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Ayurveda

A RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE EFFECT OF ERANDA MOOLA (ROOT OF RICINUS COMMUNIS) IN THE MANAGEMENT OF DYSLIPIDEMIA

Dr. Sunil S. Borkar* Phd Scholar, Department of Kayachikitsa, DMM Ayurved Mahavidyalaya, Yavatmal, Maharashtra, India. *Corresponding Author

Dr. Suryaprakash K. Jaiswal Professor & HOD, Department of Kayachikitsa, DMM Ayurved Mahavidyalaya, Yavatmal, Maharashtra, India.

ABSTRACT **Background:** Dyslipidemia is the disease condition of abnormally elevated levels of any or all lipids. Various treatment modalities like diet and life style modification, and use of lipid lowering agents Statins, Fibrates, Niacin etc are used in the management of Dyslipidemia. Lipid lowering herbs and Panchkarma procedures are mentioned in Ayurveda for management of Medo Vikaras. Complex or combined treatment modalities are effective in management but it is difficult or expensive for patient to follow or perform for long period of time. On the contrary compliance is best for natural origin lipid lowering agent which is cost effective, handy and free from side effects in the management of dyslipidemia. Hence it is decided to evaluate the effect of Eranda Moola as a lipid lowering agent in the management of dyslipidemia. **Aim and Objectives:** Study to evaluate the effect of Erand moola in the management of Dyslipidemia. **Methodology:** In this study,140 patients will be divided randomly into 2 groups (70 in each). In Group A (Intervention) – Eranda Moola (Root of Ricinus communis) 80 mg/kg b.w. in morning on empty stomach with Anupana of Honey for 08 weeks and Control group using Atorvastatin 20 mg OD (Control) for 08 weeks. Assessment will be recorded on day 0, at the end of 4th week and at the end of 8th week. **Results:** Changes will be observed in the objective outcomes. **Conclusion:** Eranda Moola will be effective in the management of Dyslipidemia.

KEYWORDS : Eranda Moola, Dyslipidemia, Direct LDL-C

INTRODUCTION:

Dyslipidemia is a condition marked by unhealthy abnormal concentrations of lipids or lipoproteins in blood. Dyslipidemia is a major risk factor for many life-threatening non communicable disorders like atherosclerotic cardiovascular disease (ASCVD), cerebro-vascular disorders and other athero-sclerogenic disorders [1]. It has been closely linked to the patho-physiology of ASCVD and is a key independent modifiable risk factor [2, 3]. ICMR- India Diabetes (INDIAB) phase 1 study shows overall high in low density lipoprotein cholesterol (LDL-C) and triglycerides is 13.3 % and 22.8% respectively [4].

Medical science fraternities are continuously in search of finding new safe and effective drug for the management of dyslipidemia. Now research interest has been focused on various herbs for their potential role in lowering lipids. Thus, there is need of searching herbal drug for dyslipidemia by adopting the Golden triangle approach (i.e., research collaboration of Ayurveda, Modern Medical Science and Modern Basic Sciences) to provide clinical benefit to society [5].

Rationale of Study:

As per Ayurveda, *Medoroga* may be considered as a Dyslipidemia, in which *Kapha dosha and Meda dhatu* are involved as a prime causative factor and *Vata and Pitta* are considered for fatal complications [6,7,8]. Various treatment modalities like diet and life style modification, conservative treatment and *Panchkarma* procedures are mentioned in Ayurveda for management of *Medo Vikaras*[9]. Pharmacological and clinical studies also reported that Ayurvedic herbal medicines are effective in lowering LDL-C [10]. *Acharya Bhavmishra*, in his text *Bhavprakash* mentioned the use of *Eranda moola* along with honey in *Sthoulya*[11]. Pharmacological study of *Eranda moola* also proved its lipid lowering properties [12,13,14,15]. But still there is no clinical trial reported regarding the lipid lowering activity of *Eranda moola*. Hence, we decided to evaluate the effect of *Eranda moola* in the management of Dyslipidemia (*Medoroga*).

AIM AND OBJECTIVES:

Aim:

Study to evaluate the effect of *Eranda moola* in the management of Dyslipidemia (*Medoroga*)

OBJECTIVES:

1) To study the effect on the change in direct LDL-C level.
2) To study the effect on the change in Triglycerides levels.
3) To study the effect on the change in other lipid parameters such as Total Cholesterol (TC), Low Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL).
4) To study the effect on the change in Anthropometric parameters like Body Weight, BMI, Waist circumference and Waist to hip ratio.

Case definition-

Diagnosed and confirmed cases of either sex between the age group of 18 to 65 years having Direct LDL-C ≥ 130 at the time of screening.

Research Question:

To evaluate the effect of *Eranda Moola* (Root of Ricinus communis) (Intervention) 80mg/kg b.w. in morning on empty stomach with *Anupana* of Honey for 08 weeks and Control group using Atorvastatin 20 mg OD (Control) for 08 weeks in the management of Dyslipidemia (Medoroga) (Patient) with primary outcome as a change in the level of LDL-C and triglycerides.

Hypothesis:

Eranda Moola has positive effect in the management of Dyslipidemia (*Medoroga*).

Null Hypothesis:

Eranda Moola is not effective than Control treatment in the management of Dyslipidemia (*Medoroga*).

Alternative Hypothesis:

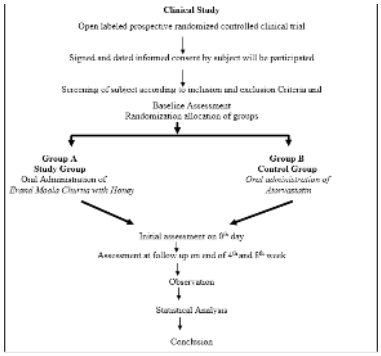
Eranda Moola is effective than Control treatment in the management of Dyslipidemia (*Medoroga*)

METHODOLOGY:

STUDY DESIGN:

Open labeled, two arms, randomized controlled trial. Interventional study of two parallel group which is having 1:1 ratio.

Table No. 1: Clinical study design flow chart



Study Setting: The study will be conducted in academic hospital of Shri Gurudeo Ayurveda College, Gurukunj Ashram (MS)

Registration Number: Trial Registration: REF/2019/02/023939. The registration number for this trial is CTRI No. CTRI/2019/02/017743

Selection of Study Subjects:
Eligibility Criteria:
Subjects of either sex (both males and females) in the age group of 18 to 65 years with Direct LDL-C ≥ 130 at the time of screening will be included in study. Subjects with uncontrolled or malignant Hypertension, Type I & II Diabetes Mellitus, uncontrolled Hypothyroidism or Hyperthyroidism, known cases of severe / chronic hepatic or renal disease, any active malignancy, history of significant cardiovascular event < 12 weeks prior to randomization, ECG demonstrating any signs of uncontrolled arrhythmia / acute ischemia, active tuberculosis, known HIV case, pregnant and lactating females and subjects currently participating in any other clinical study will not be included in study.

Sample Size: 70 subjects will be recruited in each group (Total 140 subjects).

Table No. 2: Interventions of both groups-

Group	Drug	Dosage	Anupana	Time	Frequency
Group A	*Eranda Moola* (Root of Ricinus communis)	Powder 80 mg/kg b.w.	Honey	in morning on empty stomach	Once a day
Group B	Tab.Atorvastatin	20 mg	Water	At bed time	Once a day

All the subjects will be advised to take given study product for a period of 8 weeks.

Subject Withdrawal Criteria:
Subject will be withdrawn from the study at their own request or at the request of their family members. If in the investigator's opinion, continuation in the study would be detrimental to the subject's well-being and protocol deviations that could invalidate interpretation of the results will be considered for withdrawn.

Study Outcomes:
Primary Outcome:
1. Effect on the change in direct LDL-C level at the end of study (08 weeks).
2. Effect on the change in Triglycerides levels at the end of study (08 weeks).

Secondary Outcome:
Change in other lipid parameters such as Total Cholesterol (TC) Triglycerides (TG), Low Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL) at the end of 4 and 8 weeks.
1. Change in Anthropometric parameters like Body Weight, BMI, Waist circumference and Waist to hip ratio [16] at the end of 4 & 8 weeks.
2. Overall efficacy of the study and control product as per the physician (CGI-I) at the end of study (08 weeks)
3. Safety assessment by assessing adverse drug reactions, clinically significant abnormal laboratories values at the end of 4 weeks and at the end of 8weeks.
4. Overall safety assessment of the study and control product as per the physician at the end of study (08weeks)

DISCUSSION –
The term *Medo dhatu* described in Ayurveda covers fats, lipid and adipose tissue; hence the disorders of these tissues can be considered as disorders of *Meda dhatu*. Excessive accumulation of *Meda* in body causes various diseases like *Medoroga or Sthaulya or Atisthaulya, Granthi, Galaganda and Madhumeha* [17].

On the basis of physiological consideration of *meda dhatu*, circulating lipids are considered as a *asthayi (poshak) dhatu* and where as body fats or adipose tissue can be considered as *sthayi or sthira meda dhatu*. The term lipid is better to consider in relation to physiological aspect of fat where as adipose tissue to be considered in relation to anatomical aspect. In *Medo vikaras* all the etiological factors influence and disturb (*agnimandya*) the *jatharagni* primarily and then consequently *bhutagni and dhatwagni*, which causes excess formation of *apaachit or saam meda dhatu*.

From above discussion it may be stated that Dyslipidemia (*Medoroga*) is a disease of *asthayi medo dhatu vriddhi*, means increased circulating lipids which resides in *rasa-rakta* and Obesity (*Sthoulya*) is a disease of *apaachit or saam sthayi medo dhatu vriddhi* [18]. In another aspect it is a disease of diminished j*atharagni and dhatwagni* induced *apachita or saam asthayi meda dhatu vriddhi* [6]. *Bhutagni* is the link between *jatharagni and dhatwagni*, means all three agni are diminished. So, for the management of Dyslipidemia (*Medoroga*) such drug is needed which has *deepan, pachan, kaphaghna and medoghna* properties. Medicines having *katu rasa and rukshan* properties are useful but such drug has to be use for shorter period to avoid the *karshan* of all dhatus. Hence such drug is needed which causes *pachan* of circulating *saam asthayi meda dhatu* of *rasa - rakta* but doesn't do *karshan* of remaining *dhatus*.

Eranda Moola has unique property of correcting the impaired *dhatwagni vyapara* of all *dhatu* by virtue of its *vrishya or urjaskar* property [15]. This property also ensures the long-term use of *Eranda moola* in the management of Dyslipidemia (*Medoroga*) to avoid long term complications. Dyslipidemia (*Medoroga*) is the root cause for the development of atherogenesis. *Kapha Vataj* nature of atherosclerosis needs such drugs which having both qualities of pacifying *kapha and vata* at same time. *Erand moola* is the best in these regards. *Ushna virya and Katu vipak of Eranda moola* starts *paachan* right from *rasa* as seen in disease *Aamvata. Madhur, Katu, Kashay rasa and Vata Kapha hara* properties might be helpful to avoid complications like atherosclerosis. So, disease pacifying and dhatu modifying both properties are possessed in *Eranda moola*. *Acharya Bhavaprakash* mentioned its use in the management of *Sthoulya Roga* with honey [11]. Hence it is decided to evaluate the effect of *Eranda Moola* as a lipid lowering agent in the management of Dyslipidemia (*Medoroga*).

Time duration till follow up: The patient will be followed up during treatment 08 weeks.

Follow up period– 0 day, at the end of 04 weeks, at the end of 08 weeks.

Time schedule of enrolment, interventions: Drug will be given from 0 to 08 weeks.

Recruitment: As per computer generated randomization list, subjects will be randomized to one of the two study groups i.e., Group A-Intervention, Group B-Control with the allocation ratio of 1:1. The randomization method will be a stratified block randomization. A wash out period of 15 days will be given before enrolment to subjects who are on any lipid lowering / anti-obesity drug(s) at the time of screening.

Methods:
Data collection, management, and statistical analysis.

Data collection methods:
Assessment of Efficacy Parameters
1. **Assessment of Direct LDL-C and Triglycerides (TG)** level will be checked initially, at the end of 4 weeks and at the end of the study i.e. 8 weeks. Change in Direct LDL-C and Triglycerides level will be assessed in both the group.
2. **Assessment of other lipid parameters such as Total Cholesterol (TC) and High Density Lipoprotein (HDL)** will be performed initially, at the end of 4 weeks and at the end of the study i.e.8weeks.
3. **Assessment of Body Weight, BMI, waist circumference and waist to hip ratio** [16] will be assessed initially, at every follow up visit, and at the end of the study.
4. **Assessment of overall efficacy on CGI-I (Clinical Global Impression- Improvement Scale)** will be recorded / filled at the end of the study.

Assessment of Safety:
Safety shall be assessed by clinical review of all safety parameters, including laboratory investigations like hematology, biochemistry including liver and kidney function test and vital signs including pulse rate, respiratory rate, body temperature and blood pressure, body weight. Assessment of safety of the product by the physician on global assessment scale will be assessed Adverse event reporting will be done in case of happening.

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

Statistical Methods and Data Analysis

Data will be coded & entered in MS Excel worksheet. Statistical analysis will be performed in statistical software STATA, version 10.1, 2011. For the analysis of efficacy variables, data will be analyzed from the Intent to treat population and per protocol population also. The values of the last visit will be considered for final analysis for subjects who did not complete the study schedule (Last Observation Carry Forward) for intent to treat analysis. Safety Analysis will be done on all subjects who have administered at least one dose of treatment.

A) Descriptive Analysis

Data describing quantitative measures will be expressed as median or mean ± Standard Deviation or Standard Error or the mean with range. Qualitative variables will be presented as counts and percentage.

B) Tests of significance

Comparison of variables representing categorical data like change in Quality of life, Overall Global Improvement assessed by subjects and Investigators will be performed using chi-square or Fisher's exact test or any applicable tests.

Mean differences of continuous variables like Body weight, BMI, Waist Circumference, Waist Hip Ratio, Lipid profile parameters from baseline will be examined by Student t test and comparison between two groups by independent t test or Group means of dependent sample will be compared by means of ANOVA (repeated-measures design, GLM procedure).

All p-values will be reported based on two-sided significance test and all the statistical tests will be interpreted at 5% level of significance level.

Ethics and dissemination: Research ethics approval; approval from research ethics committee has taken on dated 22.02.2018

Consent or assent: The written consent will be taken from the patient before starting the study.

Subject confidentiality statement

The identity of the study subjects will not be provided to any party except study related personnel, ethics committee and representatives of Government regulatory bodies. The data generated and recorded from the study will be kept confidential and in a coded form. The subject identity will not be revealed while publishing the study data.

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.

Strength: Patients of Dyslipidemia (*Medoroga*) are most of the time not presenting with clinical presentations of *Sthoulya* (Obesity). Such patients are more vulnerable for future complications like cardio-vascular disease or stroke. In such cases precise choice of medicine is that which corrects the vulnerable LDL cholesterol directly. If *Eranda Moola* effectively corrected the elevated level of LDL cholesterol, it will be the comparable choice instead of contemporary medicines. It also may cause radical cure and at the same time it may use for long term without side effects. So, it is decided to evaluate the effect of *Eranda Moola* as a Single herb formulation in the management of Dyslipidemia (*Medoroga*).

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