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Research Article

THE EFFICACY OF *VASAGUDUCHYADI 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.

Vasaguduchyadi Kashayam is a classical Ayurvedic formulation stated in *Ashtanga Hridayam* for the treatment of Jaundice and anemia. The study focuses on the effect of the *Vasaguduchyadi Kashayam* in ALD for restoration of normal liver function, with the help of investigating 10 subjective and 2 objective parameters. As the *Vasaguduchyadi Kashayam* is *Yakritgami, Kamalanashak* and *Pandunashak*, was used as Trial Drug.

Clinical Trials were conducted at Anandvan De-Addiction Centre, Pune. By ballot method 60 well diagnosed male 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.

The control group was allowed to partake symptomatic line of treatment advised by the centre while the trial group was administered *Vasaguduchyadi kashayam* in a dose of 15ml with luke warm water after meal for the duration of 45 days. Patients of both groups followed complete abstinence from Alcohol and *Pathyakar aahar-vihar*.

The statistical analysis revealed that Trial drug is effective in ALD. It significantly reduces *Agnimandya, Aruchi, Hrillas, Trishna Pitatva* and LFT.

KEYWORDS: Alcoholic liver disease, *Vasaguduchyadi Kashayam.*

INTRODUCTION

Alcohol consumption accounts for 5.9 % of all deaths worldwide[1] and is the prime cause of Alcoholic Liver Disease (ALD). This is characterized by macro or micro vesicular fatty changes, diffuse or massive necrosis, acute or chronic hepatitis, fibrosis and liver cirrhosis as also its malfunctioning[2].

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[2,3,4,5]. 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[5]. A number of laboratory abnormalities, including elevated AST and ALT have been reported in patients with ALD, and used to diagnose ALD[6].

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.

Contemporary management of the condition too promotes the use of hepato-protective herbal or herbo-mineral formulations. The current study is thus an endeavor to establish the efficacy of herbal formulation viz. *Vasaguduchyadi kashayam* quoted by *Vagbhatacharya*[7].

AIM AND OBJECTIVES

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

MATERIALS AND METHOD

The trial drug, *Vasaguduchyadi kashayam* was purchased from Arya Vaidya Sala Kottakal, Kerala- a standardized licensed Pharmacy (Batch No.508711). The *Vasaguduchyadi kashayam* used was as per the reference of *Ashtanga Hridayam*[7].

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/COA/1680-2/2012-13).

Source of data: For the study well diagnosed patients of 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. Clinically diagnosed patients of ALD were selected and randomly allotted to either of 2 group's viz. Trial or Control by ballot method after taking Informed Consent. The criteria of inclusion were patients suffering from ALD, sex male only of the age group of 18 to 60 years. Patients suffering from Non Alcoholic Liver Disease, Infective Hepatitis, Hypertension and other high risk conditions were exclude from the study.

A sample size of 60 patients was decided upon considering the incidence of the condition of the place of study and time duration. A total of 94 patients were screened and 72 of them were enrolled in the study, but a dropout of 12 was registered. All patients were subjected to pre and post laboratory tests of Haemogram and Liver Function Test (LFT).

Dosage: The Trial Group patients were administered 15 ml of *Vasaguduchyadi kashayam* two times a day after meals with luke warm water for 45 days. Patients of the Control Group did not receive any trial drug but followed symptomatic treatment as and when required.

Duration of study: The duration of study was 45 days.

Follow up: All patients, who were included in study, were studied daily for 45 days.

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, Spleenomegaly, Hepatocellular carcinoma etc.

Assessment Criteria

The A pilot study was conducted before the commencement of the actual trial so as to define criteria of assessment. On the basis of this, 10 subjective parameters viz. *Agnimandya* (Loss of appetite), *Aruchi* (Tastelessness), *Hrillas* (Nausea), *Trishna* (Thirst), *Manda Jwara* (Mild fever), *Daha* (Burning sensation all over the body), *Panduta* (Pallor), *Pitatva* of *Nakh-Netra-Twak_Mala* (Icterus), *Daurbalya* (Weakness) and *Bhrama* (Vertigo) formed the criteria of Assessment on enrolment and weekly follow ups.

These parameters were graded on the basis of CTCAE guidelines of 2009. Haemogram and LFT formed the objective 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

The Wilcoxon Paired Signed Rank test was carried out for each of the assessment criterion separately to assess efficacy. The Mann Whitney 'u' test was run separately for each criterion to compare the efficacy between the Trial and Control groups.

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

RESULTS

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

	Agnimandya	*Aruchi*	*Hrillas*	*Trishna*	*Daha*	*Pitatva* of *Nakh Netra Twak* and *Mala*	*Daurbalya*	*Bhrama*
Mann-Whitney U	183.000	271.50	228.000	443.000	427.000	57.000	319.000	383.00
Z	-4.212	-2.876	-3.459	-.109	-.412	-6.186	-2.080	-1.228
p-value	.000	.004	.001	.913	.680	.000	.038	.219

8 out of the pre-defined 10 subjective parameters were predominantly observed in both groups. From the above table it is observed that there is no significant difference in two groups for *Trishna, Daha* and *Bhrama* as p- value Mann-Whitney U test is greater than 0.05. While significant difference is observed in two groups for *Agnimandya, Aruchi, Hrillas, Pitatva* and *Daurbalya.*

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

				95% C.I.		t	p-value	Result
	df	Mean Difference	Std. Error Difference	Lower	Upper			
Hemoglobin	58	.49000	.16514	.15943	.82057	2.967	.001	Significant
S.G.P.T.	58	43.91000	6.91793	30.06226	57.75774	6.347	.000	Significant
S.G.O.T.	58	63.87333	9.23149	45.39450	82.35217	6.919	.000	Significant
Alkaline Phosphatase	58	74.40667	13.96333	46.45603	102.35731	5.329	.033	Significant
Total Bilirubin	58	.82100	.17793	.46484	1.17716	4.614	.000	Significant
Direct Bilirubin	58	.44833	.11159	.22495	.67171	4.018	.000	Significant
Indirect Bilirubin	58	.31400	.09966	.11452	.51348	3.151	.001	Significant

OBSERVATIONS & RESULTS

Based on the statistical analysis, the effects of the drug on various parameters were studied and following results were obtained.

Agnimandya showed 100% relief in Trial group and 29.27% in control group [Fig.1]. *Aruchi* recorded an alleviation of 100% in trial group whereas the control group showed only 27.27% alleviation [Fig.2]. *Hrillas* was reduced by 100% of the patients of trial group as compared to 61.84% in Control group [Fig.3]

Trishna was reduced by 100% of the patients of trial group as compared to 72.41% in Control group [Fig.4]. The symptom of *Daha* showed 92.31% reduction in the trial group and an 80% reduction in control group [Fig.5]. *Pitatva* was reduced by 100% of the patients of trial group as compared to 17.95% in Control group [Fig.6].

Daurbalya was reduced by 66.67% of the patients of trial group as compared to 57.63% in Control group [Fig.7]. Similarly, *Bhrama* recorded an alleviation of 83.33% in trial group whereas the control group showed only 73.08% alleviation [Fig.8].

The objective parameters viz. LFT was normalized and an elevation in the Haemoglobin % was also noted. (p-value< 0.001).

DISCUSSION

Vasaguduchyadi kashayam is a combination of 6 herbal ingredients[3] viz. *Vasa* (*Adathoda vasica*), *Guduchi* (*Tinospora cordifolia*), *Triphala* (*Emblica offcinalis, Terminalia bellerica, Terminalia chebula*), *Kutaki* (*Picrorrhiza kurroa*), *Bhunimba* (*Andrographis paniculata*) and *Nimba* (*Azadirachta indica*).

Adathoda vasica has been proved hepatoprotective against by D-galactosamine in rats[8] and paracetamol induced hepatic damage[9]. Ethyl acetate extract of *Adhatoda vasica* has potent hepatoprotective effect against CCl_4 - induced liver damage in rats[10-11] and in mice too[12].

Ethanolic extract of all the parts of *Tinospora cordifolia* showed significant hepatoprotective effect by reduction in serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TBL) in the carbon tetrachloride-induced hepatic damage in rats[13].

Triphala and its constituents show valuable hepatoprotective activity. *Triphala* showed significant protection against acute liver toxicity induced by high doses of drugs and chemicals, which might be due to high levels of phenolic and polyphenolic compounds in these plants[14].

Terminallia chebulla one of the content of test drug was found to prevent the hepatotoxicity caused by the ATT[15] and significantly reversed the t-BHP-induced cell cytotoxicity and lactate dehydrogenase leakage[16].

Another ingredient *Azadirachta indica* has exhibited potent hepatoprotective activity against Antitubercular drugs in an experimental study in rats[17] and in Paracetamol induced hepatotoxicity in rats on biochemical and histologically parameters[18-19]. It also showed protective effects against diethyl nitrosamine (NDEA) induced hepatotoxicity in male mice[20].

Picrorrhiza kurroa possesses potent hepatoprotective activity. Its alcoholic, petroleum ether and chloroform extract significantly protect hepatic damage caused by carbon tetrachloride. In alcohol induced hepatotoxicity a significant decline in activities of ALDH is seen. Its active principle Picroliv significantly prevents the decrease in activities of these enzymes. This result in decrease in the generation of free radicals, which lead to quicker repair of damaged cell membranes. It also has antioxidant activity[21]. *Andrographis paniculata* has a potent hepato-protective action on CCL_4 induced hepatic damage in rats[22].

Thus all the ingredients of test drug have been proved as a potent hepatoprotective drug in various in vivo and in vitro experimental studies and in some clinical studies as well.

In Ayurvedic perview the ingredients of *Vasaguduchyadi Kashayam* are *Tikta* (Bitter), *Katu rasatmak* (Pungent), *Deepan* (stimulators of appetite), *Pachan* (digestive), *Raktaprasadak* and *Shodhana* (blood purifier) and indicated in the treatment of *Pandu, Raktapitta* and *Kamala*[7]. It is a *Shodhan* (mild purification) *Kalpa* and has an affinity to act on *Yakrit* (liver).

The properties of *Tikta, Katu rasa, Deepan, Pachan* and *Pittashaman* render it useful in reducing the symptoms of *Agnimandya, Aruchi, Hrillas* and *Trishna* as they pacify the *Doshas* and promote *Dhatuposhan* thus reducing *Daurbalya* and *Bhrama*.

The *Raktashodhan* and *Prasadan* properties on the other hand attribute to the reduction in *Nakh-Netra-Twak-Mala Pitatva*.

The *Yakritottejak* (hepato-stimulant) and *Yakritprasadan* (hepato-protective) properties of the formulation are responsible for the better results in alleviation of elevated SGOT, SGPT, Total, Direct& Indirect Bilirubin and Alkaline phosphatase.

CONCLUSION

From the above study, an inference can thus be drawn that *Vasaguduchyadi Kashayam* is a herbal formulation that effectively reduces the symptoms of *Agnimandya, Aruchi, Hrillas, Daurbalya* and *Pitatva* observed in patients suffering from ALD. It is also effective in restoration of normal liver functions and can thus be advised as a drug of choice in clinical practice.

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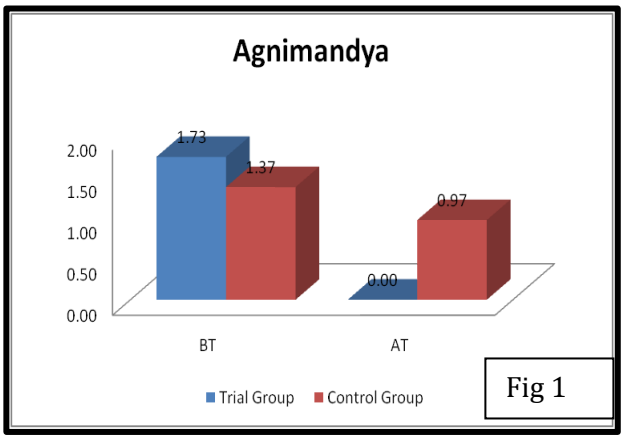

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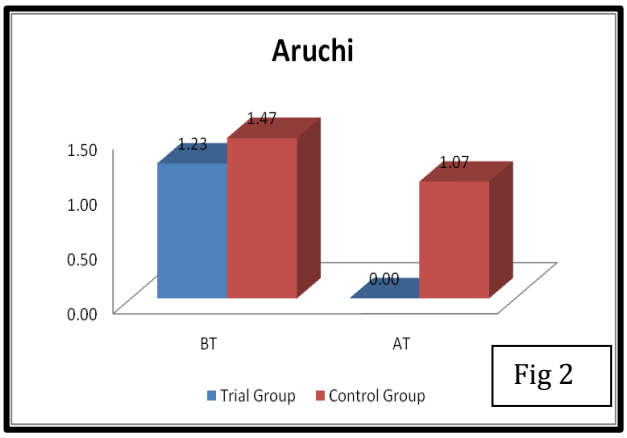

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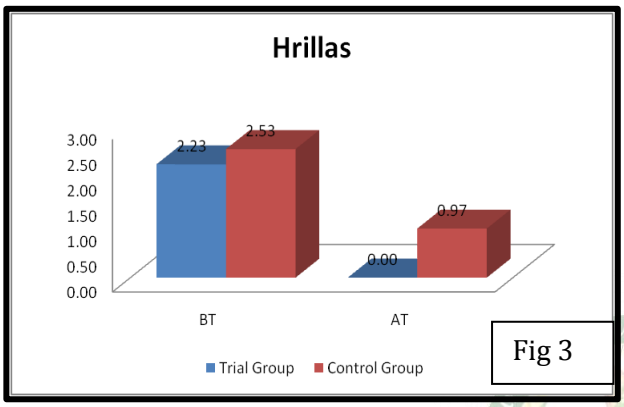

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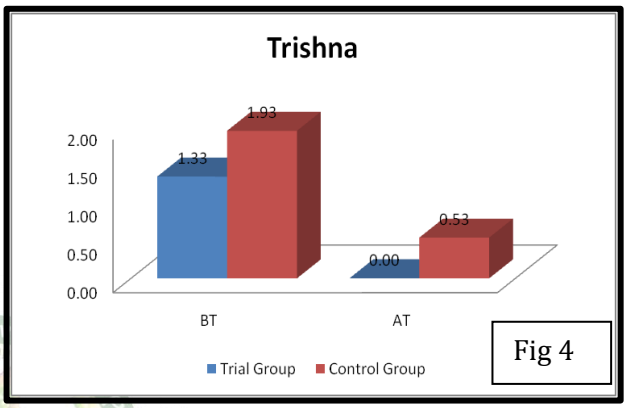

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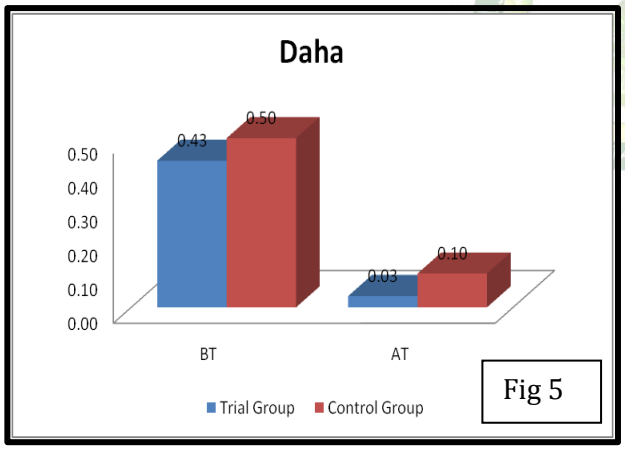

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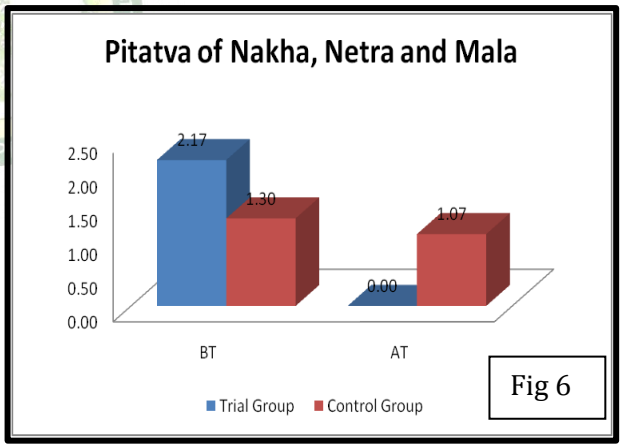

Fig 6

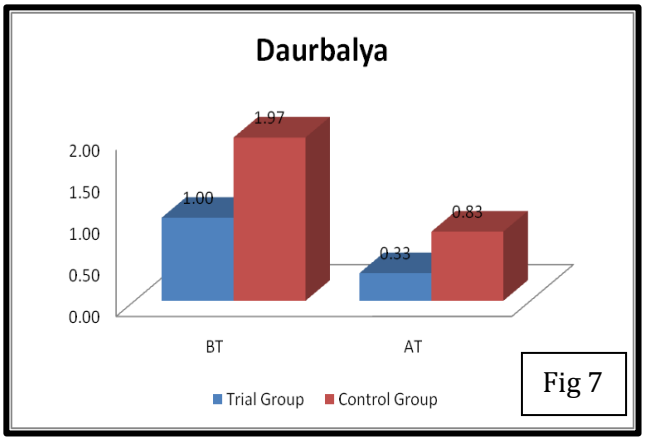

Fig 7

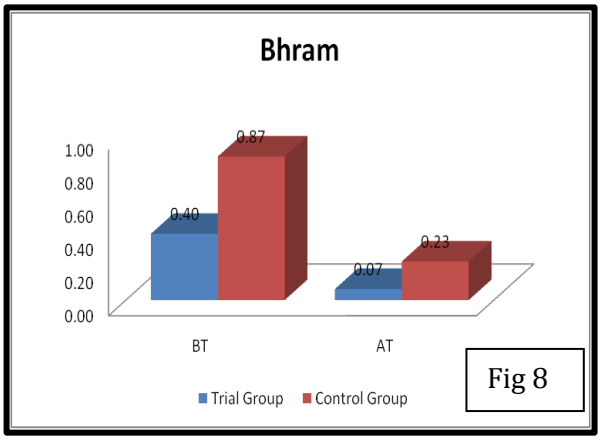

Fig 8