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Research Article

Clinical Trial of A Polyherbal Preparation (Tefroliv – Forte) In Patients With Chronic Hepatitis B

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Abstract: Hepatitis B infection is known to be a common cause of cirrhosis and hepatocellular carcinoma world wide. Though many drugs are being tried to slow down the progression of the disease, a safe, effective and universally acceptable therapy is still elusive. This study analyses the effectiveness of a polyherbal formulation in chronic hepatitis B infection. The study was conducted in 45 patients, of age group 18 to 62 years with duration of 6 months treatment. Symptomatic patients with HbsAg Positivity persistent for more than 6 months were included. Patients were given a poly herbal preparation 2 tablets 3 times a day for a period of 6 months. Seroconversion of 31% of HbsAg positivity, 42% in Anti HbcAb, 41% in HbeAg and 100% of anti HbeAb. Therapy with polyherbal preparation used by us in chronic hepatitis B infection was found to be effective and safe. No clinical deterioration observed during study period.
Keywords: Chronic hepatitis infection Polyherbal preparation (Tefroliv-forte), Seroconversion

INTRODUCTION

There are more than 450 million healthy carriers of HBV in the world out of which 45 millions healthy carriers live in India. These carriers act as a reservoir for HBV and a source for the spread of infection in our community. Hepatitis B virus is one of the serious infections of the liver mainly due to its course in acute liver disease and likelihood of development of sequelae in them[1]. Hepatitis B infection is known to be a common cause of cirrhosis and Hepatocellular carcinoma in underdeveloped countries. In spite of great in-depth studies into the etiopathogenesis and sequelae of HBV and many treatment trials already carried out, a universally acceptable, safe and effective therapy still remains elusive. The current therapy with polyherbal formulations aims principally at offering symptom relief, prolonging survival and elimination of surface antigen in a significant proportion. Seroconversion is equivalent to interferon and nucleoside analogue therapy without major side effects and absolutely safe in hepatic decompensation and in renal failure [2]. Tephrosia purpurea has been recommended for the diseases of liver. It is known as serpunkha in Ayurveda. Active components are tephrosin, dequelin, querectin, isotephrosin and rotenole. In traditional Ayurveda practice, tephrosin purpurea has also undergone clinical trials on viral hepatitis and has shown to improve liver functions. Eclipta Alba contains wedelolactone, dimethyl wedeloactone and luteolin which possess strong antiinfective and anti-hepatotoxic properties Apart from hepato protective property this also acts as an anti-inflammatory agent. Andrographolide is the active ingredient. The plant increases the biliary flow and increases liver weight. It has hepato protective and choleretic effect. It has also shown immuno modulatory and anti inflammatory activity. This drug exhibited potent stimulation of immune response and was capable of enhancing both anitigen specific and non-specific responses. Picrorhiza kurroa

Picrorhiza kurroa is the hepato protective, immuno stimulant and immuno modulatory agent. It is widely used for diseases of liver It has shown to have choleretic and marked anticholestatic effect. It also enhances immune response and phagocytic function of cells of reticuloendothelial system. Solanum nigrum:Solamargene and solasonnie are active components of this plant. This plant has been extensively used in the diseases of liver. Ethanol extract of Solanum nigrum has show remarkable hepatoprotective activity in experimental setting.Pierprine is the active alkaloid constituent of piper lonum. Piper longum is used in Ayurveda as it increases the bioavailability of other herbs. Mode of

action of herbal preparations .There herbal agents modulate cell mediated and humoral component of immune system, hepatoprotective and anti-inflammatory effect on damaged liver cells. It increases bile flow and hepatic mass index. It prevents fibrosis, cholesterol lowering agents and moderate effect on anticholestatic reaction in addition to antiviral effects[4].There is yet no safe drug which specifically acts against Hepatitis viruses, protects liver and stimulates liver regeneration. Since number of drugs used in modern medicine is derived from natural herbs, this study was aimed to find out an acceptable treatment based on Indian system of medicine[5].

Basic Concepts of the Need of the Polyherbal Drugs

Several claims have been made in the Indian system of Medicine about successful therapeutic remedies for chronic hepatitis. These claims have been supported by some clinical trials using different preparations. In view of the above there is need to explore the scope of cost effective therapy with least side effects. With these in mind, a combination of indigenous herbal and ayurvedic formulation has received attention of various authors. A number of plants have been used traditionally to treat the chronic Hepatitis B virus infection namely Siddha, Ayurveda and Unani medicines. Some of these herbal formulations have been extensively tried by modern research techniques and found to be useful either in elimination of virus or prevention of ongoing liver disease. Tefroliv Forte is one such formulation that has already been used in treating liver disorders[6].

DRUG COMPOSITION PRESCRIBED IN THE STUDY

Each prescribed tablet contains the following:

1.	*Tephrosia purpurea*	120 mg
2.	*Phyllanthus niruri*	100 mg
3.	*Eclipta alba*	60 mg
4.	*Andrographic paniculata*	60 mg
5.	*Picrorhiza kurroa*	60 mg
6.	*Solanum nigurm*	20 mg
7.	*Piper longum*	10 mg
8.	*Terminalia chebula*	10 mg
9.	*Ocimum sanctum*	10 mg

MATERIALS AND METHODS

Totally 45 patients were included in our study among them male population was around 32 years, and female population was around 13 years. The mean age group of the population was around 38.34±20.08.The total duration of the drug treatment was around 6months. The study period was around 6months from December 2011-July2012. The study was conducted in Melmaruvathur Adiparasakthi Institute of Medical Sciences & Research, after obtaining the institutional ethical committee clearance.

Inclusion Criteria:

- Jaundice persisting for more than 6 months.
- HbsAg persisting for more than 6 months.
- Serum bilirubin and transminases elevated for more than 6 months.
- Patient available for regular follow up for 6 months.

Exclusion Criteria :

- Severe hepatic decompensation
- h/o alcoholism.
- Associated with toxic or other viral, non-viral infections.
- Patient already on antiviral treatment.
- Fatty liver syndrome of non-viral etiology.
- Obstructive jaundice
- Hepatic malignancy.

All these patients were subject to detailed history, clinical examination, basic hematological, biochemical and viral markers for hepatitis B virus by Elisa method for HbsAg. Anti HBc antibody, HbeAg, antiHBe antibody was done in all subjects. Our limitation was that HBV DNA polymerase by PCR and antiHBs were not done in our patients. Patients were given Tefroliv forte tablets – 2 tablets 3 times daily for a period of 6 months. These patients were clinically examined every month. Biochemical investigation for liver function test was done every 2nd month and viral markers repeated after completion of 6 month's therapy.

RESULTS

Table-1: Shows the Age & Sex Distribution

Age Group	Male	Female
< 20 Years	2	0
21 – 30 years	8	3
31- 40 years	13	4
41 – 50 years	6	4
51 – 60 years	3	1
> 60 years	1	0
Total	33	12

Table-2: Shows the Clinical Presentation Among The Patients

Icterus	41	90 %
Malaise	19	42 %
Loss Of Appetite	13	29 %
Weight Loss	12	26 %
Edema Legs	7	15 %
Itching	6	13 %
Ascites	5	11 %
Fever	4	9 %
Ugi Bleeding	3	6 %
Encephalopathy	2	4 %

Table-3: **Shows The Clinical Examination Finding Among The Patients.**

Jaundice	45	100%
Hepatomegaly	32	70%
Pedal Edema	7	15%
Ascites	6	13%
Splenomegaly	5	11%
Encephalopathy	4	9%
G.I. Bleeding	3	6%

Table-4: **Liver Enzymes (AST, ALT) 45 Cases**

Rise In No. Of Times	No. Of Patients	Percentage
2 – 5	13	29 %
6 – 10	17	38 %
11 - 20	11	24%
21 - 30	3	7%
>31	1	2%
Total	45	100%

Table-5: Shows The Viral Markers Status (Pretreatment) 45 Cases

Markers	Positive	Negative
HbsAg	45 (100%)	-
AntiHBc (Total)	33 (73 %)	12 (27 %)
HBe Ag	17 (37 %)	28 (73 %)
Anti HBe antibody	10 (22%)	28 (78 %)

During follow up period patients were on polyherbal drugs in a standardized dose of 2 tablets three times daily along with supportive and sympotomatic treatment. Conservative treatment for hepatic encephalopathy grade I – II and non variceal bleeding were done as an inpatient procedure. Salt restriction, diuretics and human serum albumin were given for patients with persistent ascites lasting for more than a week.

Table-6: Shows the Clinical Outcome After 6 Month's Therapy

Clinical Condition	No. Of Patients	%
Normal	23	51%
Improved	12	26%
Static	10	23%
Deterioration	NIL	NIL

Table-7: **Shows the Level Of Serum Bilirubin After 6 Month's Therapy**

Clinical Condition	No. Of Patients	%
Normal	24	53%
Decreased	13	29%
Static	8	18%
Progression	NIL	NIL

Table-8: Shows the Serum Level After 6 Month's Therapy

Serum Level	No. Of Patients	%
Normal	25	56%
Decreased	14	31%
Static	6	13%
Progression	NIL	NIL

Table-9: Shows The Viral Markers After 6 Month's Therapy

Markers	Total	Seroconversion	Persistent
HbsAg	45	14 (31%)	69%
Anti HbcAb	33	14 (42%)	58%
HbeAg	17	7 (41%)	59%
Anti HBeAb	10	10 (100%)	Nil

DISCUSSION

There is as yet no safe drug which specifically acts against hepatitis viruses, protects liver damage, stimulates liver function and helps in hepatic regeneration. The use of available antiviral drugs has not yielded total success.Interferon and nucleosides analogs have shown beneficial results in a selected group of patients only[7]. However, the prohibitory cost, prolonged treatment and side effects have restricted their use. P.Amarus and Eclipata alba also were shown to bring out in vitro inactivation of Hepatitis B surface antigen.Interpreted as exhibiting HbsAg binding property, Phyllanthus extracts inhibit endogenous DNA polymerase of HBV.P.amarus treatment initiates an immunomodulatory trigger resulting in higher antiHBs titre which may help in the clearance of HBV in carriers [8]. In our study HbsAg clearance rate among chronic hepatitis B infection by treatment was 31% which is as good as with interferon in chronic hepatitis B and in different report studies on treatment with P. amarus ranging from 20% to 59 % in a study conducted by Thyagarajan et al.. In 1988 stated the coorelation of positive results around (69%) [9]. HbsAg positive carriers who were also HbeAg Positive were less likely to respond than those without HbeAg. (3/17 (18%) versus 11/28 39%) as shown in our study). HbeAg seroconversation rate was 17/27 (59%) equivalent to what is reported in literature. No clinical deterioration was observed in our study during trial period.

CONCLUSION

Based on literature references and our clinical trial the following conclusion were derived. Polyherbal drug therapy (Tefroliv forte) for 6 month's period in patients with chronic hepatitis B is reasonably safe. It is effective against chronic hepatitis B virus and is as good as interferon or nucleoside analog therapy possible mode of action of this polyherbal drug has

been shown to be HbsAg binding, immunomodulatory, inhibition of DNA polymerase and ant hepatotoxic potentials. The active potential of these agents may be present in more than one fraction. However a word of caution: Larger doses over longer duration of therapy may be tried to see if it yields quicker and better results. Species identification and bioprocessing of plants will also play major role in drug activation.

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REFERENCES

1. Anonymous : formulary of Siddha Medicine IMCOPS Madras,1972.
2. Anonymous: formulary of ayurvedic Medicine IMCOPS Madras, 1981.
3. Anonymous: formulary of Unani Medicine IMCOPS Madras, 1982.
4. Mitra R, Jain SK; Concept of phyllanthus niruri in indian flora. Bull. Bort surv. India, 1985; 27:161:175.
5. Lee CD, Mott SP, . Thyagarajan DA, Sharfritz RD, Gupta BK; Amarus down regualates hepatitis B Virus mrna transcription and replication. European Journal of clinical investigation, 1996; 26:1069-1076.
6. Jayaram S, Thyagarajan SP, Madanogopalan N, Panchanadam M, Subramanian S; Anthiepatitis B Virus properties of Phyllanthus nirurui linn and eclipa alba hasek, in vitro and vivo safety studies. Biomedicine, 1987;7:9-16.
7. Thygarajan SP, Subramanaian S, Thirunalsundari T, Blumberg BS; Effect of Phyllanthus amarus on chronic carriers of Hepatitis B. lancet, 1998;1:764-766.
8. Singh B, Sexana AK, Chandren BK, Agarwal SG, Anand KK; In vivo hepatoprotective activity of active fraction from ethanolic extract of Eclipta alba leaves. Indian J Physiol pharmacol, 2001;45(4):435-441.
9. Thyagarajan SP, Subramanian S, Thirumalsundari T, Venkateswaran PS, Blumberg BS; Effects of Phyllanthus amarus on Chronic carriers of Hepatitis B Viruses. Lancet, 1988: 2(74):766.