HEPATOLOGY

Evaluation of efficacy and safety of LiverCare Capsules in hepatitis

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Viral hepatitis is a major public health problem all over the world. However, as yet, specific treatment is not available to manage this condition. A number of indigenous agents and their combinations are claimed to be beneficial. LiverCare is one such formulation containing pure herb extract and is claimed to be useful in various hepatic disorders. The present study has evaluated the efficacy and safety of this formulation in 70 patients of viral hepatitis in a randomised clinical trial. Response to treatment was assessed by clinical examination and liver function tests. Adverse effects likely to be attributed to drug treatment were recorded. Results indicated the clinical and biochemical efficacy and safety of LiverCare in patients of viral hepatitis. LiverCare produced faster recovery of liver function tests. None of the patients with hepatitis B virus (HBV) showed seroconversion. The drug was well tolerated.

INTRODUCTION

Hepatitis continues to be one of the most frequently reported diseases all over the world. Hepatitis A, caused by HAV, a RNA Picomavirus, can produce either asymptomatic or symptomatic infection in humans after an average incubation period of 28 days. The illness caused by HAV infection typically has an abrupt onset of symptoms that can include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine and jaundice. Signs and symptoms can last up to 2 months although 10-15% of symptomatic persons have prolonged or relapsing disease lasting up to 6 months.[1] In infected persons, HAV replicates in the liver, is excreted in bile and shed in the stools. Peak infectivity of infected persons occurs during the 2-week period before onset of jaundice or elevation of liver enzymes, when the concentration of virus in stool is highest.[2,3] Hepatitis B virus is spread when blood or body fluid from an infected person enters the body of a person who is not immune. Its incubation period is around 45-160 days and chronicity is very common. Herbal products are gaining popularity all over the world. However, profound disagreements exist between conventional and alternative medicine practitioners regarding their value. Western medical advocates cite deep concerns about the purity of most herbals because of lack of standardised production, the paucity of pharmacokinetic data, the fact that few well designed randomised,

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Table 1: Composition of LiverCare

Each LiverCare capsule contains:

	Name of the plant	Quantity
Exts.	*Capparis spinosa*	49 mg
	Cichorium intybus	49 mg
	Solanum nigrum	25 mg
	Terminalia arjuna	25 mg
	Cassia occidentalis	13 mg
	Achillea millefolium	13 mg
	Tamarix gallica	13 mg

Table 2: Demographic data of patients on entry

Features	LiverCare (n=34)	Placebo (n=36)
Age (years)	23.40 ± 8.5	24.11 ± 9.3
Sex (M/F)	22/12	26/10
Weight (kg)	51.80 ± 10.7	49.86 ± 10.98
Duration of illness (days)	11.33 ± 4.9	10.25 ± 4.2
Severity of illness (score)	14.96 ± 4.5	15.2 ± 4.2
Serum bilirubin (mg/dl)	10.49 ± 16.01	10.81 ± 6.0
SGPT (U/L)	120.5 ± 74.2	130.5 ± 65.2
Serum alkaline phosphatase (U/L)	17.1 ± 8.1	16.8 ± 8.3
HbsAg status (+ve/-ve)	8/26	10/26

Figures are mean ± SD, no significant difference between the groups

controlled trials of these products have been performed and the evidence that some herbals have been responsible for adverse effects. Nevertheless, many in the public, even in western countries turn to the use of herbals, believing that they must be safe and effective because they are natural.[4] Particularly with regard to safety, adequately powered randomised controlled clinical trials with well selected end points are needed to assess the role of herbal therapy for liver disease.[5] Despite rapid advancement in modern scientific medicine, there is no specific treatment available for this disease. Primary goal of management of acute viral hepatitis is to provide adequate nutrition to prevent further damage of the liver and to prevent transmission of infection to others. However, early normalisation of hepatic function and symptomatic and clinical recovery are very important in the clinical management of acute hepatitis. A number of indigenous agents are claimed to be useful for the treatment of liver diseases including viral hepatitis. LiverCare is one such formula containing extracts of 7 herbs (Table 1). LiverCare has been studied for its efficacy in the experimental models of hepatitis. Present study is aimed at evaluating the safety and efficacy of LiverCare capsules in patients of viral hepatitis.

MATERIAL AND METHODS

Patients of viral hepatitis referred to Naidu Hospital, Pune were included in the study which extended from June – December 2007. Seventy consecutive adult cases were randomised after obtaining their consent.

Study Design

This study was a prospective double blind randomised placebo-controlled clinical trial. The study protocol was approved by local ethics committee. The drug related information and informed consent form in local language (Marathi) was used during this clinical trial. The patients were free to opt out from this study if they so desired.

Study Procedure

On admission into the study, informed consent was obtained from the eligible patients after explaining to them the nature of the study. Randomisation was undertaken by using computer generated random number allocation and each arm had approximately equal number of patients (Table 2). Detailed medical history was obtained from all enrolled patients. The patients were subjected to haematological and biochemical investigations including liver function tests.

Study Drug

LiverCare or matching placebo capsules were administered to the patients in a dose of 1 capsule twice a day orally for 4 weeks. No other medication was administered to these patients. No dietary restriction was imposed.

Follow-up and Monitoring

The following information was obtained before starting the treatment twice in the 1st week and then at weekly intervals for the next 3 weeks: State of patient's well-being, loss of appetite, presence of any nausea, vomiting, fever, pruritus, rashes, joint pain, abdominal discomfort, tiredness, colour of urine, hepatic tenderness and hepatic enlargement. Liver function tests (serum bilirubin, SGPT, SGOT, alkaline phosphatase and prothrombin concentration) and haematology (haemoglobin, total and differential WBC count, serum protein total, albumin, globulin and routine urine examination) were done initially and then at the end of 4 weeks. Hepatitis B surface antigen (HbsAg)

Table 3: Response to treatment

Parameters	LiverCare (n=34)	Placebo (n=36)
Weight loss (kgs)	1.25 ± 0.95*	2.15 ± 1.10
Time for clinical recovery (days)	12.70 ± 7.18*	20.17 ± 9.70
Time for 50% fall in serum bilirubin (days)	8.46 ± 3.54*	15.05 ± 8.07
No. of patients recovered by 28 days (%)	25 (73%)*	9 (25%)

**p<0.05 as compared to placebo*

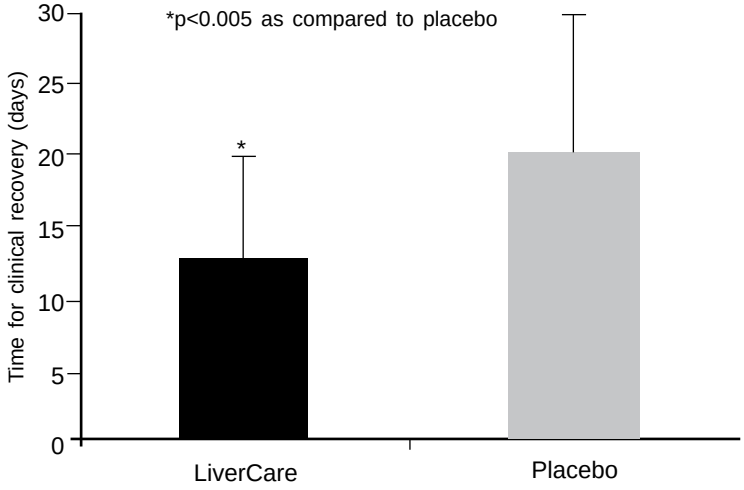

Fig. 1: Time for clinical recovery

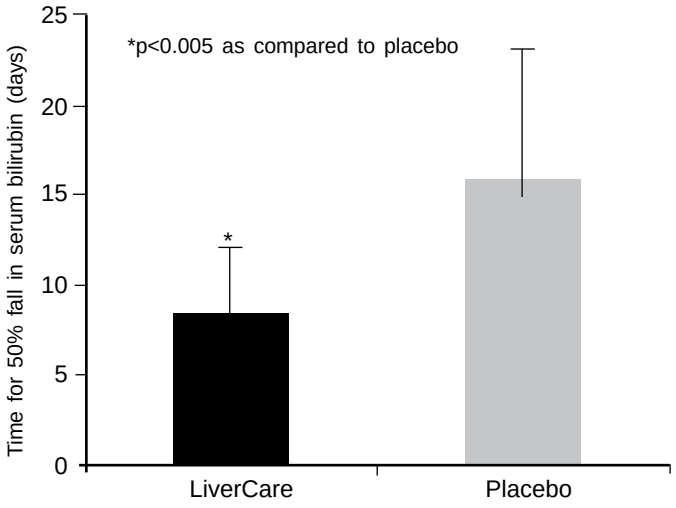

Fig. 2: Time for 50% fall in serum bilirubin

was determined at the beginning and at the end of the 1st month if positive, by counter immunoelectrophoresis. Clinical features were recorded with the help of an arbitrary scoring system namely absent 0, mild 1, moderate 2 and severe 3. Side effects likely due to the treatment were also recorded. Compliance to therapy was assessed by direct questioning.

Statistics

Data was analysed by Student's unpaired 't' test.

RESULTS

Seventy-eight patients were screened for the study out of which 8 patients were excluded from the study because of exclusion criteria. Out of 70 patients who remained in the study, 34 patients received LiverCare and 36 patients were on placebo. Patients in both the groups are comparable as far as the demographic data on entry is concerned.

Table 3 outlines the results of treatment. Treatment with LiverCare was associated with significantly ($p<0.05$) less loss in body weight and rapid clinical recovery as compared to placebo. In drug-treated patients, there was a significant ($p<0.05$) rapid biochemical recovery as suggested by short time required for 50% decline in serum bilirubin levels (Figures 1 and 2). By the end of 4 weeks, 25 patients had recovered from symptoms in LiverCare group as compared to 10 patients in placebo group (Figure 3). Eight patients from placebo group and none from LiverCare groups had relapse of hepatitis during 7th week of follow up from which they recovered uneventfully. None of the patients from LiverCare group or placebo group had seroconversion from HbsAg. All the patients tolerated the drug very well with good compliance.

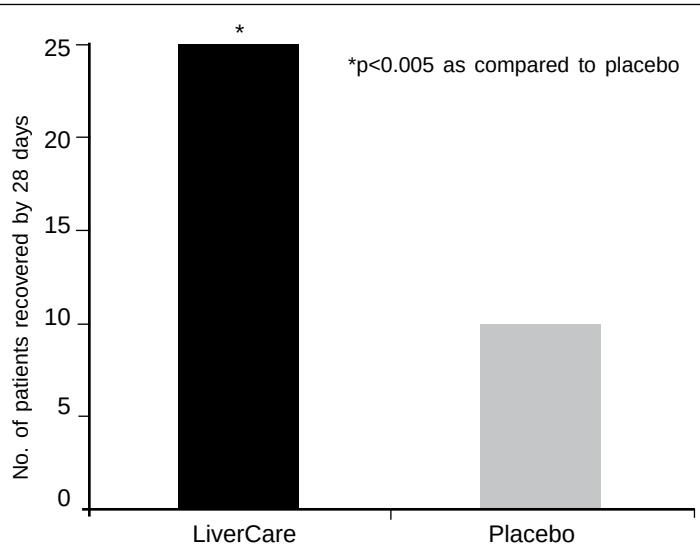

Fig. 3: Effect of LiverCare in viral hepatitis

DISCUSSION

Medicinal plants, since time immemorial have been used in virtually all cultures as a source of medicine. The use of traditional medicine and medicinal plants in most developing countries as a normative basis for the maintenance of good health has been widely observed.[6]

The practice of traditional medicine is wide spread in many of the Asian countries. Interest in medicinal plants as re-emerging health system has been fuelled by the rising costs of prescription drugs in the maintenance of personal health and well being. Based on the current research, medicinal plants will seemingly continue to play an important role as a health aid.

The results of the present study indicate a rapid clinical as well as bio-chemical recovery from acute viral hepatitis during the treatment with LiverCare. The dramatic decrease in total serum bilirubin was evident from the 4th day of treatment suggesting that LiverCare might be enhancing bilirubin clearance by stimulating either hepatic or extrahepatic clearance of bilirubin. The exact mechanism of action of LiverCare cannot be identified. Al-Said *et al* demonstrated the strong anti-inflammatory activity of *Capparis spinosa*.[7] Bonina *et al* have documented the anti-oxidant activity of this plant.[8] Zafar *et al* observed hepatoprotective effect of *Cichorium intybus* against CCl4-induced hepatotoxicity and reported prevention of malondialdehyde formation.[9] *Solanum nigrum* was investigated for its hepatoprotective activity against CCl4-induced hepatic damage. Sultana *et al* demonstrated that *Solanum nigrum* protects DNA against oxidative damage.[10] Similarly, Akhtar *et al* observed gastric mucosal cytoprotection by *Solanum nigrum*. It is possible that the beneficial

effects of LiverCare are due to the total effects of its ingredients.[11] LiverCare was well tolerated and did not produce any side effects.

CONCLUSION

Present study indicates safety and efficacy of LiverCare in patients of viral hepatitis. LiverCare was well tolerated. It did not produce any seroconversion in patients with hepatitis.

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