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"Efficacy of Kutaki in the Management of Dyslipidemia-A Randomized Control Trial"

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ABSTRACT: *Dyslipidemia is the disorder of lipoprotein metabolism manifested by elevation of the total cholesterol, the low density lipoprotein (LDL) cholesterol and the triglyceride concentrations and a decrease in the high density lipoprotein (HDL) cholesterol concentration in the blood. In Ayurveda, direct reference of Dyslipidemia is not found but it can be correlated with Medodushti and can be included under Santarpanjanya Vyadhi as "Medoroga". Agni is responsible for all metabolic processes in the body. Decreased Agni leads to "Ama" (undigested/partially digested food) production, which is the main cause of all diseases. To study the efficacy of Kutaki in the management of Dyslipidemia and to compare the effects of Kutaki and Atorvastatin on BMI, serum lipid levels, AST, ALT, serum creatinine and serum urea. In this study,160 patients will be divided randomly into 2 groups (80 in each).In Group A (Experimental) – Kutaki vati 500 mg will be administered twice a day with water before meal for 60 days and Group B (Control) – Atorvastatin10 mg will be administered at bed time for 60 days.Assessement will be recorded on 0 and 60th day. Changes will be observed in objective outcomes. Kutaki vati will be more effective than Tab. Atorvastatin.*

Keywords *–Atorvastatin, Ama, Dyslipidemia, Medoroga, Kutaki.*

I. Background and rationale

Among the lifestyle disorders Dyslipidemia is the disorder of lipoprotein metabolism manifested by elevation of the total cholesterol, the low density lipoprotein (LDL) cholesterol and the triglyceride concentrations and a decrease in the high density lipoprotein (HDL) cholesterol concentration in the blood [1].Today's unhealthy food habits and sedentary life style are the main causative factors for Dyslipidemia. In Dyslipidemia there is increased lipids in the blood resulting either from an increased rate of synthesis or from a decreased lipoprotein breakdown rate.

Dyslipidemia is an important risk factor for atherosclerosis, coronary artery disease and cerebrovascular disease, for every 1% increase in cholesterol level there is 1-2% increase in the incidence of CHD [2]. The overall prevalence of Dyslipidemia in India in various studies ranges from 10% to 73%, depending on area of residence, socio-economic strata, diet, physical activity patterns and age[3].WHO has predicted that, by 2030, cardiovascular diseases will affect approximately 23.6 million people around the world [4].

In *Ayurveda,* direct reference of Dyslipidemia is not found but it can be correlated with *Medodushti* and can be included under *Santarpanjanya Vyadhi* as "*Medoroga".* Agni is responsible for all metabolic processes in the body. Balance of all *Dosha, Dhatu or Mala* depends solely on proper functioning of *Agni.* The vitiation of *Agni*

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has serious impact on health at various levels depending on type of *Agni* involved. When *Agni* is decreased, it leads to "*Ama*" (undigested/partially digested food) production, which is the main cause of all diseases. If *Agnimandya* is present at the level of *medodhatwagni*, then successive formation of *Dhatus* will not take place and *apachita meda dhatu* formed in excess. This excess formed *meda dhatu* get accumulated in the body causing *Medoroga*[5].

Aam is the primary cause of all metabolic disorders in *Ayurveda*. This *Ama* causes obstruction in the *strotasa* leading to disease formation. Cholesterol is considered as one such product that produced due to metabolic impairment of fat metabolism.

Treatment of Dyslipidemia in *Ayurveda* involves methods to increase the *Agni* to digest the *Aam*, thus controlling the main causative factor. Drugs having lekhana and medohar properties are used to break the Samprapti. Several individual herbs and combinations of herbs are used in *Ayurveda* for the management of *Medoroga, Aam* and metabolic disorders. Hence to manage this condition the selected drugs should be of *Dipana, Pachana, Medohar, Lekhana* and *Srotoshodhaka* properties[6].

II. Rationale of the study

In modern medicine drugs used for lowering cholesterol includes statins, bile acid, nicotinic acid, cholesterol absorption inhibitors. Commonly used group is statins. Statins, act by inhibiting cholesterol synthesis and up regulate LDL receptors in liver. It reduces Atherosclerotic cardiovascular disease (ASCVD) risk by 15% to 37%, but residual 60% to 80% of ASCVD risk still remains. Common side effects of statins are myositis, arthralgias, gastrointestinal upset and elevated liver function test. Hence it cannot be given in Liver and renal disorders [7].

Thus there is a need of the effective and safe herbal antihyperlipidemic drugs with simultaneously reducing the severe side effects. *Kutaki* (*Picrorhiza kurroa* Royle ex. Benth) can be used in such conditions due to its *lekhana* and *medohar* properties [8]. It improves liver functions. Various animal research studies conducted on *Kutaki* proved its antihyperlipidemic and hepatoprotective property [9]. The main purpose of the study is to improve patient car and to reduce cost related to cardiovascular diseases. The liver is an important organ in regulating various metabolic processes. It is the main site for formation and clearance of lipoproteins. Hence liver diseases can affect plasma lipid levels in a variety of ways. Obesity, Diabetes mellitus and Stress are major secondary causes of Dyslipidemia. *Kutaki* mainly works on liver and being hepatoprotective, antioxidants, antidiabetic, anticholestatic and immune-modulating properties help in breaking pathogenesis [10-12]. Hence this study is proposed to evaluate the efficacy of *Kutaki* in the management of Dyslipidemia .

III. AIM AND OBJECTIVES

Aim: To study the efficacy of Kutaki in the management of Dyslipidemia

Objectives:

- To study the effect of Kutaki on BMI, Total cholesterol, HDL LDL & Triglycerides.
- To study the effect of Atorvastatin on BMI, Total cholesterol, HDL, LDL & Triglycerides.

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• To assess the levels of AST, ALT, S. Creatinine and S. urea in both the groups

• To compare the effects of Kutaki & Atorvastatin on BMI, S. lipid levels, AST, ALT, S. creatinine & S. urea.

Case definition-

Diagnosed and confirmed cases of either sex between the age group of 30 to 60 years having Dyslipidemia According to National Cholesterol Education Programme (NCEP) and ATP III Guidelines patients having serum cholesterol levels ≥200 mg/dl, serum triglyceride levels ≥150 mg/dl, serum HDL levels < 40 mg/dl for men and < 50 mg/dl for women and LDL cholesterol levels ≥130 mg/dl.

Research Question:

Is Kutaki effective in the management of Dyslipidemia as compared to Atorvastatin?

Hypothesis:

Kutaki may be effective in the management of Dyslipidemia due to its deepan, pachan and lekhana property.

Null Hypothesis:

Kutaki may not be effective in the management of Dyslipidemia.

Trial design: Randomized Standard controlled Double arm Open labeled Study. Interventional study on 2 parallel group having 1:1 ratio.It is a exploratory study.

IV. METHODOLOGY

Study setting : The study will be conducted in academic hospital MGACH & RC, Salod (H), Wardha.

Registration Number: REF/2018/09/021751 The registration number for this trial is CTRI/2018/10/015939.

Eligibility criteria- Age between 30 yrs to 60 yrs of either sex and any Sharirik Prakruti, diagnosed & confirmed cases of Dyslipidemia on the basis of investigation (according to Adult Treatment Panel III, 2001)[13] Patients having Total cholesterol from 200 to 280 mg/dL and/or LDL between 130 to 200mg/dL and/or Sr. Triglycerides from 150 to 280 mg/dL and/or Sr. HDL from 40-to 20mg/dL with controlled hypertension and Diabetes mellitus are included. Patients having Total cholesterol above 280 mg/dL and/or LDL above 200mg/dL and/or Sr. Triglycerides more than 280 mg/dL and/or Sr. HDL below 20 mg/dL, patients with Unstable Angina, myocardial infarction, stroke, transient ischemic attack, cardiovascular surgery or major operations within 6 months prior to screening visit and having systemic illness like Tuberculosis, Carcinoma, Endocrine disorders, Renal or Liver disorder, uncontrolled hypertension, diabetes mellitus and drug induced Dyslipidemia are excluded.

Table No. 1 Interventions of both groups-

Drug	Dose in units	*Anupana*	*Kala*	Frequency
Group A – *Kutaki vati*	500 mg	Water	*Abhakta* (60 min before)	Two times a day

Group B – Tab.Atorvastatin	10 mg	Water	At bed time	Once a day

Criteria for discontinuing or modifying allocated interventions: Subject will be withdrawn from the study if any untoward incidence, features of drug sensitivity or any other disease or problem arises, the subject will be offered free treatment till the problem subsides.

Follow up: 0 and 60th day

Primary Outcomes: We will see the effect of interventional drug on Lipid profile, Blood Sugar Level (Fasting) before and after treatment.

Secondary Outcomes : We will see AST/SGOT (aspartate aminotransferase or serum glutamic oxaloacetic transaminase), ALT/SGPT (alanine aminotransferase or serum glutamic pyruvic transaminase), Serum Creatinine, Serum urea and Blood sugar level –Fasting and any side effect of interventional drug.

Statistical analysis : The changes from baseline will be analyze by using Paired and Unpaired 't' Test for objective criteria.[21]

Time duration till follow up : The patient will be followed up during treatment 60 days.

Follow up period–0, 30th and 60thday

Time schedule of enrolment, interventions :Drug will be given from 0 to 60 days

Recruitment :160 (80 in each group) patient will be recruited by simple random sampling Lottery method, and PI will allocate and enroll the patient.

Methods : Data collection, management, and analysis

Data collection methods: Assesement criteria :

Objective criteria- Total cholesterol, LDL (Low Density Lipoproteins) and/or Sr. Triglycerides and/or Sr. HDL (High Density Lipoproteins), AST/SGOT (aspartate aminotransferase or serum glutamic oxaloacetic transaminase), ALT/SGPT (alanine aminotransferase or serum glutamic pyruvic transaminase), Serum Creatinine, Serum urea and Blood sugar level –Fasting will be assessed before and after treatment.

We will stay in touch with patient by taking contact no. and timely advice them for medication and follow up and data of follow up patient will be stored in documentation with reason.

Data management: The data entry coding will be done by PI

Statistical methods: Paired and Unpaired 't' Test for objective criteria.

Ethics and dissemination: Research ethics approval ; approval from research ethics committee has taken. No-Ref.No.DMIMS (DU)/IEC/2018-19/7329.

Consent or assent: The written consent will be taken from the patient before starting the study. During the study the confidentiality of each patient will be maintained.

Dissemination policy: The data will be disseminated by paper publication. Authorship eligibility guidelines and any intended use of professional writers

Informed consent materials: With all the information model consent form and other related documentation will be given to participants.

Expected Results: We expect to see good efficacy of *Kutaki in the management of dyslipidaemia in intervention arm.*

Discussion: If *Kutaki* works and improves hepatic functions, it directly corrects the lipid metabolism which will be helpful in radical cure of Dyslipidemia. If the proposed study results in the positive outcome then it will give the best parallel modality for the management of Dyslipidaemia with protecting organs from damage. It may cause radical cure of Dyslipidemia. A number of articles on different aspects of dyslipidemia and related conditions were reviewed [13-25].

Limitations: It is single drug therapy to evaluate the efficacy of *Kutaki* in the management of Dyslipidemia. For better results other drugs can be added and combined formulation may be prepared. More specific investigations like Apolipoproteins can be done.

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Figure no.1 Gantt Chart (Quarterly based)

Item	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**
Enrollment of Volunteer								
Data collection								
Writing the thesis parts up to methods								
Data analysis								
Writing the thesis parts up to results and Conclusions								
Submission								