 31, 1131-1141.

15. Prasad, G.C., Effect of Liv.52 on the liver *in-vitro*. *J. Res. Ind. med.* (1975): 4, 15-23.

16. Salaskar, V.H., Diagnostic evaluation of the hepatic function tests. *Probe* (1978): 17, 97-109.

17. Samuel, K.C. and Chatterjee, S.N., Modification of Fite Faraco staining for acid fast bacilli. *Ind. J. Path. Bact.* (1971): 14(2), 107-109.

18. Simons, R.D.G., Leprology today. *Excerpta med. Dermatol. Venereol.* (1956): 10, 349-354.

19. Sinha, P.K., Kumar, A. and Patney, N.L., A study of therapeutic action of Liv.52. *Probe* (1979): 18, 157-166.

20. Sule, E.A., Liver in leprosy. *J. Ind. Med. Prof.* (1968): 12, 6391.

21. Tilden, I.L., Lepromatous leprosy: a reticuloendothelial disease; histopathological aspects. *Am. J. Clin. Path.* (1945): 15, 165-177.

22. Williams, Jr. R.C., Cathart, E.S., Calkins, E., Fite, G.L., Rubio, J.R. and Choen, A.S., Secondary amyloidosis in lepromatous leprosy. *Ann. Int. Med.* (1965): 62, 1000-1008.