[*Ind. J. Med. Res*. (1976): 5, 738]

Efficacy of an Indigenous Compound Preparation Liv.52 in Acute Viral Hepatitis – A Double Blind Study

Sama, S.K., Assistant Professor
Krishnamurthy, L., S.R.O., Gastroenterology
Ramachandran, K., Associate Professor and Head of the Bio-Statistics Division
and
Krishan Lal, Senior Technician.
Department of Gastroenterology
All-India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.

ABSTRACT

A double blind study on the efficacy of an indigenous compound preparation in the treatment of acute virus A hepatitis was conducted in seventeen patients. The drug was administered in doses of 6 tablets a day for six weeks. Another group of 17 patients fulfilling all the criteria for diagnosis of acute virus A hepatitis received placebo tablets in the same dose for the same period of time. The symptomatic recovery and 50 per cent fall in bilirubin level took significantly lesser time in the group treated with the indigenous preparation as compared to the placebo group, with less weight loss in the subjects of the former. The total period of recovery was not influenced by the therapy. However, there were no side effects noted in the group treated with the indigenous preparation.

INTRODUCTION

Viral hepatitis is an endemic disease in our country assuming epidemic proportions occasionally. Though majority of patients recover completely with no residual liver damage, a small proportion of cases progress to a chronic form of the disease or have a fulminant course, resulting in death. Despite rapid advances in modern drug therapy, viral hepatitis continues to pose a problem to the clinicians. There is no specific drug therapy to date which can minimise the clinical and biochemical effects in hepatitis. Steroids have been routinely used in the past, as they bring about rapid amelioration of symptoms and a quick fall in bilirubin level in the serum. Blum *et al*. (1969) from Zurich have reviewed thirty five trials, from American, European and Russian literature till 1969. Most of these trials were uncontrolled and at least 16 trials wholeheartedly endorsed steroid therapy. But investigators who subsequently carried out controlled trials did not share the enthusiasm of these workers. In their own study Blum *et al*. (1969) reported much the same findings *i.e.* a rapid initial fall in serum bilirubin with general improvement in the symptomatology but the total number of days spent in the hospital was not materially affected. On the other hand, incidence of complications like ulcer and bleeding was high. A higher relapse rate and high incidence of chronic liver disease was also noticed. Sherlock (1972) has also decried the use of steroids routinely in acute hepatitis.

The composition of the indigenous preparation Liv.52 used in the study is indicated in Table I.

Table I: Composition of Liv.52 tablets

Capparis spinosa	65 mg
Cichorium intybus	65 mg
Solanum nigrum	32 mg
Cassia occidentalis	16 mg
Terminalia arjuna	32 mg
Achillea millefolium	16 mg
Tamarix gallica	16 mg
Mandur bhasma	33 mg

This product has been claimed to be very effective in protecting the liver of experimental animals exposed to various hepatotoxic agents (Joglekar *et al*., 1963; Joglekar and Balwani, 1967; Joglekar and Leevy, 1970; Karandikar *et al*., 1963; Kale *et al.*, 1966; Patel and Sadre, 1963; Sheth *et al.*, 1960). A number of clinical trials on this preparation have been reported with very promising results in acute hepatitis. All the trials conducted uniformly observed the efficacy of the drug in bringing about rapid amelioration of symptoms (Arora, 1968; Dave and Gupta, 1972; Ramalingam *et al*., 1971; Deshpande *et al*. 1971; Sule, *et al.,* 1968; Mehrotra and Mathur, 1973; Gupta *et al.*, 1972; Jaffari and Shyam Raj, 1969; Mukerjee and Dasgupta, 1970). Progression to fulminant and chronic course is also averted (Sule *et al*., 1968; Mukerjee and Dasgupta, 1970). However, most of these trials were uncontrolled. In view of this, a trial was undertaken with Liv.52 in acute virus A hepatitis under controlled conditions using a randomised double blind method.

MATERIAL AND METHODS

Patients of infective hepatitis attending the medical out patient and Gastroenterology clinic of the All-India Institute of Medical Sciences, were hospitalised during acute phase of illness. The diagnosis was based on clinical features of prodromata like anorexia, vomiting, malaise and fever, followed by highly coloured urine and icterus, mild to moderate hepatomegaly with elevated transaminases *i.e.* both serum glutamic oxaloacetic transaminase and pyruvic transaminase of over 200 Karmen units, the normal being 40 and 35 Karmen units respectively. Patients who had history of ingesting hepatotoxic drugs prior to the onset of symptoms those who had HBAg in the serum were excluded from the study. Only patients with jaundice of less than ten days' duration and a serum bilirubin of over 4.5 mg were included. In order to ensure that the patients were not already in the recovery phase, a serum bilirubin estimation was carried out on days 1 and 3 to demonstrate stable or rising bilirubin. Children below ten and adults above forty were excluded from the trial. Patients in whom there was a rapid deterioration of liver functions, or signs of precoma and/or bleeding tendencies were dropped from the trial and regarded as failures.

In all, thirty four patients received the treatment. They were randomised into two groups and each patient received 6 tablets (2 tablets t.d.s.) of the drug or placebo per day for six weeks according to the allocation. Accurate intake of the drug was ensured at the hospital as well as at home with the help of one reliable relative.

The response was recorded on days 3 and 7 after commencement and thereafter at weekly intervals till clinical recovery occurred. The assessment included factors like return to appetite, sense of well being, degree of icterus, reduction in the size of liver and development of any complications. Biochemical parameters studied were serum total bilirubin, serum transaminase and serum alkaline phosphatase using standard procedures. After clinical recovery patients were followed up fortnightly till full biochemical recovery occurred or for a period of 3 months. No histological criteria were used for assessment.

RESULTS AND DISCUSSIONS

Table II shows the matching of the two groups after decoding. There were seventeen subjects in each group and there is no significant difference in the mean age, duration of symptoms prior to institution of drug and mean bilirubin level. The socio economic status of both groups as evidenced by per capita income did not differ in the two groups.

Table II: Comparison of Liv.52 and placebo group*s*
Initial data on the two groups of patients at the time of admission

Treatment	Age (Yrs.)		S. Bilirubin (mg.) on admission		Duration of illness (days) on admission	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Liv.52	23.4	8.55	8.01	3.63	6.71	3.42
Placebo	23.9	6.84	9.35	3.82	8.23	2.97
(No. significant difference in the two groups)						

Table III outlines the results of treatment. Clinical recovery and a 50 percent fall in bilirubin took place in a significantly shorter time in the drug-treated group. (Text Figs. *a* and *b*). However, the total recovery, as evidenced by the normalisation of biochemical parameters especially pyruvic transaminase took more or less the same time in the two sets of patients. While weight loss was recorded in twelve of the drug-treated group and in ten of the placebo group, the degree of weight loss was significantly higher in the placebo group. One case in placebo group had to be dropped from the trial on account of impending fulminant hepatitis.

Table III: Response to treatment in the two groups

Treatment	No. studied	No. recovered	Weight loss (kg.)	Time for 50 per cent fall in bilirubin (days)	Clinical recovery (days)	Biochemical* recovery (days)
			Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.
Liv.52	17	17	1.00 0.83	6.53 2.45	9.71 4.30	36.41 11.87
Placebo	17	16	2.40 0.94	12.62 4.57	18.00 10.35	37.06 8.66
Significance		Not Significant	$p<0.01$	$p<0.001$	$p\approx0.01$	Not Significant

* Time taken for SGPT to attain normal levels

Patients receiving the drug did not show any side effects or complications for a period of three months.

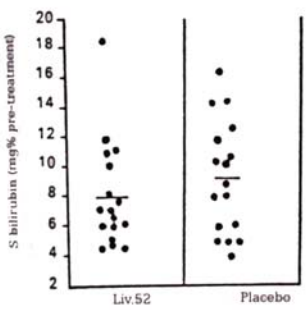

Figure 1: Diagram showing pre-treatment level of Bilirubin

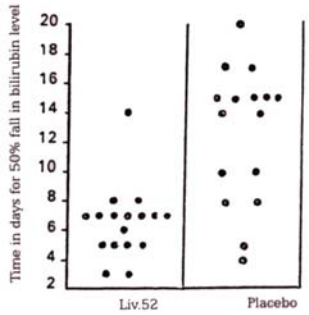

Figure 2: Diagram showing time taken for 50 per cent fall in bilirubin

Liv.52 thus seems to be a useful drug for therapy of acute viral hepatitis. There was rapid amelioration of clinical symptoms and signs, though total period of recovery was not materially affected. The response seems to be very similar to that of steroids, but without the latter's side effects. Weight loss is also minimum with Liv.52. It would be worthwhile to undertake more controlled trials in HBAg positive hepatitis and also in progressive and chronic liver disease.

REFERENCES

1. Arora, J.K. Role of various types of treatment in infectious hepatitis. *Armed Forces Med. J.*(1969): 3, 362-368.

2. Blum, A.L., Stutz, R., Haemmerli, U.P., Schmid, P. and Grady, G.F. A fortuitously controlled study of steroid therapy in acute viral hepatitis. I. Acute disease. *Am. J. Med.* (1969): 47, 82-92.

3. Dave, D.S., Rajput, V.J. and Gupta, M.R. Clinico-biochemical study of infective hepatitis with special reference to Liv.52 therapy. *Probe* (1972): 4, 214-220.

4. Deshpande, R.S., Sheth, Shantilal C. and Joykutty, M.D. Infectious hepatitis - Study of 100 cases. *Curr. Med. Pract.* (1971): 6, 810-816.

5. Gupta, S., Khatri, R.L. and Srivastava, G. Therapy of infectious hepatitis and other liver disorders. *Probe* (1972): 2, 93-99.

6. Jaffari, S.M.H. and Shyam Raj. Liv.52 in infective hepatitis. *The Antiseptic* (1969): 5, 353.

7. Joglekar, G.V. and Balwani, J.H. Allyl alcohol induced hepatotoxicity in rats and its protection by Liv.52. *J. Expt. Med. Sci*. (1967): 11, 7-9.

8. Joglekar, G.V., Chitale, G.K. and Balwani, J.H. Protection by indigenous drugs against hepatotoxic effects of carbon tetrachloride in mice. *Acta Pharmacol. et Toxicol.* (1963): 20, 73-79.

9. Joglekar, G.V. and Leevy, C.M. Effect of an indigenous drug on ICG (indocyanine green): clearance and autoradiographic patterns in albino rats with experimentally induced hepatotoxicity. *J. Ind. med. Prof*. (1970): 12, 7480-7485.

10. Kale, A.K., Kulkarni, S.D., Joglekar, G.V. and Balwani, J.H. Effect of Liv.52 on growth and alcohol induced hepatic dysfunction in rats. *Curr. Med. Pract.* (1966): 10, 240.

11. Karandikar, S.M., Joglekar, G.V., Chitale, G.K. and Balwani, J.H. Protection by indigenous drugs against hepatotoxic effects of carbon tetrachloride-a long-term study. *Acta Pharmacol. et Toxicol*. (1963): 20, 274-280.

12. Mehrotra, M.P. and Mathur, D.C. Liv.52 trial in infective hepatitis. *The Antiseptic* (1973): 2, 114-118.

13. Mukerjee, A.B. and Dasgupta, M. Treatment of viral hepatitis by an indigenous drug-Liv.52. *Indian Practitioner* (1970): 6, 357-366.

14. Patel, J.R. and Sadre, N.L. Effect of Liv.52 on structural and functional damage caused by some hepatotoxic agents. *Probe* (1963): 1, 19-24.

15. Ramalingam, V., Sundaravalli, N. and Balagopal Raju, V. Liv.52 studies in acute hepatitis. *Indian Paediat*. (1971): 12, 839-842.

16. Sheth, Shantilal, C., Northover, B.J., Tibrewala, N.S., Warerkar, U.R. and Karande, V.S. Therapy of cirrhosis of liver and liver damage with indigenous drugs experimental and clinical studies. *Indian J. Paediat*. (1960): 149, 202-210.

17. Sherlock, S. The course of long incubation hepatitis. *Brit. Med. Bull.* (1972): 28, 109-113.

18. Sule, C.R., Pai, V.R., Damania, R.F. and Joshi, V.S. Studies with Liv.52 therapy in infective hepatitis. *J. Indian Med. Prof.* (1968): 14, 6391-6397.