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Research Article

AN OPEN RANDOMIZED STUDY OF *PATOLA KATUROHINYADI KASHAYAM* IN ALCOHOLIC LIVER DISEASE

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ABSTRACT

Alcoholic liver disease (ALD) is a leading cause of morbidity and mortality in India. Chronic consumption of alcohol results in variations in alcohol metabolism, oxidative stress, antigenic adducts formation and acetaldehyde toxicity. These factors cause inflammation, fatty changes, fibrosis of liver cells and raising the transaminases in the blood. There is no specific treatment for ALD.

Patola Katurohinyadi Kashayam, a classical Ayurvedic formulation has been reported by many practitioners to be effective in treatment of liver disorders. This study focuses on the effect of the *Patola Katurohinyadi Kashayam* in ALD for restoration of normal liver function by investigating 10 subjective and 5 objective parameters. As *Patola Katurohinyadi Kashayam* is *Raktaprasadak, Yakritgami, Deepan, Jwaraghna, Kamalanashak* and *Pandunashak* it was used as Trial Drug.

Clinical Trials were conducted at Anandvan De-Addiction Centre, Pune. By random allotment method 20 well-diagnosed patients of ALD were included in both Control and Trial group each. The diagnosis of ALD was made by documentation of alcohol excess and evidence of liver disease. Trial group was administered the Trial drug in a dose of 15ml with luke warm water after meal for the duration of 28 days. Control group was not given any drugs but observed for 28 days for all parameters.

The statistical analysis revealed that Trial drug is effective in ALD and significantly reduces *Panduta, Agnimandya, Hrullas, Daha* and *Daurbalya.* Besides it significantly lowers the SGOT and SGPT levels too.

KEYWORDS: Alcoholic liver disease, *Patola Katurohinyadi Kashayam,* SGOT, SGPT.

INTRODUCTION

Alcoholic liver disease (ALD), a toxic liver injury is a leading cause of morbidity and mortality in India. In 2012, about 3.3 million deaths, or 5.9% of all global deaths were attributable to alcohol consumption [1]. The spectrum of ALD varies from simple steatosis to cirrhosis. These are not necessarily distinct stages of evolution of the disease, but rather, multiple stages that may be present simultaneously in a given individual[2,3]. These are often grouped into three histological stages of ALD, including fatty liver or simple steatosis, alcoholic hepatitis (AH), and chronic hepatitis with hepatic fibrosis or cirrhosis[4].

The primary metabolite of alcohol i.e. Acetaldehyde is thought to be a major cause of alcoholic liver disease. Acetaldehyde impairs mitochondrial oxidative system resulting in variations in alcohol metabolism, centrilobular hypoxia; inflammatory cell infiltration and activation, antigenic adducts formation, reactive oxygen species formation and lipid peroxidation[5-8]. These factors cause inflammation, fatty changes, fibrosis of liver cells. The range of clinical features of alcoholic liver disease varies, from asymptomatic to end-stage liver disease with portal hypertension, jaundice and encephalopathy Patients may present symptoms such as nausea, anorexia, fever, ascites and jaundice[8]. A number of laboratory abnormalities, including elevated AST and ALT have been reported in patients with ALD, and used to diagnose ALD[9].

The symptoms of ALD often improve with the cessation of drinking. Immediate and total abstinence from alcohol is critical for patients with alcoholic liver disease. Continued drinking is associated with disease progression, while abstinence benefits patients at any stage of disease. There is no specific treatment for ALD.

According to *Charak*, *Madya* (Alcohol) is etiological factor responsible for vitiation of *Raktadhatu*[10]. Excessive alcohol consumption

ultimately causes vitiation of *Yakrit* (Liver) as *Yakrit* is *Mulasthana* of *Raktavaha Srotas*[11]. This can be correlated as Alcoholic Liver Disease. The signs and symptoms of ALD are similar to that of *Kamala Vyadhi.*

Patola Katurohinyadi Kashayam[12] is a classical Ayurvedic formulation from *Ashtanga Hridayam*, has been reported to many health practitioners to be effective in treatment of Liver disorders. It is indicated in *Kamala, Kushtha, Vaman, Aruchi, Jwara* and *Vishajanya Vyadhi* [12]. Almost all the ingredients of this *Kashaya* like *Patola, Kutki, Raktachandan, Murva, Guduchi* and *Patha* are *Raktaprasadak, Pittaghna, Kamalanashak, Pandunashak* and *Vishaghna.* This *Kashaya* is easy to administer and cost effective. Thus to counteract ALD *Patola Katurohinyadi Kashayam* was selected as it has an affinity for *Yakrit* and *Rakta Dhatu*.

AIMS AND OBJECTIVES

The study was conducted with the aim to assess the effect of *Patola Katurohinyadi Kashayam* in ALD. The objective was to ascertain the restoration of normal liver functions.

MATERIALS AND METHOD

Patola Katurohinyadi Kashayam was purchased from Arya Vaidya Sala Kottakkal, Kerala. Standardization certificate of the same was obtained prior to commencement of the clinical study. The *Patola Katurohinyadi Kashayam* used was as per the reference of *Ashtanga Hridayam* [12].

This Open Randomized Clinical Trial was conducted at Anandvan De-addiction and Rehabilitation Centre, Chandan Nagar, Pune, India after the permission of the Institutional Ethics Committee (vide letter no: BVDU/Exam/2185/2011-12).

Patients diagnosed with ALD were randomly selected from the in-patient departments of Anandvan De-addiction and Rehabilitation Centre, Chandan Nagar, Pune, India.

Method of collection of data

Detailed clinical history and clinical examination was carried out before assessing the case and starting the proper trial. The diagnosis of ALD was made by documentation of alcohol excess and evidence of liver disease using the special Proforma. The patients were divided into two groups - Control group and Trial group. The both groups consisted of 20 patients each. Thus, the total sample size of the study was 40, calculated on the basis of rate of incidence of the condition. A total 112 patients were screened and 62 of them were enrolled in the study, but a dropout of 22 was registered. Informed Consent of each patient was taken prior to their enrolment in the clinical trials.

The Trial Group patients were administered 15 ml of *Patola Katurohinyadi Kashayam* two times a day after meals with luke warm water. Patients of the Control Group did not receive any trial drug. All patients, who were included in study, were studied daily for 28 days. All patients were subjected to pre and post laboratory investigations of Haemogram and Liver Function Test (LFT).

Inclusion Criteria

a) Clinically diagnosed patients of Alcoholic Liver Disease were selected

b) Age group - above 18 years (as patients below this category were negligible in the centre)

c) Sex - Male (as female were not admitted in this particular centre)

Exclusion Criteria

a. Age below 18 years

b. Sex - Female

c. Patients suffering from non alcoholic hepatitis

d. Patients with high risk diseases and severe illness

e. Patients who are diagnosed as Liver cirrhosis, Hepatic coma, Ascites, Portal hypertension, Splenomegaly, Hepatocellular carcinoma etc.

Assessment Criteria: The patients were assessed using the following parameters.

Subjective Parameters

1. Assessment of *Agnimandya* (Loss of Appetite)
   0 : Absent
   1 : Present
2. Assessment of *Aruchi* (Tastelessness)
   0 : Absent
   1 : Present
3. Assessment of *Hrillas* (Nausea)
   0 : Absent
   1 : Nausea
   2 : Nausea with excess salivation
   3 : Nausea with regurgitation
   4 : Nausea with vomiting
4. Assessment of *Trishna* (Thirst)
   0 : Absent
   1 : Mild
   2 : Moderate
   3 : Sever but reduces after water intake
   4 : Sever but don't reduces after water intake
5. Assessment of *Manda Jwara* (Mild Fever)
   0 : Absent
   1 : Present
6. Assessment of *Daha* (Burning sensation)
   0 : Absent
   1 : Present
7. Assessment of *Panduta* (Pallor)
   0 : Absent
   1 : Present
8. Assessment of *Pitatva* (Icterus)

0 : Absent
1 : Present

9. Assessment of *Daurbalya* (Weakness)
0 : Absent
1 : Dyspnoea after moderate to severe work
2 : Dyspnoea after mild to moderate work
3 : Dyspnoea after mild work
4 : Dyspnoea at rest

10. Assessment of *Bhrama* (Vertigo)
0 : Absent
1 : Occasionally
2 : Frequently
3 : Often and with short disorientation
4 : More often and with prolonged disorientation

Objective Parameters

1. Haemogram
2. Liver Function Test

STATISTICAL ANALYSIS

Statistical analysis was carried out in terms of Mann-Whitney U test, paired t-test and finally results were incorporated in term of probability (p).

Table 1: Showing effect on subjective parameters between Trial and Control group

Symptoms	Group	Median grade at				
		Day 0	Day 7	Day 14	Day 21	Day 28
Agnimandya	Trial	1	1	1	0	0
	Control	1	1	1	1	1
	p-value	0.999	0.999	0.289	0.06	0.006
Aruchi	Trial	1	1	0	0	0
	Control	1	1	1	0	0
	p-value	0.602	0.602	0.108	0.999	0.289
Hrillas	Trial	3	2.5	2	0.5	0
	Control	3	2	1.5	1	1
	p-value	0.62	0.01	0.999	0.03	0.006
Trishna	Trial	2	2	1	0	0
	Control	2	1	0	0	0
	p-value	0.841	0.052	0.253	0.289	0.602
Manda Jwara	Trial	1	1	1	0	0
	Control	1	1	0	0	0
	p-value	0.602	0.799	0.602	0.999	0.799
Daha	Trial	1	1	0	0	0
	Control	1	1	1	0	0
	p-value	0.799	0.799	0.602	0.183	0.03
Panduta	Trial	1	1	1	0	0
	Control	1	1	1	1	1
	p-value	0.999	0.999	0.152	0.003	<0.001
Pitatva	Trial	1	1	1	0	0
	Control	1	1	1	1	0
	p-value	0.999	0.999	0.602	0.183	0.108
Dourbalya	Trial	2	2	1	1	1
	Control	3	2	2	1	1
	p-value	0.231	0.341	0.091	0.341	0.049
Bhrama	Trial	0	0	0	0	0
	Control	1	0	0	0	0
	p-value	0.102	0.678	0.429	0.799	0.799

Out of total 10 subjective parameters highly significant result was observed in the symptom *Panduta* (p-value < 0.001) Significant results were observed in 4 symptoms *Agnimandya, Hrillas, Daha* and *Daurbalya* (p-value < 0.05).

Table 2: Showing effect on objective parameters between Trial and Control group

Biomarkers	Group	N	Mean	SD	p-value
HB_BT	Trial	20	12.67	2.60	
	Control	20	13.45	1.67	0.267
HB_AT	Trial	20	13.60	1.94	
	Control	20	13.81	1.51	0.698
Bil_Total_BT	Trial	20	1.79	1.13	
	Control	20	1.49	0.66	0.310
Bil_Total_AT	Trial	20	0.79	0.22	
	Control	20	0.82	0.16	0.637
Bil_Direct_BT	Trial	20	0.86	0.84	
	Control	20	0.85	0.54	0.952
Bil_ Direct _AT	Trial	20	0.46	0.67	
	Control	20	0.42	0.15	0.795
Bil_Indirect _BT	Trial	20	0.93	0.40	
	Control	20	0.64	0.22	0.009
Bil_Indirect _AT	Trial	20	0.49	0.19	
	Control	20	0.41	0.11	0.117
SGPT_BT	Trial	20	89.70	50.82	
	Control	20	92.70	29.86	0.821
SGPT_AT	Trial	20	31.24	6.46	
	Control	20	47.28	9.80	< 0.001
SGOT_BT	Trial	20	108.10	57.58	
	Control	20	79.73	27.37	0.057
SGOT_AT	Trial	20	24.44	9.03	
	Control	20	36.94	7.35	< 0.001
ALP _BT	Trial	20	288.70	68.78	
	Control	20	202.87	52.71	< 0.001
ALP _AT	Trial	20	151.54	40.98	
	Control	20	136.83	37.65	0.244

HB = Haemoglobin, Bil = Bilirubin, SGOT = Serum glutamic oxaloacetic transaminase, SGPT = Serum glutamic pyruvic transaminase, ALP = Alkaline phosphatase, BT = before treatment, AT = after treatment, N= number of patients, SD =Standard Deviation, p = Probability Value

In objective parameters, highly significant results were observed in the SGOT and SGPT (as p-value < 0.001)

OBSERVATIONS & RESULTS

Based on the statistical analysis, the effects of the drug on various parameters were studied and following results were obtained. The symptom *Panduta* showed complete i.e. 100% reduction in Trial group while 25% reduction in Control group [Fig.1]. *Agnimandya* showed 90% relief in Trial group and 40% in Control group [Fig.2]. *Hrillas* was reduced by 85% in Trial group as compared to 35% in Control group [Fig.3] while *Daha* showed 100% reduction in the Trial group and 60% reduction in Control group [Fig.4]. *Daurbalya* was reduced by 35% in Trial group and 20% in Control group. *Bhrama* recorded an alleviation of 100% in Trial group whereas the Control group showed only 80% alleviation. Similarly *Aruchi* showed 90% reduction in Trial group while 80% reduction in Control group [Fig.5] whereas *Pitatva* was reduced by 100% in Trial group as compared to 70% in Control group [Fig.6].

The Liver Function Test viz., Total Bilirubin, Indirect Bilirubin, SGPT [Fig.7], SGOT [Fig.8] and Alkaline Phosphatase showed a greater decrease in the mean difference in Trial group indicating the efficacy of Trial drug.

DISCUSSION

Patola Katurohinyadi Kashayam is a combination of 6 herbal ingredients [12] viz. *Patola* (*Trichosanthes dioica), Katurohini (Picrorhiza kurroa), Raktachandan (Pterocarpus santalinus), Murva (Marsdenia tenacissima), Guduchi (Tinospora cordifolia), Patha (Cissampelos pareira).*

Patola root decoction is having hepatocurative and mild hepatoprotective activity due to its *Rechaka* property. It's *Pittasaraka* (cholagogue), *Deepan, Pachan, Anuloman* and *Bhedan* properties help to alleviate ALD [13].

Katurohini is useful in jaundice, nausea anorexia, dyspepsia and periodic fevers and proven as a hepatoprotective agent in experimental & clinical studies. It has shown hydrocholeretic effect in rats and dogs [14]. Its extract revealed strong antioxidant activity and also significantly inhibited lipid peroxidation **[15]**. Picroliv, its active constituent has been evaluated as a hepatoprotective agent against ethanol-induced hepatic injury in rats [16-17].

The ethanol and aqueous stem bark extract of *Raktachandan* afforded significant protection against CCl_4 induced hepatocellular injury[18].

Murva has *Deepan, Vishaghna, Anuloman, Amapachan, Shulaprashaman* and *Pittasaraka* property. It also has anti-inflammatory, antibacterial, antimutagenic, anticancer and anti-pyretic action.

Various Ayurvedic preparations of *Guduchi* are indicated in *Pandu* (anaemia) and *Kamala* (jaundice). A clinical study has shown that *Guduchi* plays an important role in normalization of altered liver functions (ALT, AST).The anti hepatotoxic activity of *Tinospora cordifolia* has been demonstrated in CCl_4 induced liver damage, normalising liver function as assessed by morphological, biochemical (SGPT, SGOT, serum alkaline phosphatase, serum Bilirubin) parameters[19-20].

Hepato protective activity of *Patha (Cissampelos pareira)* against carbon tetra chloride induced hepatic damage was found in vitro and in vivo study [21].

All liver disorders are due to the vitiation of *Pitta* and *Virechana* is the choice of treatment for all the *Pittaja rogas*. *Patola Katurohinyadi Kashayam* is a *madhyam shodhan* formulation stated in *Ashtanga Hridayam Shodhanadi ganasangrah adhyaya*. It is *Tikta* (bitter) *rasa* predominant which is *Pittashamaka* in nature. This predominance also attributes to the *Vishanasaka* (Anti-toxic) property as stated by classics. Similarly *Laghu guna* (light) allows easy absorption and assimilation. The *Bhedana* property of Trial drug is especially correlated with choleretics. The drug which has choleterics property will stimulate the secretion of bile and the excessive bile cause *Virechana*. In short trial drug has choleretic, hepatoprotective, hepatocurative and antioxidant property.

CONCLUSION

From the above study, an inference can thus be drawn that *Patola Katurohinyadi Kashayam* is a very potent polyherbal formulation that effectively reduces the symptoms of *Panduta*, *Agnimandya, Aruchi, Hrillas, Trishna, Daha* and *Bhrama* observed in patients suffering from ALD. It is also effective in restoration of normal liver functions as it reduces elevated SGPT and SGOT. Thus it can be advised as a drug of choice in clinical practice.

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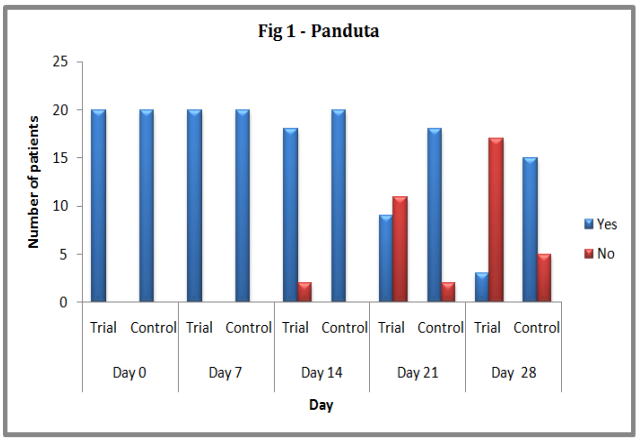
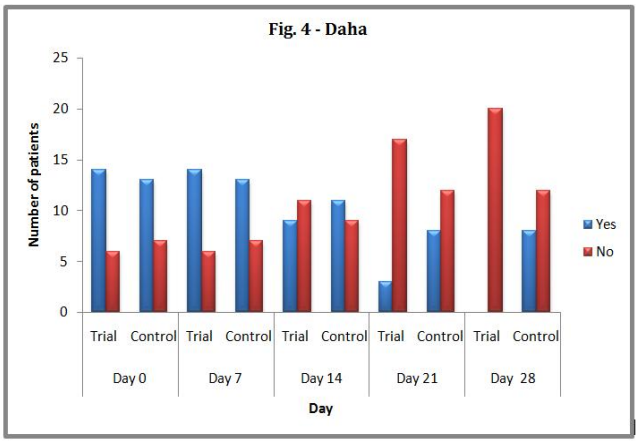
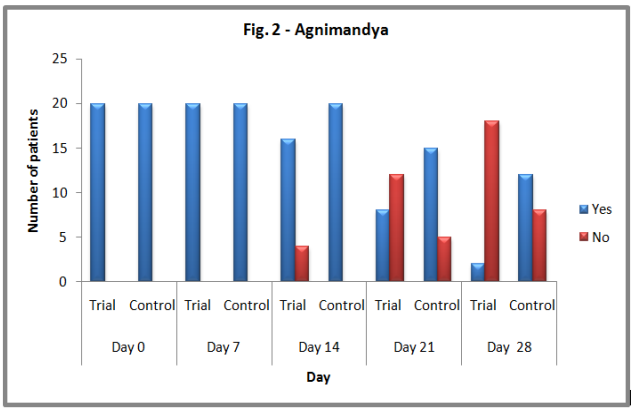
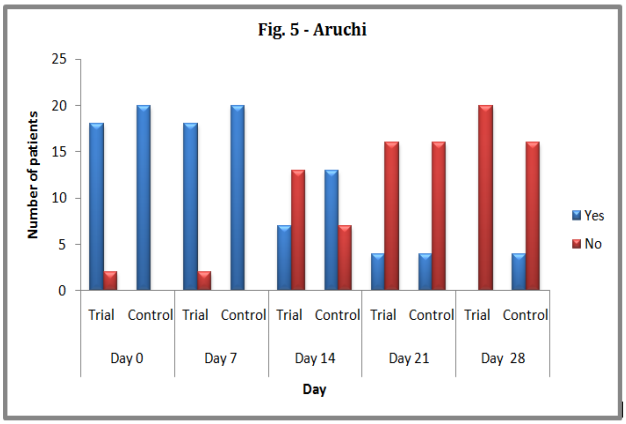
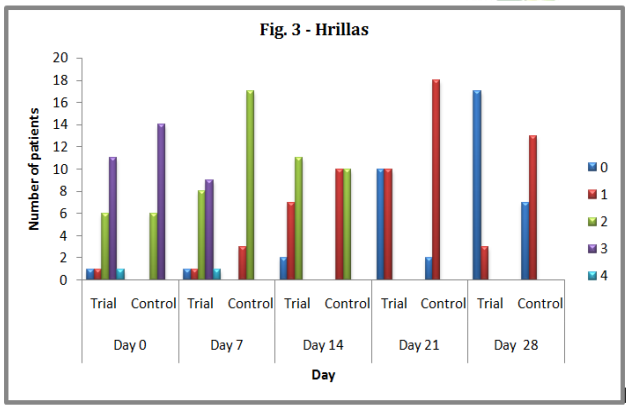
Graphs

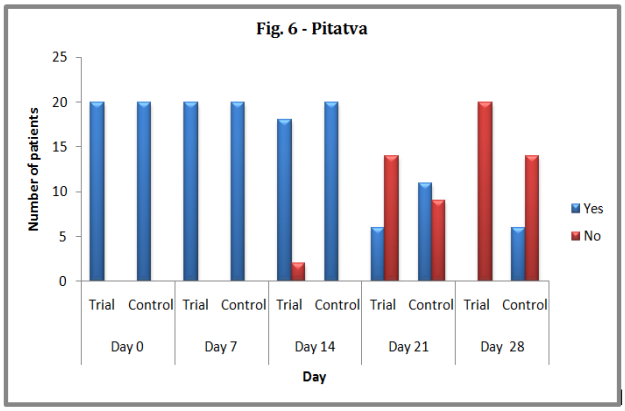


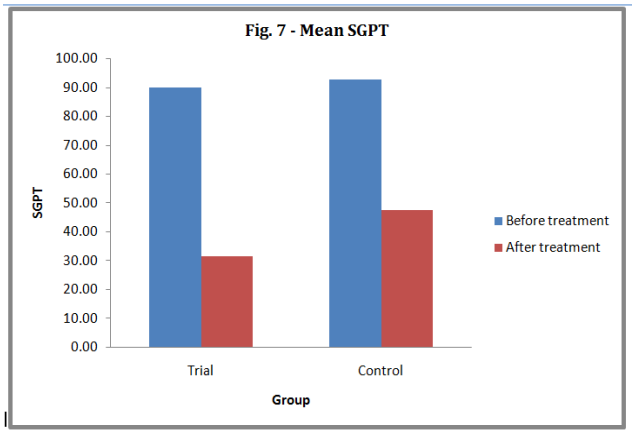


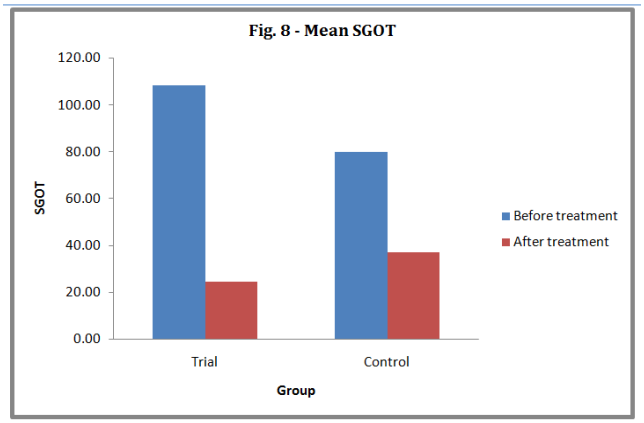












Graph 1: Showing effect on subjective parameters between Trial and Control group