

Alternative treatment in Hepatitis B by using polyherbal formulation

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Abstract: The hepatitis B is most prevalent diseases (along with morbidities) in Asian countries. This research study has been conducted to provide an alternative treatment which is safe, effective and cost-effective to comprehend relations of disease, symptoms, patients response and the clinical response via better management of hepatitis B. The goal of this research is to evaluate efficacy and safety of herbal medicine as compared to allopathic medicine in patients suffering from hepatitis B. This was a single blind, randomized controlled clinical trial conducted at Shifa-ul-Mulk Memorial Hospital Hamdard University, Karachi and Dar ul Shifa Unani Dawakhana Karachi, Pakistan. The patients of both genders ranging from 25 to 50 years with symptoms and diagnosed for hepatitis B that fulfilled the criteria for membership, and consented for participation were registered. Ethical committee clearance and permission was obtained from the concerned committee at Faculty of Eastern Medicine, Hamdard University, Karachi, Pakistan. No significant difference was identified after treatment and it was found that the efficacy of Alpha (Control drug) is same as Safoof akseer e jigar (Test drug). The data offered support to the null hypothesis and therefore research hypothesis was rejected. According to the statistical analysis by chi square, hepatitis B was recorded as negative in 26 patients (57.77%) out of 45 patients by the use of Interferon Alpha (control therapy) and in 27 patients (64.28%) out of 42 patients by the use of Safoof akseer e jigar (test drug). Comparison of the data recorded of the patients was determined as both drugs showed significant improvement and p value>0.05. The efficacy response is equal in both drugs while test drug showed more safety response. It is concluded that Safoof akseer e jigar possesses as effective a therapeutic value in treating hepatitis B as allopathic medicine.

Keywords: Hepatitis B, natural medicine, interferon therapy.

INTRODUCTION

Hepatitis B virus causes liver damage in humans. It is a DNA virus composing of a DNA codes for enzyme DNA polymerase. The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity. Hepatitis B surface antigen is the marker checked in Hepatitis positive patients after 6 to 16 weeks of infection. The infection is self-limiting by natural immunity within 1 to 2 months after the onset of symptoms. Persistence of HBsAg for >6 months show development of either a chronic carrier state or chronic HBV infection. HBV is spread via percutaneous or parenteral contact with the infected blood, body fluids, and by sexual intercourse (Baker, 1996; William 2006). The virus also causes sporadic infections which cannot be attributed to parenteral modes of spread (Kidd-Ljunggren *et al.*, 2006). Liver cirrhosis may lead to hepatocellular carcinoma. The virus replicates in liver cells which are known as hepatocytes. Hepatitis B virus particles bind with host cell through PreS viral antigen surface and then directly through endocytosis are internalized. PreS receptors are mainly hepatocytes, whereas, DNA of the virus and proteins are found in hepatic sites, thus suggesting the cellular receptors are located in hepatic

cells (Pungpapong *et al.*, 2007 and Zuckerman, 1996). The virus spreads vertically from mother to child in the immediate perinatal period (Chang, 2007).

About 350 million people were infected by the virus all over the world in 2004. Prevalence ranges less than 1% (in Northern Europe and United States) to over 15% in Asia. The route of infection includes sexual contact, intravenous drug use and blood transfusion (Petersen *et al.*, 1976). In traditional Asian systems there are several foods and spices which are known to have hepatoprotective properties. This study was undertaken to introduce five effective medicinal plants having hepatoprotective properties.

These plants were selected after literature survey focused on the known hepatoprotective activities: *Achillea millefolium* Linn. Was reported as hepatoprotective in many studies and is prescribed in hepatitis B (Chaudhary, *et al.*, 2007; Alam & Naeem, 2007) reported the hepatoprotective effects of *Artemisia absinthium*. The clinical observations showed 80-90% symptoms getting relief from viral Hepatitis (Anwar, 1998). The *Rosa damascena* water and methanol extracts had shown anti HIV infection activities *in vitro* (Mahmood *et al.*, 1996). In a clinical trial, anti-HIV action of the 09 compounds 2-phenylethanol-O-(6-O-galloyl)- β -D-glucopyranoside

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which was identified in the methanol extract and evaluated on C8166 human T lymphoblastoid cells infected with HIV-1MN and H9 human T-cell lymphoma cells with HIV-1IIIB chronic infections. Kaempferol 1 and its 3-O- β -D-glucopyranosides 3 and 6 showed the maximum activity against HIV infection of C8166 cells, whereas kaempferol-7-O- β -D-glucopyranoside showed no effect. Similarly, quercetin-7-O- β -D-glucopyranoside was inactive compared to quercetin 2. Compound 8, a new natural product exhibited moderate anti-HIV activity, presumably due to the presence of the galloyl moiety since 2-phenylethanol-O- β -D-glucopyranoside was inactive. Similarly, another study was conducted to investigate the hepatoprotective role of *Tamarix gallica* Linn. in Patients of an acute viral hepatitis and prospective results were found Dange *et al.*, 1989). Activity of the liver and therapeutic results of this drug have also been reported for *Rheum emodi* Wall due to changes in serum SGPT and SGOT levels (Popovici *et al.*, 2008 and Potrich *et al.*, 2008). This study tried to show synergistic action of the above mentioned plants for the treatment of hepatitis B infection.

MATERIALS AND METHODS

Study design

A multicenter, randomized, single blind, controlled study was done in patients residing near Shifa-ul-Mulk Memorial Hospital Hamdard University Karachi and Dar ul Shifa Unani Dawakhana Karachi Pakistan during March 2008 to December 2011. Diagnosis was established on the basis of clinic serological and biochemical consideration (LFT's, HBsAg, HBeAg) of hepatitis B as shown in table 1.

Treatment

The patients were divided into two group i.e. control and the test. Control group received Interferon Alpha and the test group was treated with Safoof Akseer e Jigar. Blood samples were taken and HbsAg and HBeAg tests were performed for the detection and confirmation of active hepatitis B infection in the screening. Different parameter i.e. age, sex, and other clinical signs and symptoms were studied and compared the two treatment groups (Interferon Alpha and Safoof Akseer e Jigar) at baseline and end of therapeutic clinical administration. Consent of patients was taken at the start of treatment in both groups.

Criteria of inclusion

- Cases suffering from hepatitis B were selected
- Patients of 25 to 50 years of age.
- Patients without pathological findings on checkups.
- Patients of all socio-economic categories.

Criteria for exclusion

- Patients suffering from chronic hepatitis B diseases.
- Patients having physical illness e.g. uncontrolled hypertension and diabetes mellitus.

- Patients having cancer of the liver and liver cirrhosis were excluded.
- Diabetes patients.

Sample size

Trial was conducted on 87 patients suffering from hepatitis B from both groups (45 patient from the control and 42 from the test group) ranging from 25-50 years of age (selected irrespective of their socioeconomic status).

Ethical issues

Ethical committee, Faculty of Eastern Medicine, Hamdard University clearance and permission was obtained

RESULTS

Hepatitis B surface antigen (HBsAg) is first antigen appearing after infection and it is used more often for the screening of positive infection. In case infection is in its earlier stage the antigen is not detected as this is diluted out by the host. People having mild infection may clear it within a few weeks to months. There are several herbal medicinal products protecting the hepatic cells and clinical trials have demonstrated the ability of herbs to normalize the liver enzymes including ALT and AST in people who are affected. It has been previously reported that *Achillea millefolium* and *Artemisia absinthium* have anti hepatitis B effect and are commonly used in treating hepatitis B infection. Thus, by taking advantage, coded herbal formulation Safoof akseer e Jigar, consists of five ingredients in which *Achillea millefolium*, *Artemisia absinthium*, *Rosa damascene*, *Tamarix gallica* and *Rheum emodi* were formulated for the treatment of hepatitis B infection/disease.

A weekly record of changes in signs and symptoms in hepatitis patients was maintained and analyzed the improvement in hepatitis B associated symptoms in both arms. Accordingly disappearance of loss of appetite, feeling of fatigue, pain in the liver, jaundice, dark urine and pale-colored stools were especially noted. Routine examination of different investigations mentioned in clinical trial protocol especially LFT's was done for monitoring the improvement. According to the statistical analysis hepatitis B was recorded as "negative" in 26 patients (57.77%) out of 45 patients by the use of Interferon Alpha (Control therapy), and in 27 patients (64.28%) out of 42 patients by the use of Safoof akseer e Jigar (Test poly herbal drug). The manifestation of hepatitis B eradication is at par in the control and the test groups. But there was a significant reduction in hepatitis B associated symptoms in the test treated group as observed in the two treated groups at the end of therapy.

Different trial records have been cited where herbal medicines have been utilized for the treatment of hepatitis B. Different trial records have been cited where herbal medicines have been utilized for the treatment of hepatitis B.

Table 1: Working plan

Activity	Out Line	Description
1) No. of the drugs	Safoof Akseer e Jigar (Test)	Interferon Alpha (Control)
2) No. of patients	87	Both genders
3) Laboratory test	LFT's, HBsAg, HBeAg	
4) Time period	6-month	6 months follow up
5) Total study time duration	3years	2008-2011
6) Present action of report	After every 3 month interval	

Table 2: Configuration

Hepatitis B	Test Drug Configuration	Control Drug
Composition	Safoof Akseer e Jigar 1. <i>Achillea millefolium</i> 2. <i>Artemisia absinthium</i> 3. <i>Rosa damascene</i> 4. <i>Tamarix gallica</i> 5. <i>Rheum emodi</i>	Interferon Alpha
Dosage	1-2g twice daily	Intradermal Implantation : 3 million units/day

Table 3: HBsAg in total patients

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
HbsAg test At Baseline	Positive	42	45	87	0.95
	Negative	00	00	00	
	Total	42	45	87	
HbsAg test After Treatment	Negative	27 (64.28%)	26 (57.77%)	25	0.344
	Positive	15 (35.71%)	19 (42.22%)	72	
	Total	42	45	87	

64.28% of patients showed as negative *hepatitis B* surface antigen after taking Safoof akseer e Jigar and 57.77% of patients were negative of the Interferon therapy. There was no difference between test and the control groups as p value is calculated as 0.344

Pradhan & Girish, 2013) worked on the effects of Sho-saiko-to (Xiao-Chai-Hu-Tang) on HBeAg clearance in children with chronic Hepatitis B Virus Infection and with sustained liver disease. Seven out of fourteen patients did not display negative HBeAg within 0.47 years. Therefore, Sho-saiko-to was effective in clearing HBeAg in children with chronic HBV infection and with sustained liver disease (Tajiri *et al*, 1991; Sandeep and associates, 2013). cited work on herbal drug which inhibited Hepatitis B Surface Antigen Secretion in Transfected Human Hepatocarcinoma PLC/PRF/5 Cells. The test drug HD-03/ES exhibited strong anti-HBV activity by inhibiting the secretion of hepatitis B surface antigen in PLC/PRF/5 cells, which can be prescribed for the treatment of acute and chronic hepatitis B infections. Chang & Huang, 2007) reviewed an account of complementary and alternative treatment of chronic hepatitis B (Hepatitis B virus). It is due to the high costs of hepatitis B medications, the herbs formulated as polyherbal medicine used for treatment of chronic hepatitis B in developing countries.

DISCUSSION

The alternative anti-HBV therapies have shown that these could be a better option for Hepatitis B treatment.

HbsAg test analysis

Both preparations led to eradication of hepatitis B. as shown in table 3. 64.28% of patients showed as negative hepatitis B surface antigen after taking Safoof akseer e Jigar and 57.77% of patients were negative of the Interferon therapy. There was no difference between test and the control groups as p value is calculated as 0.344

Liver function test (LFT's) Analysis

The results obtained after statistical evaluation showed that test group is got more effective herbal than the control as $p < 0.05$. The 83.33% of patients showed improvement in LFT's after using Safoof akseer e Jigar and 62.22% of patients using Interferon therapy as depicted in table 4.

Symptomatic analysis

The results obtained after symptomatic evaluation for anorexia, nausea, vomiting and fever were remarkably improved superior in test group on statistical ground as p value calculated in each case is less than 0.05, however, in the case of fatigue the efficacy was at par in case of the control group as shown in tables 5-8.

Table 4: LFT's in cumulative patients

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
LFT's At Baseline	Abnormal	42	45	87	0.95
	Normal	00	00	00	
	Total	42	45	87	
LFT's After Treatment	Improved	35 (83.33%)	28 (62.22%)	63	0.0241
	Not improved	07 (16.66%)	17 (37.77%)	24	
	Total	42	45	87	

Table 5: Anorexia analysis

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
Anorexia At Baseline	Yes	35	36	71	0.451
	No	07	09	16	
	Total	42	45	87	
Anorexia After Treatment	Complete improvement	33 (94.28%)	23 (63.88%)	56	0.001
	No improvement	02 (05.71%)	13 (36.11%)	15	
	Total	35	36	71	

Table 6: Fatigue analysis

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
Fatigue At Baseline	Absent	10	04	14	0.504
	Present	32	41	73	
	Total	42	45	87	
Fatigue After Treatment	Improved	28 (87.5%)	29 (70.73%)	57	0.074
	Not Improved	04 (12.5%)	12 (29.26%)	16	
	Total	32	41	73	

Table 7: Nausea and vomiting analysis

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
Nausea and vomiting At Baseline	Absent	24	21	45	0.95
	Present	18	24	45	
	Total	42	45	87	
Nausea and vomiting After Treatment	Improved	22 (91.66%)	09 (75.00%)	31	0.000
	Not Improved	2 (8.33%)	12 (25.00%)	14	
	Total	24	21	45	

Table 8: Fever analysis

Treatments		Treatment groups		Total (n)	p value
		(Safoof akseer e Jigar) Test	(Interferon therapy) Control		
Fever At Baseline	Present	20	33	53	0.0124
	Absent	22	12	34	
	Total	42	45	87	
Fever After Treatment	Improved	14 (70%)	11 (33.33%)	25	0.010
	Not Improved	6 (30.0%)	22 (66.66%)	28	
	Total	20	33	53	

Adverse effects profile

All the patients enrolled identical in the study. Side effects were defined as sign and symptoms that first occurred or became more severe during the course of treatment. The likely drug reactions in patients administered with Interferon Alpha showed side effects such as chills (04 patients), malaise (07 patients), headache (04 patients), muscle aches, pains (03 patients) and allergic reaction (02 patients) were the most common drug related events and in test drug related symptoms includes: headache (07 patients) and allergic reaction (03 patients). No life threatening side effects were recorded in either of the group. It is because of the fact that plant drugs selected for the treatment of hepatitis B infection do not contain any toxic chemical agent that may trigger the adverse drug reaction response. It can be explained further that chemical components of the plant drugs altogether are low in quantity and frequency of occurrence, but when administered together, these in turn act synergistically to exhibit pronounced type of effective response for curative action.

CONCLUSION

The findings of this study demonstrated the following salient clinical assessment; that no statistically significant difference in comparison with the effects of herbal medicine Safoof akseer e Jigar (Test drug) to Interferon Alpha (Control therapy) in treating hepatitis B is noted. It is concluded that Safoof akseer e Jigar possesses a therapeutic value in treating hepatitis B infection/disease and its associated symptoms. It is as effective as the Interferon Alpha therapy.

There was no untoward manifestation associated with the use of Safoof akseer e Jigar and this has found good acceptability by all the treated patients. The principal objective of herbal medicine Safoof akseer e Jigar as compared to Interferon Alpha is to determine if they can represent a base in developing new therapies. This was an exercise for the application of latest investigations and clinical study to a product that was in use since long period of time. The efficacy of herbal formulation is a feature of mixture of compounds found in various herbs used as multiple dosage form design. This study outlines an approach of traditional and conventional medicines, so in its ultimate dictate; this is worth an exercise, because it may lead to new category of therapies.

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