Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 15 (3), 2024; 689-697

Evaluation of Comparative Efficacy of *Kutaki (Picrorhiza kurroa* Royle ex. Benth) versus Atorvastatin in the Management of Dyslipidemia - A Randomised Controlled Trial

Research Article

Sadhana Misar Wajpeyi[1*], Vaishali Kuchewar[2], Ketki Wajpeyi[3]

1. HOD and Professor, 2. Dean and Professor, Department of Kayachikitsa,
Mahatma Gandhi Ayurved College Hospital and Research Centre, Salod (H), Wardha,
3. Fellowship in Oncopathology (Scholar), Senior Resident,
Department of Pathology, Jawaharlal Nehru Medical College, Sawangi (M),
Datta Meghe Institute of Higher Education and Research (Deemed To Be University), Sawangi (M), Wardha, (M.S.). India.

Abstract

Introduction: Dyslipidemia is a lipoprotein metabolism condition marked by elevated blood levels of triglycerides, total cholesterol, and low-density lipoprotein (LDL) cholesterol as well as decreased levels of high-density lipoprotein (HDL) cholesterol. It can be correlated with (*Medoroga) Medodushti* Aim and objectives: To evaluate comparative effectiveness of *Kutaki* (*Picrorhiza kurroa Royle ex. Benth*) and Atorvastatin in the management of Dyslipidemia. Methodology: Total 160 patients were randomly divided into two equal groups. Patients in Study Group A were treated with *Kutaki Vati* and patients in Control Group B were treated with Atorvastatin for 60 days. Data was collected by assessment of Objective parameters like body weight, BMI, lipid levels (TCH-Total serum cholesterol , HDL-High-density lipoproteins, LDL-Low-density lipoproteins, TG- Serum Triglycerides, VLDL-Serum Very Low-density lipoproteins, AST, ALT, S.Urea, S.Creatinine, Fasting blood sugar on the day 0, 30 and 60. The analysis was done with the help of inferential and descriptive statistics. Observation and Result-*Kutaki* and Atorvastatin both showed significant improvement in lipid levels but *Kutaki* showed reduction in body weight and BMI with correction in deranged Agni and bowel habit(constipation) which was not seen in Atorvastatin group. *Kutaki* showed no rise in AST, ALT, S Creatinin and S.urea indicating its hepatoprotective and nephroprotective properties. Conclusion-Both groups are equally effective in the management of Dyslipidemia (Medoroga).But *Kutaki* is effective in reducing bodyweight and BMI and safe as it showed no rise in AST, ALT, S Creatinin and S.urea.

Keywords: Atorvastatin*, Dyslipidemia,* Hypolipidemic*, Kutaki, Picrorhiza kurroa* Royle ex. Benth.

Introduction

Among lifestyle related conditions, dyslipidemia is a disorders of lipoprotein metabolism that is characterised by elevated blood levels of triglycerides, total cholesterol, and low-density lipoprotein (LDL) and HDL cholesterol, as well as decreased blood levels of High density lipoproteins (1). The primary causes of dyslipidemia nowadays are sedentary lifestyles and unhealthy eating habits. It is an important contributor to risk for coronary artery disease, cerebrovascular disease and atherosclerosis for every 1% increase in cholesterol, the chance of developing coronary heart disease increases by 1% to 2% (2). The prevalence of Hypercholesterolemia is relatively high over the world. According to recent estimates, over 28.5 million adults (aged 20 and more) had high levels of total serum cholesterol, with a reported prevalence of 11.9 percent (3).

In Modern Medicine, the first approach to hypercholesterolemia is lifestyle changes. Lipid-lowering drug therapy is used in patients who have failed to adequately respond to dietary therapy or have a cardiovascular risk. Pharmacological therapy used in Dyslipidemia mainly consists of HMG-CoA reductase inhibitor (statins), Fibrates, Nicotinic acid, or Niacin, Bile acid sequestrates, Cholesterol absorption inhibitor and Omega 3 fatty acids.

There is no mention of Dyslipidemia in Ayurvedic literature, however it may be associated to *Medodushti* and classified as "*Medoroga*" under *Santarpanjanya Vyadhi*. All of the body's metabolic functions are regulated by Agni. The right functioning of *Agni* is the only factor that determines the equilibrium of any *Dosha, Dhatu,* or *Mala*. Depending on the form of Agni involved, Agni vitiation can have different negative effects on health at different levels.

*** Corresponding Author:**

Sadhana Misar Wajpeyi

HOD and Professor, Department of Kayachikitsa, Mahatma Gandhi Ayurved College Hospital and Research Centre, Salod (H), Wardha, DMIHER (Deemed To Be University) Sawangi (M), Wardha, 442001, (M.S.)

Email Id: sadhanamisar@gmail.com

Reduced *Agni* is the primary cause of all ailments since it causes "*Ama*" (partly or not digested food) production. *ApachitaMedaDhatu* created in excess when *Agni* of *Medodhatu* is reduced, preventing the subsequent production of *Dhatu*. The body accumulates this extra *Meda Dhatu*, which results in *Medoroga* (4).

In Ayurvedic medicine, treating dyslipidemia includes strategies for digesting *Ama* and correcting Agni, which regulates the primary contributing elements. *Samprapti* is broken by drugs with *Deepan, Pachan, Lekhan,* and *Srotoshodhak* qualities (5). Ayurveda describes a number of single herbs and combinations of plants with these qualities that can be used to treat dyslipidemia.

Acharya Charak described *Lekhaniya Mahakashaya* that is a drug having scraping action which helps in reducing excessive *Kapha* and *Meda*. *Kutaki (Picrorhiza kurroa* Royle ex. Benth) is one amongst *Lekhaniya Mahakashaya* (5). In *Samhita*, *Kutaki* is described as having *Katu, Tikta Rasa, Ushna Virya, KatuVipaka, Agnideepan, Pachan* and *Lekhan* properties and it is mainly used in all types of *Yakrutvikar, Kamala* and *Raktavikar*.

Several studies on animals have demonstrated the hypolipidemic, hepatoprotective and liver-regenerative qualities of *Kutaki* (6). It has choleretic, cholegauge, anticholestatics stimulating and strengthening effects on the liver. Research studies were conducted on Dyslipidemia on formulations having *Kutaki* as one of the ingredients but to date, no study conducted on a single *Kutaki*.

Although risk of (ASCVD) atherosclerotic cardiovascular disease is reduce by statins by 15 to 37 percent, the risk of ASCVD remains between 60% and 80% (7,8).Myositis, arthralgia's, gastrointestinal distress, and increased liver biomarkers are all common adverse effects of statin. It also increases insulin resistance and insulin secretion thus the risk of causing Diabetes mellitus (9). Therefore, those with hepatic and renal diseases cannot receive it. Therefore, this study was carried out to assess effectiveness of *Kutaki* in comparison with Atorvastatin in the treatment of Dyslipidemia.

This study was conducted with the aim to assess comparative effectiveness of *Kutaki* (*Picrorhiza kurroa*) and Atorvastatin in treating Dyslipidemia. The Primary objectives were **t**o study and compare the effect of *Kutaki* and Atorvastatin on bodyweight, body mass index (BMI), Serum Total Cholesterol (TC), HDL-High-Density Lipoprotein, LDL -Low-Density Lipoprotein, (TG) Triglycerides and (VLDL) Very Low-Density Lipoproteins. Secondary objectives were to evaluate and compare AST levels, ALT levels, Serum Creatinine, Serum urea levels and *Agni* and bowel habit (Constipation) of in each group.

Material and Methods

a) Type or Nature of study- Single-blind (assessor blind) Randomised controlled study.

b) Commensurate Sample Size

Formula-Following formula for equivalence clinical design, for continuous variable(numerical) (F4) is used.

$$n = 2 \times \left[\frac{Z_{1-\alpha} + Z_{1-\beta}}{\triangle} \right]^2 \times S^2$$

Where $Z_{1-\alpha}$ is the standard normal deviation for one or two -sided = 1.96

$Z_{1-\beta}$ is the power of the test = 80%=0.84

$\triangle$ = Real difference between the two treatment groups which is clinically acceptable

Margin =20%= 0.20

S is the pooled standard deviation of both comparison groups= 0.41 (Calculated by pilot study)

$$n = 2 \times \left[1.96 + 0.84/0.20^2 \right] \times 0.41^2$$

n=69.14 =70 patients in each group

Assuming dropout rate of 10% that is 7

Total sample size is = 70 + 7 = 77

=80 patients needed in each group

Drug preparation

The dry raw rhizomes of *Kutaki* (*Picrorhiza kurroa* Royle ex. Benth) were purchased from Authenticated shop. After procurement of raw drug, the drug sample was authenticated and was certified. *Kutaki Vati* was made by following standard procedure mentioned by Acharya Sharangadhar (10) at Dattatraya Ayurveda Rasashala, Department of Rasashastra and Bhaishajya Kalpana, Mahatma Gandhi Ayurveda College Hospital & Research Centre Salod (H) Wardha, Maharashtra. The analytical study of *Kutaki vati* was carried out in GMP certified Dattatreya Rasashala of our Institute. *Kutaki Vati* contains powder of rhizomes of *Kutaki* drug as per Standard Operating Procedure mentioned in Sharangdhar Samhita Madhyam Khanda. **A)** Tablet Atorvastatin (10mg) were procured from Macleods Pharmaceuticals Pvt Ltd.

B) Methods

Total patients- 160

All subjects were divided in 2 groups equally

- **Group A (Study group) (n=80)**-*Kutaki* Vati
- **Group B (Control group) (n=80)**-Tablet Atorvastatin

Patient consent: Written informed consent was taken from all patients before enrolment in the study.

Diagnosis

Patients were diagnosed as per "(NCEP: ATPIII, 2001) -National Cholesterol Education Program and Adult Treatment Panel III" for recruitment in of subjects.

Blood samples collected from each individual following 12 to 14 hours fasting. Fasting glucose, lipidprofile and AST, ALT, S.Creatinine and S.Urea were estimated using Clinical Chemistry Analyser, RX Daytona,and FURUNO ELECTRIC CO.LTD.JAPAN with REDOX TCH, TG and HDL KIT. LDL and VLDL were calculated by The Friedewald 13 formula (11). The Friedewald formula LDL: TC-HDL-TG/5mg/dl, was used to calculate LDL-C and VLDLC was measured using equation: VLDL-C = TG/5.

Randomisation

Patients were allocated equally in two groups through computer generated randomised table method.

Source of data

The study was conducted at *Kayachikitsa* department of MGACH & RC, Salod (H), Wardha. Subjects fulfilling the inclusion criteria were enrolled for the study. Total 168 patients were screened, out of which 3 patients from Study group A and 5 patients from Control Group B were dropped out due to failed to follow up.

Table 1: Intervention in both Groups

Groups	No of patients	Age	Inter-vention	Dose	Dura-tion	Assess-ment
Study Group A	80	30-60 years	*Kutaki Tablet* 500mg with water	Twice a day before meal	60 days	On day 0, 30 and 60
Control Group B	80	30-60 years	Tablet Atorvastatin 10mg with water	Once at bed time		

Dietary Modification

All patients were advised not to consume excessive oily, fried food,

ghee, cheese, milk and milk products, sweets, and bakery products during treatment period. For which patients were provided diet chart and adherence was monitored during their follow up.

Assessment criteria

After completion of treatment shown in Table 17, assessmentwas done on the Variable mentioned below by the other person on day 0, 30 and 60.

Objective Criteria-

- Body weight in Kg
- BMI-Calculated by formula –Weight in kg/ (height in meter)^2

Lipid profile-

- Serum Total cholesterol
- Serum Triglycerides
- Serum Low Density Lipoproteins
- Serum High DensityLipoproteins
- Serum Glutamic Oxaloacetic Transaminase (**SGOT) or** Aspartate
- Aminotransferase **(AST)**
- Serum Glutamic Pyruvic Transaminase **(SGPT) or** Alanine Aminotransferase (**ALT**)
- Serum Creatinine
- Serum urea
- Fasting BGL(Blood Glucose Level)

Subjective Criteria

Agni

Agni was assessed and categorized *into Samagni, Mandagni, Vishmagni* and *Tikshnagni* by using standardized and validate questionnaire. The *Agnibala* was assessed by using *Agnibala* assessment tool which include validated questionnaires like ability to digest food, time of need to feel hungry, frequency of taking meal, Ability to bear hunger, capacity to digest heavy meal, bowel habit and eating habits. The design of these "self-assessment questionnaires" to record *Agni* strength is mostly based on the Charaka Samhita in Vimanasthana (chapter 6, verse 12) and its description of Agnibala (strength). There are four *Jatharagni* states mentioned in this verse: *Vishamagni, Tikshnagni, Mandagni,* and *Samagni*. Based on this method of classification, more Agni characteristics were gathered from other Ayurvedic books, and a main set of questionnaires was developed to evaluate each *Agnibala* aspect. The participants in this tool entered their responses in the relevant columns. The instructions on how to reply were laid out in detail. After calculating the total scores in the appropriate columns, the scores were transformed into percentages for additional statistical analysis. An individual's *Agni* status was determined on the basis of maximum percentage scores obtained under the different categories of *Agni* (12).

Bowel habit

Constipation was assessed by Rome III diagnostic criteria for functional constipation. According to Rome III diagnostic criteria for functional constipation, symptoms characteristics were based on abnormal stool type and stool frequency, presence of straining, sensation of incomplete evacuation, anorectal obstruction or blockage and manual manoeuvres with occurring at least 25% of defecations. The Rome III constipation diagnostic questionnaire response options were on a nominal scale of yes or no; whereas responses on an ordinal scale of never or rarely, sometimes, often, most of the time and always for individual frequency thresholds of each question were used to determine the prevalence of symptoms characteristics for functional constipation. The definition of FC requires symptoms to be present at least 25% of defecations. Furthermore, Bristol Stool Chart which is also called Bristol Stool Form (BSF) Scale was used to characterise human stools to seven classifications (13).

Inclusion and Exclusion criteria

Inclusion Criteria

Patients willing to give informed written consent, between the age group of 30-60 years of eithersex diagnosed with Dyslipidemia as per "National Cholesterol Education Program and Adult Treatment Panel III (NCEP:ATPIII, 2001)"(14) as follows- TCH equal to or greater than 200 mg/dLand/or LDL-C between 130 - 189 mg/dL and/or Sr.TG between 150 - 499 mg/Dl and/or Sr. HDL-C below 40mg/dL with Patients of controlled hypertension and diabetes mellitus type 2 having Dyslipidemia.

Exclusion criteria

Subjects having MI (myocardial infarction), Angina, Stroke, TIA (transient ischemic attack), major cardiovascular surgeries in 6 months earlier screening. Subjects diagnosed with systemic disorders such as

malignancies, tuberculosis, diseases of Endocrine, renal or hepatic diseases. Dyslipidemia caused due to drugs and pregnant and lactating female.

Approval by Institutional Ethical Committee

The research protocol was submitted to the secretary Institutional Ethical Committee, Datta Meghe Institute of Medical Sciences, (DU) Nagpur for approval. It was approved on 11-07-2018.

- **Ethics Committee Approval:** IEC /IAEC Certificate: DMIMS (DU)/IEC/2018-19/7329
- **Registration in Clinical trial registry of India (CTRI)** Number: CTRI/2018/10/015939
- **Declaration regarding Conflict of Interest:** There is no conflict of interest in this study.

Observations and Results

Data collected was recorded on specially designed proforma and data was analyzed by using the software SPSS 27.0 Version and $p<0.05$ is considered as "level of significance". The statistical tests used for the analysis of the result were: Chi square, Z test, Student's paired t test and Repeated measures of ANOVA.

Total 172 that are in group A 85 and in group B 87 patients were registered but 5 patients from group A and 7 patients from group B were dropout.

Demographic Data-

Table 2: Age wise distribution of patients

Age Group (In Years)	No of patients (N=160)	%
30 -40 Years	49	30.62%
41-50 Years	40	25%
51-60 Years	71	44.37%
Total	160	100%
Statistics of age of the patients in both groups		
Age	Mean & SD	Min /Max
Study Group A	46 ±11	30/60
Control Group B	50±9	30/60

Table 3: Gender wise distribution of patients

Gender	Study Gr A	%	Control Gr B	%	Total	P value
Female	39	48.75%	40	50.00%	79(49%)	Chisq = 0.4472, NS, p= 0.5036
Male	41	51.25%	40	50.00%	81(51%)	

Table 4: Distribution of patients as per dietary habits

Dietary Habits	Study Gr A	%	Control Gr B	%	Total	P value
Type of Diet						
Mixed	39	48.75%		54	67.50%	Chisq = 5.7776, S, p= 0.01
Vegetarian	41	51.25%		26	32.50%	

Table 5: Distribution of patients as per daytime sleep

Daytime sleep	Study Gr A	%	Control Gr B	%	P value
Absent	29	35.00%	25	31.25%	Chisq = 0.4472, NS, p= 0.5036
Present	51	65.00%	55	68.75%	

Table 6: Distribution of patients as per Psychological stress

Psychological stress	Study Gr A	%	Control Gr B	%	P value
Present	74	92.50%	73	91.25%	Chisq =5.1805, NS, p= 0.159
Absent	6	7.50%	7	8.75%	

Table 7: Distribution of patients as per Daily physical exercise (average 30 mins)

Daily physical exercise	Study Gr A	%	Control Gr B	%	P value
Yes	26	32.50%	23	28.75%	Chisq = 3.0858, NS, p= 0.3786
No	54	67.5%	57	71.25%	

Table 8: Distribution of patients as per Addiction

Addiction	Study Gr A	%	Control Gr B	%	P value
Alcohol	13	16.25%	15	22.50%	Chisq =5.1805, NS, p= 0.159
Tobacco Chewing	12	15%	14	17.50%	
Nil	55	68.75%	49	61.25%	

Table 9: Distribution of patients as per Prakriti (body constitution)

Prakruti	(Study) Gr A	%	(Study) Gr B	%	p-Value
Kaphavataja	30	37.50%	37	46%	Chisq = 1.2603, NS, p= 0.5325
Pittakaphaja	30	37.50%	26	32.50%	
Vatapittaja	20	25.00%	17	21.25%	

Table 10: Effect of therapy on *Agni* in both groups

Agni	0th day		30th day		60th day	
	Gr A (n=80)	Gr B(n=80)	Gr A (n=80)	Gr B(n=80)	Gr A (n=80)	Gr B (n=80)
Samagni	28 (35.00%)	38 (47.50%)	50 (62.50%)	38 (47.50%)	79 (98.75%)	42 (52.50%)
Mandagni	31 (38.75%	26 (32.50%	17 (21.25%	26 (32.50%)	1 (1.25%)	23 (28.50%)
Vishamagni	9 (11.25%)	7 (8.75%)	6 (7.50%)	7 (8.75%)	00 (00%)	6 (7.50%)
Tikshnagni	12 (15.00%)	9 (11.25%)	7 (8.75%)	9 (11.25%)	0 (00%)	9 (11.25%)
p	Chisq = 2.355, NS, p= 0.308		Chisq = 3.847, NS, p= 0.2785		Chisq = 49.8361, S, p= <0.001	

Gr A - Group A (Study Group) and Gr B - Group B (Control Group)

Table 11: Comparing Effect of therapy on *Mandagni* in both groups

Group	0th Day	30th Day	60th Day
Group A(n=80)	31(38.75%)	17(21.25%)	1 (1.25%)
Group B(n=80)	26(32.50%)	26(32.50%)	23 (28.75%)

Group A-Study Group and Group B- Control Group

Table 12: Comparing Effect of therapy on bowel habit (constipation) in both groups

Bowel Habits Constipation	0th Day		30th Day		60th Day	
	Gr A (n=80)	Gr B (n=80)	Gr A (n=80)	Gr B (n=80)	Gr A (n=80)	Gr B (n=80)
Present	22 (27.50%)	28 (35.00%)	18 (22.50%)	28 (35.00%)	0 (00%)	26 (32.50%)
Absent	58 (72.50%)	52 (65.00%)	62 (77.50%)	52 (65.00%)	80 (100%)	54 (67.50%)
p	Chisq = 1.0473, NS, p= 0.3061		Chisq = 3.0511, NS, p= 0.0807		Chisq = 31.0448, S, p= <0.001	

Group A-Study Group and Group B- Control Group

Table 13: Comparing Effect of therapy on Body weight in both groups

Weight Kg	Gr A(n=80) (Study group)		GrB (n=80) (Control Group)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	67.01	11.19	67.25	10.82	-0.1364	0.8916, NS
Day 30	65.18	10.67	67.05	10.87	-0.8880	0.3759, NS
Day 60	64.39	10.26	67.64	15.18	-1.4400	0.1518, NS
F Test	F=137.09		F=0.07745		**Mean Difference**	**p-Value**
P	P=< 0.0001 (S)		P=0.9255 (NS)		**2.38±0.27**	**t=8.8569, S, p<0.0001**

Table 14: Comparing Effect of therapy on BMI in both groups on Day 0, 30 & 60

BMI Kg/m²	Gr A(n=80) (Study group)		GrB (n=80) (Control Group)		Z Test	p-Value
	Mean	S D	Mean	S D		
Day 0	26.12	3.84	26.88	3.66	-0.9248	0.3565, NS
Day 30	25.56	3.62	26.83	3.68	-1.8678	0.0636, NS
Day 60	25.12	3.43	26.85	3.68	-2.7824	0.0061, S
F Test	F=125.71		F=0.6777		**Mean Difference**	**p-Value**
p	P=<0.001 (S)		P=0.5092 (NS)		**1.01±0.25**	**t=10.5791, S, p<0.0001**

Table 15: Comparing Effect of therapy on Fasting BSL in both groups

BSL (mg/dl)	Gr A(n=80) (Study group)		GrB (n=80) (Control Group)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	102.86	10.96	101.34	9.92	0.9226	0.3538, NS
Day 30	98.49	8.72	98.33	11.54	0.10048	0.5982, NS
Day 60	96.44	10.45	99.94	7.78	-2.4722	0.0177, S
F Test	F=0.8689		F=1.868		Mean Difference	p-Value
p	p=0.0002 (S)		p=0.1568 (NS)		5.0±2.98	t=3.5326, S, p<0.0005

Table 16: Comparing Effect of therapy on TCH in both groups

TCH (mg/dl)	Gr A(n=80) (Study		GrB (n=80) (Control Group)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	238.16	24.6	236.03	28.55	1.26672	0.7382, NS
Day 30	213.85	22.48	210.6	21	1.4945	0.4498, NS
Day 60	195.14	19.32	191.56	15.16	1.1919	0.2996, NS
F Test	F=75.288		F75.264		Mean Difference	p-Value
p	p=0.0001 (S)		p=0.0001 (S)		1.46±3.60	t=0.5058, NS, p=0.6136

Table 17: Comparing Effect of therapy on HDL in both groups

HDL (mg/dl)	Gr A(n=80) (Study group)		GrB (n=80) (Control Group)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	39.53	8.52	37.28	0.41	1.782	0.0894, NS
Day 30	41.04	6.86	38.66	6.56	2.2371	0.0542, NS
Day 60	42.35	6.7	39.81	6.72	2.3907	0.0537, NS
F Test	F=2.914		F=2.706		Mean Difference	p-Value
p	p=0.05 (S)		p=0.06 (S)		0.26±0.85	t=0.5020, NS, p=0.6163

Table 18: Comparing Effect of therapy on LDL in both groups

LDL mg/dl	(Study) Gr A (n=80)		(Control) Gr B(n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	160.39	23.03	162.69	30.85	0.4123	0.5445, NS
Day 30	139.25	20.75	138.85	23.4	0.1485	0.8569, NS
Day 60	122.86	17.86	120.83	16.04	0.1459	0.8161, NS
F Test	F=69.037		F=55.527		Mean Difference	p-Value
p	p=0.0001 (S)		p=0.0001 (S)		2.53±2.05	t=-0.8803, NS,

Table 19: Comparing Effect of therapy on TG in both groups

TG mg/dl	(Study) Gr A (n=80)		(Control) GrB (n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	191.71	35.99	186.44	37.73	-0.076	0.3669, NS
Day 30	171.61	35.58	165.54	32.70	-0.0173	0.2785, NS
Day 60	156.18	35.71	149.71	28.62	-0.0688	0.2084. NS
F Test	F=10.062		F=13.771		Mean	p-Value
p	p=0.0001 (S)		p=0.0001 (S)		1.18±0.66	t=-0.3352, NS,

Table 20: Comparison of Effect of therapy on VLDLin both groups on Day 0, 30 & 60

VLDL mg/dl	(Study) Gr A (n=80)		(Control)GrB (n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	38.10	7.14	37.10	7.80	-0.0314	0.3989, NS
Day 30	34.09	7.15	32.94	6.52	-0.0473	0.2894, NS
Day 60	30.60	6.66	29.53	5.81	-0.0183	0.2786, NS
F Test	F= 10.165		F=13.894		Mean Difference	p-Value
p	p=0.0001, (S)		p=0.0001, (S)		0.075±0.81	t=-0.1016,

Graph 1: Overall Effect and comparison of therapy in both groups on TCH, HDL, LDL, TG, VLDL

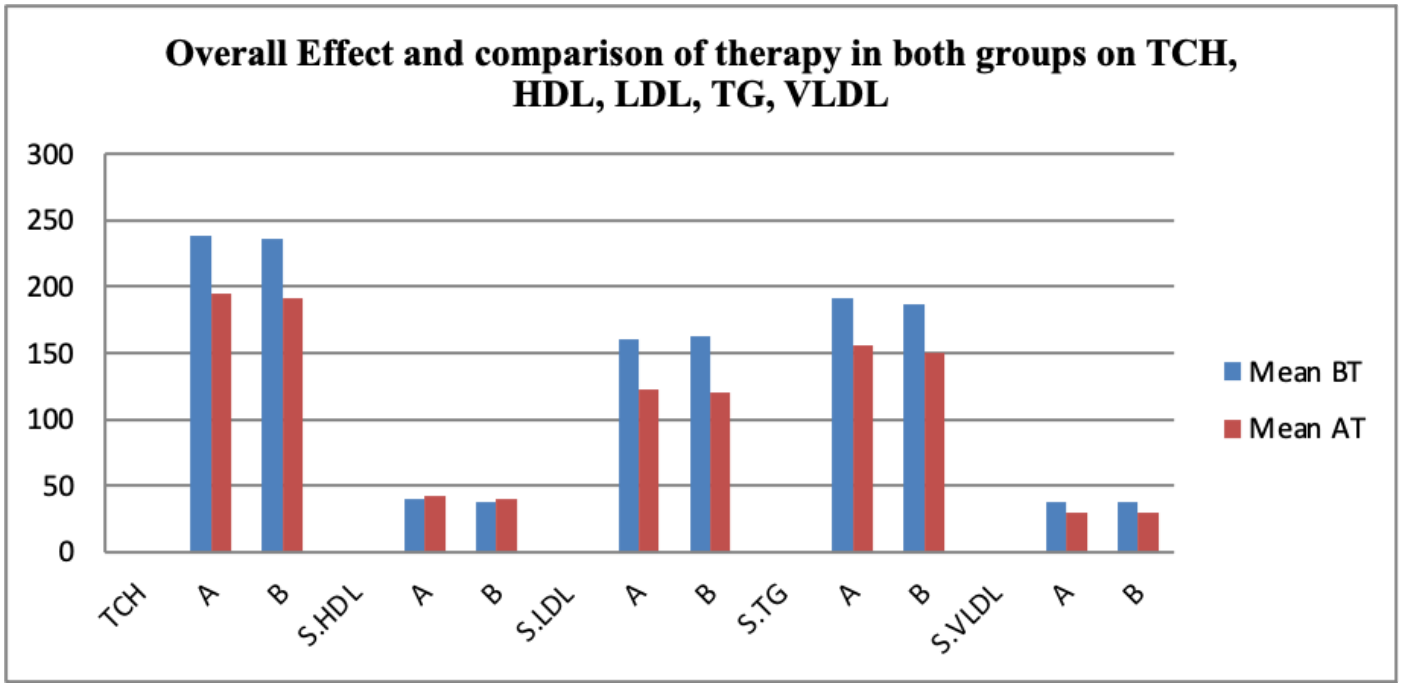

Table 21: Comparing Effect of therapy on AST in both groups

AST mg/dl	(Study) Gr A (n=80)		(Control) GrB (n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	28.08	7.26	26.60	8.12	0.8403	0.2277, NS
Day 30	25.68	5.43	26.75	7.56	-1.1874	0.3031, NS
Day 60	23.71	5.82	28.65	8.75	-3.64839	0.0001, S
F Test	F= 23.24		F=13.39		Mean	p-Value
p	p=0.0001, (S)		p=0.0001, (S)		6.41±0.75	t=7.9073, S,

Table 22: Comparing Effect of therapy on ALT in both groups

ALT mg/dl	(Study) Gr A (n=80)		(Control) GrB (n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	28.04	9.41	24.56	8.5	1.9208	0.0153, S
Day 30	25.15	8.86	25.43	7.48	-0.383	0.7855, NS
Day 60	23.74	6.17	27.11	7.79	-2.739	0.0032, S
F Test	F= 14.04		F=13.65		Mean	p-Value
p	p=0.0001, (S)		p=0.00001, (S)		6.85±2.14	t=6.1351, S,

Table 23: Comparing Effect of therapy on S.Cr. in both groups

S.Cr mg/dl	(Study) Gr A (n=80)		(Control) GrB(n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	0.93	0.26	0.86	0.22	0.1855	0.1113, NS
Day 30	0.89	0.15	0.84	0.13	2.3855	0.0190, S
Day 60	0.77	0.13	0.89	0.23	-3.9435	0.0001, S
F Test	F=31.3449		F=2.76502		Mean Difference	p-Value
p	p=0.0001, (S)		p=0.6602, (NS)		0.17±0.009	t=4.8686, S,

Table 24: Comparing Effect of therapy on S.Ureain both groups

S.Urea mg/dl	(Study) Gr A (n=80)		(Control)GrB (n=80)		Z' Test	p-Value
	Mean	S D	Mean	S D		
Day 0	25.98	7.14	25.34	6.43	1.6014	0.1112, NS
Day 30	24.33	6.42	25.29	5.41	-2.3707	0.0189, S
Day 60	23.25	6.24	26.33	5.93	-4.0403	0.0015, S
F Test	F=17.57		F=3.049		Mean Difference	p-Value
P	p=0.0001, (S)		p=0.0520, (NS)		3.71±0.19	t=-4.1569, S,

Discussion

In this study patients between 30 to 60 years of age group were included. The study showed that the majority of patients 44.37% were in the age group 51-60 years followed by the age group 30-40 years (30.62%) with incidences of disease were observed almost the same in males and females. In this study, the majority of patients 67.50% were having mixed type of dietary habit and a history of daytime sleep was present in the majority of patients (68.75%). In this study the majority of patients 91.25% had mild to moderate psychological stress and most of the patients had *Kaphavataja (*46%) and *Pittakaphajaprakriti* (32.50%). *Prakriti* was assessed as per dominance of *Doshas* by using validated questionnaire (15)**.** Thus it can be stated that the occurrence of the disease is more in *Kapha* dominant *prakriti*. In this study, it was found that the majority of the patients had no addiction and the remaining had habits of alcohol consumption, smoking and tobacco chewing, majority of patients were not doing daily physical exercise for average of 30 mins and only 30.63% of patients do regular exercise for average 30 minutes.

Comparison of both the groups regarding demographic data this study showed not significant that is both groups have normal distribution of patients in both the groups at baseline except type of food. In Control group percentage of patients having mixed type of dietary habit was more as compared to Study group A.

Probable mode of action of *Kutaki*

Medoroga (Dyslipidemia) is a disease of *Apachita* or *Sama Asthayi Meda Dhatu Vriddhi* caused by diminished *Jatharagni, Dhatwagni* and *Bhutagni*. All the three *Agni* are diminished in *Medoroga*. So for its management drugs with *Deepan, Pachan, Kaphaghna* and *Medoghna* properties are used.

Kutaki has *Katu, Tikta rasa, Laghu Ruksha guna, Ushnavirya* and *Katuvipaka*. *Kutaki* has *Deepan (*restoration of *Agni),and Pachan* (digestive) properties help in correcting deranged *Agni,* the main pathological factor of *Medoroga, Strotoshodhana* (removing obstruction) property helps in removing obstruction caused by *Ama. Kaphamedahar* (pacifies *Kapha* and *Meda)* properties reduces accumulated *Kapha* and *Meda Dhatu. Lekhan* (Scraping action) property causes scraping and helps in reducing adherent *Meda*. It has *Yakrututtejaka* (Liver stimulating) and *Pittarechaka* (Choleretic) actions enhance the excretion of bile and excess Pitta. *Yakrututtejaka* (Liver stimulating) property improves fat metabolism which play major role in *Medoroga* (16). *Katuki* possesses cholagogue (*Pittavirechaka*), cholerectic (*Pittastravi*) and anticholestatic action. Choleretic (Pittastravi) action stimulates bile production and cholagogues action (*Pittavirechaka*) promotes excretion by the flow of bile from the gall bladder into the intestines. Bile salts are required for fat and lipid absorption from the intestine; therefore, bile excretion in the feces causes a decrease in fat and lipid absorption from the gut, resulting in a fall in serum lipid content (17). The root extract of Picrorhiza kurroa, known as PICROLIV, is useful as a laxative, liver-stimulant, improving lactation, appetite stimulant, febrifuge and also has antiinflammatory action, antidiabetic and immunoregulatory functions. It reduces serum lipids (total, VLDL and LDL cholesterol). Picroliv decreased cholesterol biosynthesis in the liver while increasing bile acid excretion. Picroliv has been proven to protect against isoproterenol-induced ischemia as well as coronary artery ligation-induced ischemia (18-19).

Randomised Controlled Study conducted on a Herbal Preparation, Lekhaneeya Mahakashaya Ghanavati in Dyslipidemia, *Kutaki* is one of the ingredients of it stated that these lekhaniya drugs decreases cholesterol uptake in the intestines and thus inhibits cholesterol synthesis by hepatocytes by increasing the catabolic conversion of cholesterol to bile acids in the liver. It also limits cholesterol absorption, interfere with its entero-hepatic circulation, and enhance fecal bile acid excretion, resulting in lower cholesterol levels. Essential fatty acids are found in *Lekhaniya* medicines (polyunsaturated fatty acids). ~~Linolenic acid, for example.~~ Intake of a-linolenic acid-rich diet changes the fatty acid content of plasma lipoproteins and reduces their ability to transport lipids, particularly cholesterol, resulting in reduced levels of cholesterol in the blood. *Kutaki* has a hypolipidemic effect, and the most likely mechanism of action is through the excretion of bile in the feces, which reduces the absorption of all sorts of nutrients, including fats and lipids, in the intestine. Thus by hypolipidemic property, it helps in correcting lipid levels in the blood (20).

The correction of deranged *Agni* and scraping action helps in removing excess *MedaDhatu* causing a reduction in body weight and BMI. Antiobesity and scraping action of Bitter glycosides present in *Kutaki* reduces excess fat, and decreases the cell mass and cell size. *Kutaki* has hepatoprotective, nephroprotective and nephrocurative action. It has a stimulating action on the liver and it relieves inflammation due to its *Deepan* (corrects metabolism) and *Amapachan* (removes toxins from the liver) action. Pharmacologically *Kutkin* (Picrosides and kutkosides), the active constituent of *Kutaki*, has hepatoprotective activity. *Katuki* extract has been reported to reverse the increased AST and ALT activities towards near normalcy which suggests prevention of cellular and tissue damages. It acts probably by scavenging the free radicals and inhibiting of generation of oxygen species and due to antioxidant property causes detoxification acts as hepatoprotective and nephroprotective.It was also observed that *Kutaki* helps in reducing AST, ALT, S.Creatinine and S.Urea levels by its hepatoprotective and nephroprotective properties (21). Hence it can be given in Dyslipidemic patients having hepatic and renal disorders. Also in advanced age, there are more chances of adverse effects of Modern medicines in such conditions *Kutaki* may be effective. There were no adverse effects like loose stool, or abdominal pain noted during the study.

From the results obtained it can be concluded that both *Kutaki Vati* (500mg BD) and Atorvastatin (10mg OD) are equally efficacious in improving lipid parameters like Serum Total Cholesterol, HDL, LDL, TG and VLDL in Dyslipidemia (*Medoroga*). It was observed that improvement of *Agni*, bowel habits (constipation), and reduction in body weight and BMI was observed in Study group A treated with *Kutaki* but such improvement was not observed in Control group B. The values of parameters like AST, ALT, S Creatinine and S.urea were not found elevated in group A however they were elevated in group B but were within normal limits after completion of treatment. No adverse effect was noted in both groups during the study.

Conclusion

The Drug *Kutaki* was found to be effective in reducing body weight as well as BMI.It was also found effective in correcting deranged *Agni* like *Mandagni, Vishmagni* and *Tikshnagni*. It was found effective in improving bowel habits -Constipation of patients. *Kutaki* when compared with Atorvastatin it was found to be effective in reducing AST, ALT, S.Creatinine, and S Urea due to its hepatoprotective and Nephroprotective properties which was not observed in with Atorvastatin. In the Atorvastatin group elevation of these biomarkers was observed but the values were within normal levels.

Acknowledgement

I am very much thankful to our institute for providing conducive environment and essential facilities to conduct this research work.

Funding: No funding

Conflict of Interest: No conflict of Interest.

References

1. API Textbook of Medicine, 10th Edition, Jaypee Brothers Medical publishers, Published 2015 ; pp: 2872;pg.1690
2. Davis CE, Rifkind BM, Brenner H, et al. A single cholesterol measurement underestimates the risk of coronary heart disease. An empirical example from the lipid research clinics mortality follow-up study.JAMA. 1990;264(23):3044– 3046. [PubMed] [CrossRef]
3. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. Circulation. 2018;137:e67–492.
4. Madhavakara, Madhava Nidana with Madhukosha commentary of Vijayarakshita and Shrikantadatta, Medoroga Nidanam, published by Varanaseya Sanskrit Samsthana; Varanasi. 1993. Pg.No28.
5. Yadavji T. Charaksamhita. Sutra Sthana 4/3,Chaukhambha Orientalia Publisher: Varanasi. 2009
6. Lee HS, Yoo CB, Ku SK, Hypolipemic effect of water extracts of Picrorhizakurroa in high fat diet treated mouse. Fitoterapia. 2006; 77(7-8): 579- 584.
7. Lim S, Park YM, Sakuma I, Koh KK. How to control residual cardiovascular risk despite statin treatment: focusing on HDL-cholesterol. Int J Cardiol. 2013; 166:8–14.
8. Ahn CH, Choi SH. New drugs for treating dyslipidemia: beyond statins. Diabetes & metabolism journal. 2015 Apr 1;39(2):87-94.
9. Harrison's principal of internal medicine, 17th edition, p. 1501.
10. Srivastav S, Sharangdharsamhita. Ed reprint 2017. Madhyankhanda, chaukhambhaorientalia, Varanasi 117 p.
11. Anwar M, Khan DA, Khan FA. Comparison of Friedewald formula and modified Friedewald formula with direct homogeneous assay for low density lipoprotein cholesterol estimation. J Coll Physicians Surg Pak. 2014 Jan 1;24(1):8-12.
12. Singh A, Singh G, Patwardhan K, Gehlot S. Development, validation, and verification of a self-assessment tool to estimate agnibala (digestive strength). Journal of Evidence-based Complementary & Alternative Medicine. 2017 Jan;22(1):134-40.
13. Lim YJ, Rosita J, Chieng JY, HaziziAS.The prevalence and symptoms characteristic of functional constipation using Rome III diagnostic criteria among tertiary education students.PloS one. 2016 Dec 20;11(12):e0167243.
14. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (AdultTreatmentPanelIII)finalreport.Circulation. 2002;106(25):3143–421. (accessed on 17.03.2018 at 012.54pm)
15. Vinotha S. A Study Of The Standard Tool For Prakritiassessment In Indigenous MedicinE, World Journal of Pharmaceutical Research, 2019, 8 (5), 574-582
16. Sharma P, Dravyaguna-Vijnana, Vegetable Drugs, ChaukhambhaBharati Academy, Varanasi, Reprint: 2006, II
17. Vasudevan DM, Sreekumari S, Vaidyanathan K. Textbook of biochemistry for medical students. JP Medical Ltd; 2013 Aug 31.
18. Khanna AK, Chander R, Kapoor NK, Dhawan BN. Hypolipedaemic activity of picroliv in albino rats. Phytotherapy Research. 1994 Nov;8(7):403-7..
19. Verma PC, Basu V, Gupta V, Saxena G, Rahman LU. Pharmacology and chemistry of a potent hepatoprotective compound Picroliv isolated from the roots and rhizomes of Picrorhiza kurroa royle ex benth. (kutki). Curr Pharm Biotechnol. 2009 Sep;10(6):641-9. doi: 10.2174/138920109789069314. Epub 2009 Sep 1. PMID: 19619118.
20. Deepak BSR, Jadhav Lakshmiprasad, Girish KJ, Narayana Prakash, Randomised Controlled, Open Labeled Study of A Herbal Preparation, Lekhaneeya Mahakashaya Ghanavati in Dyslipidemia Patients, J of Ayurveda and Hol Med (JAHM).2015;3(4):1-23.
21. Kumar A, Rajpal VR, Ambika, Devarumath RM, Kumari A, Thakur R, Chaudhary M, Singh PP, Chauhan SMS, Raina SN. Isolation and HPLC assisted quantification of two iridoid glycoside compounds and molecular DNA fingerprinting in critically endangered medicinal *Picrorhiza kurroa* Royle ex Benth: implications for conservation. Physiol Mol Biol Plants. 2021 Apr;27(4):727-746. doi: 10.1007/s12298-021-00972-w. Epub 2021 Mar 26. PMID: 33967459; PMCID: PMC8055752.

*****