Original Article

Efficacy of *Sharapunkhadi* powder (a polyherbal formulation) and lifestyle modification in the management of nonalcoholic fatty liver disease-A randomized placebo-controlled clinical trial

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Abstract

Background: Nonalcoholic fatty liver disease **(**NAFLD) is an expanding health problem, which varies in prevalence among ethnic groups, occurring with an estimated global prevalence of 25%. In high-risk populations, the prevalence of NAFLD may be as high as 70%–90%. No established pharmacological treatment is available for NAFLD in modern medicine and hence, there is a search for alternative treatment modalities in other systems of medicine, which is safe and cost-effective. **Aim:** The aim is to evaluate the efficacy of *Sharapunkhadi* powder and lifestyle modification in the management of NAFLD. **Materials and methods :** Patients suffering from any of the components of metabolic syndrome, i.e. hypertension, diabetes mellitus, hypertriglyceridemia, elevated body mass index (>25 kg/m^2), truncal obesity, or presenting with the symptoms of indigestion, abdominal discomfort, flatulence. were screened with liver function tests and ultrasonography (USG) of the abdomen. A total of 93 patients confirmed with fatty liver Grade 1-3 were selected for the present trial and were randomly divided into two groups. After *Mridu Virechana* (mild purgation) with *Haritaki* powder (6–8 g) according to *Koshtha*, in group A (n = 46), 2 capsules (500 mg each) filled with *Sharapunkhadi* powder thrice a day before food with warm water along with lifestyle modification were administered for 8 weeks. In group B (n = 47), capsules filled with roasted Sooji powder in the same dose as mentioned for group A was given along with lifestyle modification and were maintained as a placebo. Relief in subjective parameters such as indigestion, abdominal discomfort, and flatulence and improvement in the grades of fatty liver evident from USG was considered for the overall assessment of the therapy in both the groups. SigmaStat 3.1 software was used for statistical calculation. Wilcoxon signed-rank test for subjective criteria and Student's paired t-test for objective criteria were applied to check the level of significance in a single group before and after treatment, while Student's unpaired t-test for objective criteria was applied to assess the level of significance of difference observed between two groups. **Results:** After 8 weeks of treatment, it was found from USG findings that there was a statistically significant improvement by about 39.25% in group A and 31.82% in group B, in the grade of fatty liver. The combination of *Sharapunkhadi* powder along with lifestyle modification provided comparatively better relief in subjective and objective parameters over the placebo control group. **Conclusion:** *Sharapunkhadi* powder is a promising herbal preparation for the management of NAFLD and the combination of *Sharapunkhadi* powder along with lifestyle modification can yield more significant results in the management of NAFLD than lifestyle modification alone.

Keywords: Ayurveda, diet and lifestyle, nonalcoholic fatty liver disease, *Sharapunkhadi* powder

Introduction

Nonalcoholic fatty liver disease (NAFLD) encompasses a spectrum of chronic liver diseases, characterized by excessive hepatic fat accumulation (steatosis) in the absence of significant alcohol consumption, occurring with or without hepatic inflammation and fibrosis.[1] NAFLD is now the most

Access this article online

Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.AYU_281_19

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How to cite this article: Remya E, Goyal M, Varsakiya J. Efficacy of *Sharapunkhadi* powder (a polyherbal formulation) and lifestyle modification in the management of nonalcoholic fatty liver disease-A randomized placebo-controlled clinical trial. AYU 2020;41:98-106.

Submitted: 02-Oct-2019 **Revised:** 11-Feb-2020
Accepted: 23-Mar-2021 **Published:** 23-Oct-2021

prevalent form of chronic liver disease, affecting 20%–30% of the general population.[2] Within the next 10 years, it is expected to become the leading cause of liver pathology, liver failure, and indication for liver transplantation. It is thought to be the hepatic manifestation of more widespread metabolic dysfunction and is strongly associated with several metabolic risk factors, including insulin resistance, dyslipidemia, cardiovascular disease, and most significantly obesity.[3] The clinical burden of NAFLD is not only confined to liver-related morbidity and mortality but also involves multi-system disease affecting extra-hepatic organs and regulatory pathways. Although the primary liver pathology in NAFLD affects hepatic structure and function to cause morbidity and mortality from cirrhosis and hepatocellular carcinoma, the majority of death among NAFLD patients is attributable to cardiovascular diseases. Increasing evidence indicates that the presence and severity of NAFLD are associated with an increased prevalence and incidence of cardiovascular and chronic kidney disease, independently of multiple cardio-renal risk factors.

The challenge for the development of therapies for NAFLD is related to the complexity of the disease, which is directly associated with visceral obesity, dyslipidemia, hyperglycemia, insulin resistance, and oxidative stress. Effective treatments are needed to prevent the progression of simple steatosis to chronic liver disease, considering that fatty liver disease is a reversible condition which if not treated early can lead to terminal liver disease.

The treatments presently available are not satisfactory, therapies that limit liver injury and the occurrence of inflammation and fibrosis are particularly attractive for this condition. Currently, it is a great challenge for the pharmaceutical industry to develop a combined therapy that is effective in NAFLD patients exhibiting obesity, insulin resistance, dyslipidemia, and oxidative stress. Therefore, serious efforts have been directed to explore novel therapeutic agents that may be directed to multiple targets. Natural products extracted from medicinal plants being rich sources of biologically active substances are having effects on health benefits and disease prevention in humans. Therefore, experimental and clinical researches focused on herbal extracts and natural products with antihyperlipidemic and hepatoprotective effects against NAFLD is the need of the hour.

One of the key causes of NAFLD is an improper diet based on caloric oversupply, the excessive intake of fats, and at the same time, the low intake of grains, fruits, vegetables, proteins and omega-fatty acids.[4] Several empiric treatment strategies such as dietary restriction, physical exercise, and weight reduction form the first line of treatment. Therefore, the correction of lifestyle itself serves the first purpose of treatment. However, adherence to lifestyle changes may not provide complete remission in the long run. In such cases, pharmacological intervention is required as the next step toward the management of NAFLD. Considering this, *Sharapunkhadi* powder was formulated comprising equal quantities of *Sharapunkha* (*Tephrosia purpurea* Linn)*., Bhoomiamalaki* (*Phyllanthus niruri* Linn.)*,* and *Katuki* (*Picrorhiza kurroa* Royle ex Benth.).[5,6] [Table 1] All the three ingredients are established hepatoprotective experimentally and clinically.

To find out the efficacy of *Sharapunkhadi* powder alone and also to compare its efficacy with lifestyle modification in the management of NAFLD, the present clinical trial was planned with the objectives to assess the clinical efficacy of *Sharapunkhadi* powder and lifestyle modification in the management of NAFLD. It was expected that the trial drug can reverse fatty changes of the liver thus may reduce the risk of NASH, fibrosis, liver cirrhosis, ascites and further complications of end-stage liver disease and thus improve quality of life of cases of NAFLD.

Materials and methods

Plan of clinical study

The present clinical trial was an open-labeled randomized placebo-controlled, interventional trial. Patients of either sex attending out patient department and inpatient Department of Kayachikitsa department, IPGT and RA, Gujarat Ayurved University, Jamnagar and patients referred from other OPD's of the hospital, having age between 25 and 60 years and suffering from any of the components of metabolic syndrome, i.e. hypertension, diabetes mellitus, hypertriglyceridemia, elevated body mass index >25, truncal obesity or presenting with the symptoms of indigestion, abdominal discomfort, flatulence, etc., were screened with liver function tests and ultrasonography (USG) of the abdomen. A total of 196 patients were screened. Among them, 93 patients fulfilling inclusion criteria were selected for the present clinical study. Randomization was done by computer-generated randomization method to reduce allocation bias (www.randomization.com) and subjects were randomized into two groups. Forty-six patients were allocated to group A (*Sharpunkhadi* powder) and Forty-seven patients to group B (Placebo) [Figure 1]. Lifestyle

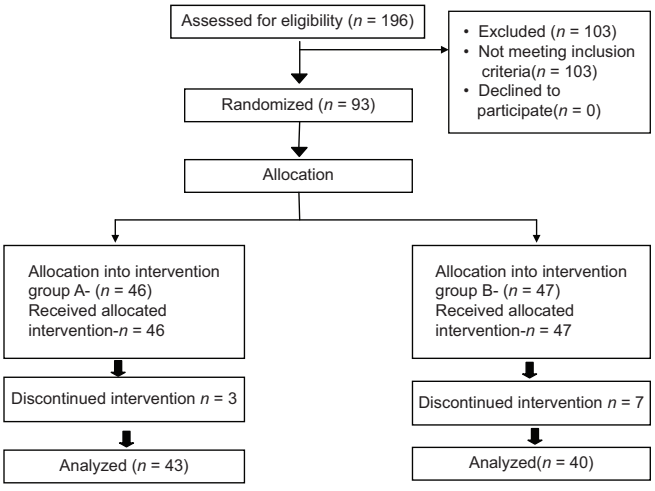

Figure 1: CONSORT flow chart

Table 1: Ingredients of *Sharapunkhadi* powder

Drug	Latin name	Part used	Ratio/mg	Form
Sharapunkha	*Tephrosia purpurea* Linn.	Water extract of whole plant	1 part/166.67 mg	Powder
Bhoomiamalaki	*Phyllanthus niruri* Linn.	Water extract of whole plant	1 part/166.67 mg	Powder
Katuki	*Picrorhiza kurroa* Royle ex Benth.	Alcoholic extract of root (50% ethanol)	1 part/166.67 mg	Powder

modification was advised in both the groups. Three patients from group A and 7 patients from group B left the study due to personal reasons.

Patients on oral hypoglycemic agents and antihypertensive drugs were allowed to continue their conventional treatment. However, patients who were taking anti-hyperlipidemic medicines were asked to stop these medicines during the treatment. After preliminary registration, diagnostic medical history was taken according to both Ayurvedic and modern clinical methods. A detailed clinical research pro forma, incorporating all the points of history taking, physical examination, and assessment of the treatment was maintained for record and analysis. Informed written consent was taken from all subjects before the recruitment of subjects in the present clinical trial and approval from the Institutional Ethics Committee was obtained vide letter No. PGT/7-A/Ethics/2015-16/2625 dated December 11, 2015 before registration of the patients. The study has also been registered in the Clinical Trial Registry of India (CTRI) with no. CTRI/2016/02/006623 dated 11/02/2015, prospectively. Raw herbal materials were collected from authentic vendors and approved by Quality Control Lab. After authentication, extraction of *Sharapunkha* and *Bhumiamalaki* was done with water and that of *Katuki* with 50% ethanol at Konark Herbals and Healthcare, Daman. Equal quantities of extracts of *Sharapunkha, Bhumiamalaki* and *Katuki* were mixed to prepare a homogeneous mixture and it was filled in 500 mg capsules, packed and dispended in asrtight containers. For the preparation of the placebo capsule, sooji powder was procured from the local market, roasted, and filled in 500 mg capsules.

Criteria of diagnosis

Abdominal USG findings suggestive of fatty liver grade 1, 2 and 3 without the evidence of fibrosis and cirrhosis was the major criteria for the diagnosis of NAFLD. The normal liver parenchyma has a homogeneous echotexture with echogenicity equal to or slightly greater than that of the renal cortex and spleen. The liver shows echogenicity higher than the renal cortex and spleen due to fatty infiltration. Various (0-3) grades of steatosis have been proposed based on visual analysis of the intensity of the echogenicity, When the echogenicity is just increased, it is the grade 1; when the echogenic liver obscures the echogenic walls of portal vein branches, it is grade 2 and when the echogenic liver obscures the diaphragmatic outline, it is grade 3 fatty infiltration.[7]

Elevation of serum transaminases and alkaline phosphatase is not a rule of thumb in the diagnosis of NAFLD. It was planned to recruit cases of USG changes of fatty liver with or without elevated serum transaminases and alkaline phosphatase into the trial. However, not a single case of fatty liver was reported with elevated liver enzymes. Hence, laboratory investigations were done before the recruitment of the patients but performed after the trial in willing patients only. Hematological investigations such as hemoglobin, total leukocyte count, differential white blood cell count, red blood cell (RBC) count, platelets count and erythrocytes sedimentation rate, biochemical examinations, i.e. lipid profile– total cholesterol, serum triglyceride, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein, fasting and postprandial blood sugar, liver function test–serum glutamic-oxaloacetic transaminase, serum glutamic pyruvic transaminase, serum alkaline phosphatase, direct, indirect and total bilirubin, total protein, serum albumin, serum globulin, albumin/globulin ratio, serum uric acid) and renal function test (blood urea and serum creatinine) were done. Along with this, physical, chemical and microscopic urine examination was also performed. USG of the abdomen was done in all the cases before the initiation and after completion of the trial. A careful history of addictions was taken to exclude alcohol use, as the trial refers to nonalcoholics only.

Inclusion criteria

- Patients of either sex of age group, >25 years and <60 years with USG findings suggestive of fatty liver grade 1, 2, and 3
- Both freshly detected and previously diagnosed cases of NAFLD were included.

Exclusion criteria

- Patient aged <25 years and >60 years or pregnant ladies
- Patients having fasting blood sugar (FBS) ≥200 mg/dl and postprandial blood sugar (PPBS) ≥250 mg/dl, despite taking oral hypoglycemic agents, Stage II hypertension, i.e., systolic blood pressure ≥160 mmHg and diastolic blood pressure ≥100 mmHg, despite taking antihypertensive drugs
- Patients with complications of metabolic syndrome such as a cerebrovascular accident, myocardial infarction, chronic kidney disease, suffering from cirrhosis, ascites, variceal hemorrhage, coagulopathy, hepatorenal syndrome, consuming hepatotoxic medicines, alcohol or other narcotic substances.

Posology

In both the groups, *Mridu Virechana* (mild purgation) was done with *Haritaki* (*Terminalia chebula* Retz.) powder at a dose of 6–8 g along with lukewarm water on an empty stomach, depending on the *Koshtha* of the patient for 3–5 days

till *Samyak Lakshanas of Koshtha Shuddhi*[8] (symptoms of appropriate purgation) were achieved.

Thereafter, in group A-*Sharpunkhadi* powder was administered as 2 capsules of 500 mg each, thrice daily in an empty stomach, i.e. ½ h before breakfast, lunch and dinner with lukewarm water for 8 weeks along with diet and lifestyle modification. Similarly, in group B (placebo group), 2 capsules of 500 mg containing roasted sooji powder were given thrice daily before food with the lukewarm water for 8 weeks along with diet and lifestyle modification. A detailed lifestyle modification sheet was prepared and given to patients in the local language. Patients were advised to eat freshly prepared light food. They were asked to take, *Mudga* (green gram), *Kulatha* (horse gram), *Yava* (barley), vegetables like *Karavellaka* (bitter gourd), *Patola* (pointed gourd), *Shigru (*drumstick), *Kushmanda* (ash gourd), *Lashuna (*garlic), *Ardraka (*ginger), fruits like *Dadima (*pomegranate*), Draksha (*Vitis vinifera); boiled warm water and buttermilk. Patients were advised to perform consistent physical exercise like brisk walking daily ½ h in fresh air or do *Yoga* postures such as *Dhanuraasana, Gomukhaasana, Ardhamatsyendraasana, Bhujangasana or Pavanamuktasana, Asanas*[9,10] which stretch abdominal organs thus promote healthy digestion.

On the other hand, patients were asked to avoid reheated and untimely food, excessively spicy, oily, salty, sour, fatty diet, pickles, pulses like black gram, yellow gram or fish, meat preparations, full-fat milk, curd, junk food, aerated drinks, chocolates, ice creams, bakery items, artificial sweeteners, jams. They were also asked to stop excessive and day time sleeping and smoking. After completion of the trial, patients were called for follow-up for four weeks at a gap of the fortnight and during this period, no specific treatment was given to the patients. They were advised to adhere to lifestyle modifications during the follow-up period.

Assessment criteria

The efficacy of the treatment was assessed based on improvement in the subjective as well as objective parameters. Relief in chief complaints of NAFLD like *Agnivaishamya* (impaired digestion), fatigue, nausea, belching, vomiting, abdominal pain, burning in the abdomen, burning in the chest, abdominal heaviness, abdominal distension, flatulence, diarrhea, constipation etc., was assessed based on changes in a scoring pattern developed in the form of a graph, for grading of subjective parameters. Patients were asked to select a number from the graph to describe the intensity of each complaint before the treatment after the treatment, and during follow-up. Scoring from 1 to 4 was considered as mild, 5–8 as moderate, and 9–10 as severe. Improvement in the grades of fatty liver was assessed by the USG changes evident from USG of the abdomen as described in [Table 2].

Presentation of data and statistical analysis

The epidemiological data of recruited patients were collected and appropriately placed in the master chart prepared with Microsoft excel worksheet. Sigma Stat[11] 3.1 software was used for statistical calculation. Wilcoxon signed-rank test for subjective criteria and Student's paired't' test for objective criteria were applied to check the level of significance in a single group before and after treatment, while Student's unpaired *t*-test for objective criteria was applied to assess the level of significance of difference observed between two groups. $P < 0.05$ was considered as statistically significant change.

Table 2: Grades of fatty liver evident from ultrasonography

Grade of fatty liver	Findings in USG-abdomen
Normal liver	Homogeneous echo texture with echogenicity equal to or slightly greater than that of the renal cortex and spleen
Grade I fatty liver	Echogenicity is just increased
Grade II fatty liver	Echogenic liver obscures the echogenic walls of portal vein branches
Grade III fatty liver	Echogenic liver obscures the diaphragmatic outline

USG: Ultrasonography

Results

Statistically significant improvement in grade of fatty liver was observed in both the groups; i.e., 39.25% in group A ($P < 0.001$) and 31.82% in group B ($P < 0.001$) [Table 3]. Among the subjective parameters, statistically significant relief was observed in following symptoms in both the groups; impaired digestion (group A– 72.1%, group B-23.36%), fatigue (group A-77.48%, group B-38.03%), nausea (group A-74.11%, group B-29%), belching (group A-76.19%, group B-29.76%), itching (group A– 74.94%, group B– 24.07%), abdominal pain (group A-73.64%, group B-21.49%), burning sensation in the abdomen (group A– 56.34%, group B– 22.73%), abdominal heaviness (group A-80.82%, group B-28.37%), abdominal distension (group A-78.89%, group B-27.21%), flatulence (group A-71.45%, group B-26.87%), diarrhea (group A-68.75%, group B– 26.22%), constipation (group A-67.69%, group B-18.01%). Only group A has shown statistically significant relief in vomiting (73.33%) [Table 4].

On applying the unpaired *t*-test for comparing the effect of therapy between two groups, it was found that the difference of percentage decrease in the above-mentioned symptoms of both groups was statistically significant and hence, group A provided better relief than group B [Table 5]. Comparing the effect of therapies on fatty liver grade in USG between the groups, the difference in the improvement of grades in both the groups was statistically significant, thus group A yield better results than group B [Table 6].

Although the hematological and biochemical parameters remained within the normal range before and after treatment, group B has shown a statistically significant rise in

Table 3: Effect of therapy on grade of fatty liver in ultrasonography

Group	Mean score		Mean diff	Percentage of diff	Paired *t*-test			Wilcoxon signed rank test				
	BT	AT			SD	SE	*t*	W	*t*+	*t*−	*P*	Signigicant
A (*n*=43)	1.07	0.65	0.42	39.25↓	0.55	0.08	5.039	−153	0	−153	<0.001	HS
B (*n*=40)	1.1	0.75	0.35	31.82↓	0.48	0.08	4.583	−105	0	−105	<0.001	HS

↓: Decrease, HS: Highly significant, SD: Standard deviation, SE: Standard error, BT: Before treatment, AT: After treatment

Table 4: Effect of therapy on chief complaints

Chief complaints	Group	Mean score		Mean diff	Percentage of diff	Paired *t*-test			Wilcoxon signed rank test				
		BT	AT			SD	SE	*t*	W	*t*+	*t*−	*P*	Significant
Agnivaishamaya	A (*n*=30)	6.2	1.73	4.47	72.1↓	0.82	0.15	29.9	−465	0	−465	<0.001	HS
	B (*n*=26)	6.4	4.92	1.5	23.36↓	0.81	0.16	9.41	−300	0	−300	<0.001	HS
Fatigue	A (*n*=33)	5.24	1.18	4.06	77.48↓	0.66	0.12	35.42	−561	0	−561	<0.001	HS
	B (*n*=29)	4.897	3.03	1.862	38.03↓	0.83	0.16	12.03	−406	0	−406	<0.001	HS
Nausea	A (*n*=21)	5.33	1.38	3.95	74.11↓	0.81	0.18	22.51	−231	0	−231	<0.001	HS
	B (*n*=14)	4.93	3.5	1.43	29↓	1.09	0.29	4.907	-66	0	−66	<0.001	HS
Belching	A (*n*=25)	5.88	1.4	4.48	76.19↓	1.01	0.2	22.29	−325	0	−325	<0.001	HS
	B (*n*=27)	5.41	3.74	1.67	29.76↓	0.92	0.18	9.415	−300	0	−300	<0.001	HS
Vomiting	A (*n*=10)	4.5	1.2	3.3	73.33↓	0.68	0.21	15.46	−55	0	−55	<0.002	HS
	B (*n*=6)	3.83	3	0.83	21.74↓	0.41	0.17	5.0	−15	0	−15	0.06	IS
Itching	A (*n*=13)	4.31	1.08	3.23	74.94↓	0.56	0.17	19.44	−91	0	−91	<0.001	HS
	B (*n*=13)	4.15	3.15	1.00	24.07↓	0.58	0.16	6.25	−66	0	−66	<0.001	HS
Abdominal pain	A (*n*=30)	6.07	1.6	4.47	73.64↓	1.17	0.21	20.971	−465	0	−465	<0.001	HS
	B (*n*=24)	5.63	4.42	1.21	21.49↓	1.29	0.26	4.608	−120	0	−120	<0.001	HS
Abdominal heaviness	A (*n*=38)	5.63	1.08	4.55	80.82↓	0.80	0.13	35.294	−741	0	−741	<0.001	HS
	B (*n*=34)	5.71	4.09	1.62	28.37↓	0.74	0.13	12.761	−595	0	−595	<0.001	HS
Abdominal distension	A (*n*=41)	5.78	1.22	4.56	78.89↓	0.84	0.13	34.845	−861	0	−861	<0.001	HS
	B (*n*=35)	5.66	4.11	1.54	27.21↓	0.89	0.15	10.303	−561	0	−561	<0.001	HS
Burning abdomen	A (*n*=25)	5.68	2.48	3.2	56.34↓	0.87	0.17	18.48	−325	0	−325	<0.001	HS
	B (*n*=20)	5.5	4.25	1.25	22.73↓	0.97	0.22	5.78	−120	0	−120	<0.001	HS
Flatulence	A (*n*=26)	5.92	1.69	4.23	71.45↓	0.71	0.14	30.369	−351	0	−351	<0.001	HS
	B (*n*=19)	5.47	4	1.47	26.87↓	0.91	0.21	7.099	−153	0	−153	<0.001	HS
Constipation	A (*n*=21)	6.19	2.0	4.19	67.69↓	0.81	0.18	23.603	−231	0	−231	<0.001	HS
	B (*n*=18)	5.83	4.78	1.05	18.01↓	0.8	0.19	5.581	−105	0	−105	<0.001	HS
Diarrhea	A (*n*=8)	6.00	1.875	4.125	68.75↓	0.64	0.23	18.205	−36	0	−36	0.008	S
	B (*n*=6)	6.33	4.67	1.66	26.22↓	0.52	0.21	7.906	−21	0	−21	0.03	S

↓: Decrease, HS: Highly significant, SD: Standard deviation, SE: Standard error, S: Significant, BT: Before treatment, AT: After treatment, IS: Insignificant

FBS (14.46%), PPBS (11.47%), serum cholesterol (9.8%), Hb (2.69%) and RBC (2.59%). S. protein had a significant rise in both groups (group A– 5.4%, group B– 4.45%). All the other parameters had insignificant change in both the groups [Table 7].

Discussion

NAFLD is a type of fatty liver which occurs when fat is deposited in the liver due to causes other than excessive alcohol use. Conventionally, NAFLD has been considered as the hepatic manifestation of the metabolic syndrome, recently, it has been suggested as a precondition to the development of type 2 diabetes and metabolic syndrome.[12] Fatty liver is mainly generated from the excessive caloric intake and lack of physical activity, pointing to correction of unhealthy life style as the first-line approach in the prevention and treatment of NAFLD. When lifestyle correction is insufficient, drug therapy becomes a strategic line.[13] Effective treatments are needed to prevent progression of simple steatosis to chronic liver disease, considering that fatty liver disease is a reversible condition which if not treated early can lead to a terminal liver disease.

There is no direct mention about NAFLD in Ayurvedic classics. After analyzing the etiology, pathogenesis, symptomatology, and complications, it can be stated that NAFLD is not a single entity, it can be explained under the broad headings of *Agnivikriti* (deranged digestion) and *Medoroga* (disturbed fat metabolism). Both these conditions can be reverted to normal with strict adherence to *Pathyasevana* (lifestyle modification). At the same time, *Agnivikriti* and *Medoroga* are capable enough for progressing into life terminating events, if environmental and host factors are favourable for the development of disease.

Table 5: Comparison of effect on chief complaints between the groups

Chief complaint	Group	Mean score		Mean diff	Percentage of diff	Unpaired *t*-test				
		BT	AT			SD (±)	SE (±)	*t*	*P*	Significant
Agnivaishamya	A (*n*=30)	6.2	1.73	4.47	72.1↓	0.82	0.15	13.567	<0.001	HS
	B (*n*=26)	6.42	4.92	1.5	23.36↓	0.81	0.16			
Fatigue	A (*n*=33)	5.24	1.18	4.06	77.48↓	0.66	0.12	11.59	<0.001	HS
	B (*n*=29)	4.897	3.034	1.862	37.96↓	0.83	0.16			
Nausea	A (*n*=21)	5.33	1.38	3.95	74.11↓	0.81	0.18	7.888	<0.001	HS
	B (*n*=14)	4.92	3.5	1.43	29.07↓	1.09	0.29			
Belching	A (*n*=25)	5.88	1.4	4.48	76.19↓	1.01	0.2	10.54	<0.001	HS
	B (*n*=27)	5.41	3.74	1.67	30.87↓	0.92	0.18			
Itching	A (*n*=13)	4.31	1.08	3.23	74.94↓	0.60	0.17	9.667	<0.001	HS
	B (*n*=13)	4.15	3.15	1.00	24.1↓	0.58	0.16			
Abdominal pain	A (*n*=30)	6.07	1.6	4.47	73.64↓	1.17	0.21	9.750	<0.001	HS
	B (*n*=24)	5.63	4.42	1.21	21.49↓	1.29	0.26			
Burning abdomen	A (*n*=25)	5.68	2.48	3.2	56.34↓	0.87	0.17	7.129	<0.001	HS
	B (*n*=20)	5.50	4.25	1.25	22.73↓	0.97	0.22			
Abdominal heaviness	A (*n*=38)	5.63	1.08	4.55	80.82↓	0.8	0.13	16.162	<0.001	HS
	B (*n*=34)	5.706	4.088	1.618	28.37↓	0.74	0.13			
Abdominal distention	A (*n*=41)	5.78	1.22	4.56	78.89↓	0.84	0.13	15.242	<0.001	HS
	B (*n*=35)	5.66	4.11	1.54	27.21↓	0.89	0.15			
Flatulence	A (*n*=26)	5.92	1.69	4.23	71.45↓	0.71	0.14	11.454	<0.001	HS
	B (*n*=19)	5.47	4.0	1.47	26.87↓	0.91	0.21			
Diarrhea	A (*n*=8)	6.00	1.88	4.12	68.67↓	0.64	0.23	7.687	<0.001	HS
	B (*n*=29)	0.68	0.74	−0.06	8.82↑	0.35	0.07			
Constipation	A (*n*=21)	6.19	2.00	4.19	67.69↓	0.81	0.18	12.072	<0.001	HS
	B (*n*=29)	0.248	0.252	−0.0345	1.39↑	0.16	0.03			

↑: Increase, ↓: Decrease, HS: Highly significant, SD: Standard deviation, SE: Standard error, BT: Before treatment, AT: After treatment

Table 6: Comparison of effect on grade of fatty liver in ultrasonography between the groups

Group	Fatty liver grade in USG				Unpaired *t*-test				
	Mean score		Mean difference	Percentage of difference	SD (±)	SE (±)	*t*	*P*	Significant
	BT	AT							
A (*n*=43)	1.07	0.65	0.42	39.25↓	0.55	0.83	0.605	<0.001	HS
B (*n*=40)	1.1	0.75	0.35	31.82↓	0.48	0.08			

↓: Decrease, HS: Highly significant, USG: Ultrasonography, SD: Standard deviation, SE: Standard error, BT: Before treatment, AT: After treatment

Further, NAFLD can be considered as *Santarpanajanya Vyadhi* (disease cause by over nourishment) having etiology and pathogenesis similar to *Sthaulya* (obesity). Initial pathology lies at *Agnivikriti* which results in the improper formation of digestive end product which again leads to the vitiation of *Kapha Dosha* and unequal formation and deposit of *Meda* (fat tissue) in *Yakrit* (liver), leading to fatty liver. Vitiated *Kapha* and *Meda* results in *Srotorodha* (blockage of channels) which provokes *Vata*. Vitiated *Vata* again results in *Agnivikriti* and this cycle repeats.[14] During this phase, clinical presentation is exactly resembling with that of *Ajirna* (indigestion) and *Sthaulya*. Therefore, the treatment of NAFLD shall encompass all these factors.

All the ingredients of *Sharpunkhadi* powder, like *Sharpunkha, Bhumiamalaki and Katuki* are having bitter taste. As per *Ayurveda, Tikta (*bitter*) Rasa* possesses *Deepana* and *Pachana* (correction of digestion and metabolism), *Lekhana* and *Medashoshana* (correction of lipid metabolism) properties. In this trial, this is evident by the significant reversal of fatty liver changes in USG in group A patients. Experiments also support that, bitter substances increase the flow of bile and stimulate repair of gut wall lining. *Sharapunkha* and *Katuki* have *Deepana* property which promotes digestive enzymes and prevent formation of *Ama*. *Deepana*, *Pachana* properties of *Sharapunkhadi* powder had corrected the digestive process and *Pachana* of *Ama* thus, corrects the process of *Dhatu* formation and therefore highly significant relief was obtained on *Agnivaishamya,* i.e. increased, decreased or altered appetite; and associated complaints like nausea, vomiting, diarrhea. Group A (*Sharapunkhadi* powder and lifestyle modification) produced statistically significant improvement in the management of vomiting, while group B (lifestyle modification alone) could not produce any significant change in vomiting. *Bhoomiamalaki* and *Katuki* due to its *Lekhana* property can

Table 7: Effect of therapy on hematological and biochemical parameters

FBS (mg/dl)	Fasting blood sugar (mg/dl)					Paired *t*-test				
	Group	Mean score		Mean diff	Percentage of diff	SD (±)	SE (±)	*t*	*P*	Significant
		BT	AT							
CBS	A (*n*=27)	94.19	102.59	−8.4	8.92↑	25.88	4.98	−1.688	0.103	IS
	B (*n*=28)	100.57	115.11	−14.54	14.46↑	37.06	7.00	−2.076	0.048	S
PPBS	A (*n*=21)	105.67	116.38	−10.71	10.14↑	25.31	5.52	−1.94	0.067	IS
	B (*n*=19)	111.9	124.74	−12.84	11.47↑	26.46	6.07	−2.116	0.049	S
Serum cholesterol	A (*n*=27)	170.7	183.59	−12.89	7.55↑	46.13	8.88	−1.452	0.159	IS
	B (*n*=29)	160.48	176.21	−15.73	9.8↑	41.14	7.64	−2.058	0.049	S
Serum protein	A (*n*=27)	6.85	7.22	−0.37	5.40↑	0.84	0.16	−2.279	0.03	S
	B (*n*=29)	6.96	7.27	−0.31	4.45↑	0.85	0.16	−1.974	0.05	S
Hb	A (*n*=33)	12.9	12.99	−0.9	6.98↑	1.27	0.22	−0.413	0.68	IS
	B (*n*=34)	13.02	13.37	−0.35	2.69↑	0.88	0.15	−2.274	0.03	S
RBC	A (*n*=32)	4.74	4.66	0.08	1.69↓	0.29	0.05	1.631	0.11	IS
	B (*n*=34)	4.64	4.76	−0.12	2.59↑	0.29	0.05	−2.277	0.02	S

↑: Increase, ↓: Decrease, IS: Insignificant, S: Significant, SD: Standard deviation, SE: Standard error, PPBS: Post prandial blood sugar, FBS: Fasting blood sugar, BT: Before treatment, AT: After treatment, RBC: Red blood cell count, Hb: Hemoglobin

remove fat and open the obstructed channel and thus has provided relief in symptoms such as belching, flatulence, constipation, abdominal pain; heaviness, and distension.

Meda is one of the prime factor in pathogenesis of NAFLD. Excessive amount of *Meda* accumulated can be removed only by means of *Shoshana* (absorption), which is done by *Tikta Rasa* and *Ruksha Guna. Tikta Rasa* and *Ruksha Guna* can perform *Lekhana* of abdominal *Meda* and thus reverse fat (fat) accumulation in the liver. This is evident from the statistically significant improvement in the grades of fatty liver in group A. *Katuki* and *Sharapunkha* are having *Yakriduttejaka* (liver stimulating) and *Pittavirechaka* (bile secretion) properties,[15,16] respectively and thus excessive triglyceride and cholesterol can also be removed with bile from liver. *Bhoomiamalaki* and *Katuki* are having *Medohara* property, thus decrease the level of circulating lipids and prevent hepatic accumulation of lipids.

T. purpurea contain flavonoids and polyphenolic compounds, which possess potent antioxidant, anti-inflammatory and free radical scavenging activity responsible to prevent cellular leakage and loss of functional integrity of the liver cell membrane, protects the tissues from the oxidative damage caused by various hapato-toxic agents like free radicals, lower the activity of liver enzymes and significantly reduce elevated serum bio-marker levels in the body and it is supported by extensive data from preclinical studies in acute and chronic hepato-toxic models.[17]

Hepatoprotective and antioxidant activity of *Phyllanthus niruri* has been attributed to two novel lignin phytochemicals named *phyllanthin* and *hypophyllanthin*.[18,19] Water, ethanol and hexane extracts of *P. niruri* exhibited marked anti-inflammatory properties due to the presence of lignan-rich fraction, or lignans phyltetralin, nirtetralin, and niranthin.[20]

Hepato-protective effect of *Katuki* is probably due to the increased activities of the antioxidant enzymes, or to a counteraction of free radicals by the presence of the electrophilic constituents picroside I, picroside II, and kutkoside (Kumar *et al*., 2001; Ramesh *et al*., 1992), which are present in rich quantities in the roots and rhizomes of *P. kurroa*.[21] A bitter extract rich in iridoid glycosides (kutkoside, kutkin) has hepatoprotective, anticholestatic, antioxidant, anti-inflammatory and immune modulating activities.[22] *Katuki* is a potent immune-stimulant, exhibits choleretic activity in dogs and alcoholic extract of isolated active principles have shown significant hepatoprotective activity. NAFLD in rats was cured by giving standard hydro-alcoholic extracts of P*icrorhiza kurroa*. It reduced the lipid content of liver significantly at the dose of 400 mg/kg.[23]

Therefore, the therapeutic action on NAFLD of *Sharapunkhadi Powder* may be attributed to phyto constituents present in it which are proved on pharmacological basis in different studies.

All the international guidelines report that lifestyle changes that include diet and exercise are the only therapeutic approach recommended for NAFLD. A moderate weight loss and physical activity induces a reduction in insulin resistance, and considered as the current therapeutic strategy for patients with NAFLD who are overweight or obese.[24] Vigorous physical exercise reduces insulin resistance, helps maintain weight loss over time and improves hepatic histology. Mild or moderate exercise intensity does not provide a significant benefit over protection in the development of NAFLD.[25] In the present trial, patients in both groups were instructed to avoid sedentary life, day sleep or awakening late in night, suppressing natural urges of defecation and urination or excessive exposure to extreme conditions of weather, as all these habits disturb *Agni* and provoke *Vata* and increase the amount of *Sthayi* (deposited) and *Asthayi* (circulating) *Medo Dhatu.* Fructose intake through soft drinks and artificial sweeteners increases the accumulation of fats in the liver and of triglycerides in plasma.[26] In this study, around 35.48% of patients prefered the intake of

Madhura Rasa (sweet taste) predominant food. Dyslipidemia, insulin resistance and oxidative damage induced by high fructose intake may contribute to increased risk of CVD that is evident in patients with NAFLD.[27] Restriction of fructose is very important to limit liver steatosis and CVD in NAFLD patients.

Patients were advised to practice *Kalabhojana* (food intake in proper quantity and at proper time) for proper functioning of *Agni* and *Upavasa* (fasting) at times to burn out excess *Meda*. Intake of vegetables and fruits rich in flavonoids and polyphenols was encouraged. *Rooksha Dravas* like buttermilk, hot water, etc., were recommended as they are having *Medoshoshana* property. *Yoga* and *Pranayama* practice can provide mental and spiritual health, in addition to physical health which will help to abandon unhealthy behaviors and acquire healthy lifestyle. Stress precipitating factors like anger, fear, worries, etc., are also to be avoided, instead *Dhyana, Patana* (meditation, prayer, reading) etc., are to be followed.

Strict adherence to lifestyle modification can prevent the incidence of NAFLD in normals, reverse the pathology, regain normalcy and can prevent progression to further stages such as NASH in NAFLD patients. This was the reason why patients of group B had significant reduction in grades of fatty liver and relief in subjective parameters such as *Agnivaishamya*, fatigue, nausea and belching.

Conclusion

Although one-to-one comparison of NAFLD is not available in Ayurvedic literature, NAFLD can be considered as *Santarpanajanya Vyadhi* having etiology, pathogenesis and clinical presentation similar to *Agnivikriti* and *Medoroga*. Although lifestyle modification alone (group B) had produced good results in subjective and objective criteria of NAFLD, *Sharapunkhadi* powder combined with lifestyle modification (group A) had provided statistically more significant reduction in grade of fatty liver and in subjective parameters such as *Agnivaishamya*, fatigue, nausea, belching, vomiting, itching, burning in the abdomen, abdominal pain, heaviness and distension, flatulence, diarrhea and constipation. Due to the present hectic day-to-day schedule, it is difficult for most of the subjects to adhere to strict lifestyle modification and *Sharapunkhadi Yoga* is a formulation which is quite safe for internal administration. Hence, *Sharapunkhadi Yoga* can be suggested as a promising herbal formulation for the management of non-alcohlic fatty liver disease specially and grade I to grade II.

Data access and responsibility

The corresponding author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Financial support and sponsorship

Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar, supported for drugs, investigations and equipment required for present clinical trial.

Conflicts of interest

There are no conflicts of interest.

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