

Protocol of Comparative Evaluation of Efficacy of Kulattha Gutika with Atorvastatin in the Management of Dyslipidemia (Medoroga)

Abstract:

Introduction-The term 'Dyslipidemia' can be referred to Medoroga included under santarpanajanyavyadhi as per Ayurveda. In *Dyslipidemia* there is involvement of *Tridosha* with *kapha* dominance. Intake of unhealthy food, alcohol, cigarette smoking, stress and lack of physical activity are the main etiological factors of Dyslipidemia. According to *Ayurveda Guru, Madhur, Sheet, Snigdha, Kapha Meda Vardhaka Ahar, Avyayam, Diwaswapa, Achinta* and *Bijadosha* are the main causative factors for *medoroga*. **Aim and objectives**-Comparative evaluation of Efficacy of *Kulattha Gutika* and Atorvastatin in the management of Dyslipidemia (*Medoroga*). **Material and Methods** – Study contains 60 patients of Dyslipidemia which will be divided into two equal groups (each contains 30 patients). Group A (Interventional) patients will be treated with *KulatthaGutika* 1 gm thrice a day after meal with warm water for 45 days and Group B (Experimental group) will be given Tab, Atorvastatin 10mg at bedtime with warm water for 45 days. Objective parameters like BMI, Lipid profile and Fasting Blood Sugar will be assessed before and after treatment. Incidence of Dyslipidemia as per prakriti will be assessed by analysing prakriti of each patient. **Discussion**- *Kulattha* is indicated for *medoroga* in *Bhavprakash* due to its *kaphamedohar* property which may help in improving objective parameters. **Result** – Subjective and Objective outcomes will be statistically analysed by appropriate method. **Conclusion** – Conclusion will be drawn from result obtained.

Keywords: Dyslipidemia, *Medoroga, Kulattha Gutika, Atorvastatin, Santarpanajanya vyadhi.*

Introduction:

In terms of food, living standards, and the environment, human life is rapidly changing. A majority of the population suffers from metabolic diseases as a result of changes in eating habits and a sedentary lifestyle. Metabolic diseases are caused by changes in normal metabolic processes caused by aberrant chemical interactions in the body. *Dyslipidemia* is defined as a group of metabolic diseases involving lipoprotein metabolism, evidenced by an increase total cholesterol, triglycerides (TGs), or both, or a reduction in high density lipoprotein levels, or all three, can all lead to atherosclerosis at any age.^(1,2) According to the ICMR-INDIAB study, hypercholesterolemia was prevalent in 13.9 percent of the population, hypertriglyceridemia was prevalent in 29.5 percent, low HDL-C was prevalent in 72.3 percent, and high LDL-C levels were prevalent in 11.8 percent. Ayurvedic texts do not provide any descriptions of dyslipidemia. As a result, it cannot be compared to a specific condition in Ayurveda. It falls under the category of *SantarpanjanyaVyadhi*. Due to similarities in their etiopathogenesis and clinical features, *Shonitabhishyandana, RasagataSnehaVridhhi* (raised plasma lipid levels), *RasaRaktagata Sneha Vridhhi* (raised plasma and blood lipid levels), *Medovridhhi* (elevation of generalised fat), *Medoroga* (obesity), and *AamMedodhatu* (abnormal). The main etiological causes of Dyslipidemia are poor eating habits, a sedentary lifestyle, the existence of Dyslipidemia in the family, alcohol

consumption, cigarette smoking, and stress.^(3,4) According to Ayurveda the main causes of *Medoroga* are *Guru, Madhur, Sheet, Snigdha, Kapha Meda Vardhaka Ahar, Avyayam, Diwaswapa, Achinta, and Bijadosha*.⁽⁵⁾ All of these *Hetus* aggravate the *kapha* and *Meda*, resulting in *Stotorodha*. The regular movement of *Vayu* is obstructed due to *Stotorodha*. This obstructed *Vayu* enters the *Koshtha*, causing *Jatharagni sandhukshana* (increased digestive capacity), which causes early digestion of ingested food, resulting in insatiable appetite and a desire for huge amounts of food. *Agnimandya* and *Ama* production, according to *Dalhan*, are to blame for the situation. The effective functioning of *Agni* is essential for all metabolic activity in the organism.⁽⁶⁾ Food digestion is hampered by *Agnimandya*, which creates *Ama*. *Ama* is thought to be a crucial element in the aetiology of metabolic problems in Ayurveda. This *ama* obstructs the *Strotas* (metabolic process channels), resulting in disease development. Excess fat accumulates in the blood and adipose tissue due to a malfunction in fat metabolism. The creation of aberrant *Poshaka Medodathu* in huge quantities is caused by *Medodhatwagnimandya*. This improperly produced *Poshaka Medodathu* accumulates in vast quantities in *Rasadhatu*. The accumulation of *Poshaka Medodathu* leads to the development of a condition known as *Dhamanipraticchaya*. *Dhamanipraticchaya* is one of *KaphaDosha's 20 NanatmajaVyadhis*.⁽⁷⁾ *Medoroga Samprapti* begins with inflamed *Kapha* and *Medas* accumulating in the various *Strotasa*, resulting in *Stotorodha*. *Shonitabhishyandana* is a condition in which there is an excessive concentration of *Kapha* and *Medas* in the *Rasadhatu* (plasma) and *Raktadhatu* (blood, and blood vessels).^(8,9) It adheres to the *Upalepa* and forms it within the *dhamani's* walls.⁽¹⁰⁾ *Acharya Charak* prescribes *karshana* and *kaphamedanashanachikitsa* in Ayurveda to eradicate the *Kapha Meda Aparpanaupalepa*. *kulattha* is mentioned in *Bhavprakash*⁽¹¹⁾ for the management of *Medoroga* which helps in *Sampraptivighatana*. *Kulattha* possesses *Laghu, Ruksha* and *Tikshnaguna, Kashaya Rasa* and due to its *Ushna* potency, it exhibits *Vata-Kaphanashak Karma* and *Lekhan Karma*, it also exhibits *Medohar* quality⁽¹²⁾. As, *Atoravastin* is a standard drug used in the treatment of dyslipidemia. So, in this study, *Atoravastatin* is used in control group.

Research Gaps Analysis –Animal studies conducted on *Kulattha* showed its antihyperlipidemic, nephrolithic and antioxidant activity. Also, *Kulattha* is mentioned to exhibit *medohar* quality by its *Lekhankarma*. There are large numbers of research studies available on Dyslipidemia. *Shodhanachikitsa* like *Vamana, Virechana* and *Basti (Lekhana Basti)* showed good results in improving lipid levels^(13,14). But all patients are not willing for procedures of *Shodhanachikitsa*. It is expensive, patients have to visit frequently to hospital, and have to follow pre and post operative procedures. *Shodhanachikitsa* cannot be used in patients having contraindicated for it. In such patients *Shamanachikitsa* can be given. In *Shamanachikitsa* most of the formulations have *guggul* as main ingredient. In *Bhavaprakash Samhita* it is mentioned to avoid long term consumption of *guggul*. The long term consumption of which have adverse effects like abdominal discomfort⁽¹⁵⁾, impotency⁽¹⁶⁾. The *Lekhana* drugs available for dyslipidemia can also cause abdominal irritation in some patients. The patients having intolerance to *Guggul* and *Lekhana* drugs cannot consume it for a longer duration. *Kulattha* is described in *Dhanyavarga* so it can be safely used for long duration. It is cost effective and easily available. So present study is planned to evaluate efficacy of *Kulattha* in the management of Dyslipidemia in human beings.

Trial plan: The study design is Double arm Randomized Standard controlled single blind clinical trial. It is an interventional study having 1:1 ratio on both parallel groups.

Research Question: Whether *Kulattha Gutika* is as effective as *Atorvastatin* in the management of Dyslipidemia?

Hypothesis

Null hypothesis(H0)-

- *KulatthaGutika* is not as effective as atorvastatin in the management of Dyslipidemia.

Alternate hypothesis(H1)-

- *KulatthaGutika* is as effective as Atorvastatin in the management of Dyslipidemia.

Aim and objectives

Aim: Comparative evaluation of Efficacy of *KulatthaGutika* and Atorvastatin in the management of Dyslipidemia (*Medoroga*).

Objective : 1. To assess the efficacy of *KulatthaGutika* on Total cholesterol, Triglyceride, HDL, LDL, VLDL & BMI.

2. To assess the efficacy of Atorvastatin on Total cholesterol, Triglyceride, HDL, LDL, VLDL & BMI.

3. To compare the efficacy of *KulatthaGutika* and Atorvastatin on Total cholesterol, Triglyceride, HDL, LDL, VLDL & BMI.

4. To study the incidence of dyslipidemia as per *prakruti*.

Methodology :

Type of trial - The trial is a parallel-group, randomized, single-blind, standard - controlled trial. It will include, a 45 days treatment period, and a 15th, 30th 45th day week follow-up period.

Allocation ratio – Total 60 patients will be selected for the study which will then be equally divided into two groups. Group A is experimental group whereas Group B is standard control.

Drug collection / authentication- The raw material will be procured from reliable source and will be authenticated from Department of *Dravayguna* of Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H) ,Wardha.

Formulations:

KulatthaGutika:

Table: 1

Sr.No.	Ingredient	Botanical Name	Part Used	Quantity
1.	<i>Kulatthi</i>	<i>Dolichos biflorus</i> Linn.	Grains	1 Part

Preparation of Material (*KulatthaGutika*) :- The *kulatthaGutika*, will be prepared as per the standard operating procedures, mentioned in Sharangdhar Samhita, *MadhyamKhand*⁽¹⁷⁾.

Properties of durgs⁽¹⁸⁾ –

Table: 2

Sr. No	Drug	Rasa	Guna	Virya	Vipak	Karma
1.	<i>KulatthaGutika</i>	<i>Kashaya</i>	<i>Laghu, Ruksha, Tikсна</i>	<i>Ushan</i>	<i>Katu</i>	<i>KaphavataSamakaMedohara</i>

Study setting:

Selection of patients will done from OPD (~~Room No. 30~~) and IPD of Department. of Kayachikitsa , Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H) , Wardha. Also patients will be selected from various specialized peripheral camps.

Diagnosticcriteria :Diagnostic Criteria ⁽¹⁹⁾ [ATP-III National cholesterol education program(NCEP) criteria]:

- Serum Total Cholesterol \geq 200 mg/dl & or
- Serum Triglycerides = 150-499 mg/dl & or
- Serum HDL(HIGH DENSITY LIPID) $<$ 40 mg/dl & or
- Serum LDL Cholesterol (LOW DENSITY LIPID)= 130 -189 mg/dl

Assessment criteria: The patients will be assessed by objective parameters like lipid profile (Total cholesterol, Triglycerides, Low density lipoproteins, High density lipoproteins and Very low density lipoproteins), fasting blood sugar level and body mass index,.

Prakruti will be assessed as per software application AYUVYA to study the incidence of dyslipidemia as per *prakruti*.

Eligibility criteria: Selection of patients in between the age group of 30– 60 yrs of both gender and irrespective of the *SharirikPrakruti* will be considered. Patients with fulfilling the diagnostic criteria of Dyslipidemia are included in the study. Patients with Pre-diagnosed cases of major illness like cardiovascular disorder, diabetes mellitus and renal disorders, Patients taking the medication like glucocorticoids and also pregnant and lactating women will be excluded.

Randomization- An independent statistician will create a block randomization sequence. Qualified individuals will be randomly assigned to either the experimental group or the conventional controlled group in a 1:1 ratio, with randomization stratified by site. A remote and web-based randomization system will be used by the researchers to assess the treatment allocation for each eligible participant. Total 60 patients will be selected for the study which will then be divided into two groups. Group A is experimental group where as Group B is standard controlled.

Blinding- Treatment allocations will be kept a secret from participants, the researcher will apply for a randomised assignment for each qualified patient by Random Sampling Computerized table method and will enrol him in study or control group. The blinding will not be broken during the trial and will be kept strictly confidential.

Interventions:

Group A (Experimental)-*KulatthiGutika*500mg 2 tab. thrice a day before meal with warm water for 45 days.

Group B (Standard Control) – Tab. Atorvastatin 10 mg once a day at bed time with warm water for 45 days.

Screening investigations (base line): Lipid profile, fasting blood sugar level

Investigation during treatment: Not applicable

Investigation (end line): Lipid profile, fasting blood sugar level

Criteria for discontinuing or modifying allocated interventions: From the study if any untoward incidence, features of drug sensitivity or any other disease or problem arises, Subject will be withdrawn and free treatment will be offered to the subject till the difficulty subsides. We will measure quantity of *Gutika* for the consumption of appropriate dose for assessment and to check drug adherence during treatment the subject will be followed up.

Follow up: Patients will be followed up on 15th day, 30th day and 45th day during the period of treatment. Patient will be advised to take normal routine activity and routine diet and no any specific precautions for food intake will be advised.

Primary Outcomes: The primary outcome of the trial is to check the efficacy of interventional drug (*Kulattha Gutika*) on serum levels of Total cholesterol, Triglyceride, HDL, LDL, VLDL & BMI

Secondary Outcomes: The secondary outcome of the trial is to study the incidence of dyslipidemia as per prakriti.

Relief and relapse incidents- Relapse is defined as a rise in lipid levels, blood sugar levels, or body mass index in patients with dyslipidemia (*Medoroga*) who had responded to treatment. When the patient's symptoms disappear, it signifies the treatment has been successful. The time until relief, time until first relapse, and total relapse times are the relief and relapse incident outcomes. The time between patients obtaining therapy and experiencing therapeutic success is referred to as the time until relief. The time to first relapse refers to the period of time between a patient's treatment success and the reintroduction of elevated cholesterol, sugar levels, or BMI. The sum of relapse times during both the treatment and follow-up periods is the total relapse time.

Long-term effectiveness- Long-term effectiveness responders are those who provide adequate relief on a weekly basis for at least 45 days throughout the follow-up period.

Statistical analysis: A statistically significant level of type I error is 5% (two-sided). Data of prakriti analysis be analysed with the help of Wilcoxon test. Paired as well as Unpaired t test will be used to analyse the data having objective criteria. The McNamara's test will be used to analyse the data with subjective criteria.

Total follow up : Patient will be followed up thrice during the trial, First on 15th day after initiating the treatment, second on 30th day after initiating the treatment, and third on 45th day i.e. after completion of the treatment.

Follow up time: The assessment of the patients will be done before and after completion of treatment.

Enrolment and intervention time schedule: Drugs will be given from 0 to 45 days with follow up on day 15th, day 30th and day 45th to check adherence of drug.

Recruitment: By computerized random chart sampling method 60 patient will be recruited (30 in each group)

Implementation: Principle investigator will enroll and allocate the patient.

Methods: Data collection , analysis and management

Data collection method :

Objectives–Serum levels of Total cholesterol, LDL, HDL, VLDL, triglycerides, and BMI(Body Mass Index)

Prakriti Assessment: Prakriti will be assessed as per software application AYUVYA to study the incidence of dyslipidemia as per prakriti.

Plan to promote participants retention and complete follow up- We will stay in touch with the patient by taking contact number and timely advice them proper medication practices and follow up and the data regarding follow up will be stored in the documentation with valid reasons.

Data management: The data will be collected from patients by assessor by doing investigations and assessment after taking written consent form from the patient. Prakriti will be assessed with the help of software application AYUVYA will be collected using structured questionnaire filled during interview of the patient. Data will be entered in master sheet and analysed by using appropriate statistical technique and data coding will be done by principal investigator.

Safety assessment-

On a consent form, details about adverse events will be noted, and on case sheet other details of patients will be noted. If there are any major adverse events, they must be reported to the principal investigator and the ethics committee within 24 hours, and any necessary therapy will be given as quickly as possible. All major adverse occurrences will be investigated and tracked until they are remedied.

Ethics and dissemination :

Research Ethics Approval : Approval for the trial from research ethics committee has been taken. Ref. No. MGACHRC / IEC / July – 2021/ 339

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

Dissemination policy : The data will be disseminated by paper presentation and publication.

Informed consent materials: The participants will be given model consent form and all related documentation with providing all information.

Result: Expected outcome result in control group with intervention *Kulattha Gutikas* per oral is potentially added effectual in improving the serum lipid levels antilipidemic.

Discussion:

In modern science, some health behaviours have been demonstrated to have an impact on lipid levels. Excess use of alcohol and Tobacco, unhealthy food habits, lack of physical activity and obesity are all are risk factors for causing Dyslipidemia. A lack of fruits, nuts/seeds, and vegetables, as well as a high consumption of saturated fats, are all nutritional risk factors. Genetic abnormalities might potentially induce dyslipidemia. Autosomal dominant mutations in LDL receptors cause the majority of cases of familial hypercholesterolemia, resulting in a rise in LDL-C levels. Other mutations in the cholesterol pathway have been reported, but they are **less common.**^(20, 21)

In Ayurveda main etiological factors which bring vitiation in *medoroga* are lack of physical exercise, day sleep, excessive intake of fatty foods, excess drinking of *Varuni* (a kind of wine).⁽²²⁾ *Medovaha Srotodushti* occurs due to vitiation of *Kapha* dosha and decreased functioning of *medo Dhatvagni*. This leads to excessive *Meda* and eventually to dyslipidemia.^(23,24) Dyslipidemia is one of the major causes of cardiovascular and cerebrovascular diseases. Many research works have been conducted on it, but none of the research study showed complete cure. In modern medicine, various classes of drugs like Atorvastatin are used but there are some limitations. Long term use of it leads to nephrotoxicity and hepatotoxicity^(25, 26). Animal studies conducted on *Kulattha* showed its antihyperlipidemic activity⁽²⁷⁾ but no studies are conducted on human beings. *Kulattha* is included in *AnnaVarga*. It is safe, cost effective and easily available⁽²⁸⁻³⁰⁾.

In this study we will observe how *Kulatthi Gutika* helps in effectively improving serum lipid levels in *Dyslipidemia*. *Kulatthi Gutika* consists exclusively of *kulattha* which has properties like *Laghu*, *Ruksha* and *Tikshnaguna*, *KashayaRasa* and *Ushna* potency. The *ushna*, *teekshnaguna* will ignite the *medodhatvagni* and also act against the vitiated *Kaphadosha*. Due to exhibition of *LekhanKarma*, it will scrap the excessively accumulated *Meda*. Thus, it may also exhibit *Medohar* quality. The following *guna-karma* will do the *Samprapti- Vighatan* and help in arresting the disease in that stage.

By assessing the *Medohar* effect of *Kulatha Gutika*, we will study the changes in Lipid Profile, BMI (Body Mass Index) of the subjects⁽³¹⁻³⁸⁾. Since, the disorder involves *Kaphadosha* we will assess the *prakriti* of subjects so that a conclusion can be made that which subjects are more prone to dyslipidemia.

Conclusion: *Kulatthi Gutika* may prove more efficacious in improving serum lipid levels in *Dyslipidemia (Medoroga)* as compared to tablet Atorvastatin with minimum side effects.

NOTE:

The study highlights the efficacy of "Ayurveda" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

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