Section: Pharmacology

Original Research Article

EVALUATION OF CHOLESTEROL LOWERING EFFECTS OF RAW GARLIC AS AN ADD-ON THERAPY TO STATIN TREATMENT

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ABSTRACT

Background: Hypercholesterolemia is a highly prevalent disease condition all over the world, with incidence of more than 10 million cases per year in India. Disorders such as atherosclerosis and Coronary Artery Disease (CAD) are the consequence of hypercholesterolemia. Even though Garlic is found to have beneficial role in reducing cholesterol levels, the potency of raw garlic against standard drug therapy like statins are less studied. Therefore, this study aims to determine the cholesterol lowering efficacy of raw garlic, as an add – on therapy to standard statin therapy.

Materials and Methods: This study is a prospective, randomized, open labelled with active controlled 2 arm parallel group. 120 patients were enrolled in this study and randomized to control group [Standard therapy] and Study Group [Garlic along with standard therapy]. The patients of Control Group were given Atorvastatin while those in Study Group were given garlic in addition to Atorvastatin for 8 weeks. Study parameters are Total cholesterol level (mg/dl) and adverse drug effects for the study products.

Results: The results collected were analyzed by percentage comparison, mean with standard deviation, Paired T-Test, One-Way ANOVA test and repeated measures of ANOVA. The study shows there is reduction of mean cholesterol values in both the study group (baseline 250.2 ± 44.58 to 8 wks 179.8 ± 26.43 and control group (baseline 235.1 ± 25.31 to 8 wks 181.8 ± 26.50). Percentage of reduction in serum cholesterol level is 70.4% in garlic + statin group compared to statin alone 53.3% (p value- 0.0001).

Conclusion: Raw garlic has beneficial effect in lowering serum cholesterol levels when given along with standard statin therapy in hypercholesterolemic patients.

Keywords: Raw Garlic, Hypercholesterolemia, Statins, Total Cholesterol.

INTRODUCTION

Hypercholesterolemia is a highly prevalent disease condition all over the world, with incidence of more than 10 million cases per year in India. Disorders such as atherosclerosis and Coronary Artery Disease (CAD) are the consequence of hypercholesterolemia. These conditions are responsible for high rate of morbidity and mortality in the world, causing nearly 2.6 million deaths as reported by WHO (1). Studies reveal that the highest rate of Low Density Lipoprotein Cholesterol (LDL), which is harmful to the body, is seen in Tamil Nadu with an incidence rate of 18.3%.[1] Recently garlic, fish oil, red yeast rice, niacin, chromium, milk thistle and essential oils have been studied for their cholesterol lowering effects.

Aims and Objectives

Analysis of cholesterol lowering effect of raw garlic when used as an add - on treatment to standard statin therapy.

Pathophysiology of Hypercholesterolemia

Elevated levels of cholesterol are most important factors in promoting atherosclerosis, which is characterized by deposition of cholesterol from lipoproteins into the artery wall, thus leading to

coronary artery disease. There is an inverse relationship between HDL concentrations and coronary artery disease. Dyslipidemia can be due to a variety of factors such as genetics, diet and lifestyle. Familial hypercholesterolemia, an inherited disorder of metabolism, occurs due to a defect in LDL receptor, thus preventing clearance if LDL. Consumption of excessive quantities of saturated fatty acids are also an important cause. Lifestyle features such as high blood pressure, smoking, male gender and a lack of exercise also contribute to increased levels of cholesterol.

Drug therapy of hypercholesterolemia

Several treatment options exist for hypercholesterolemia, which may be instituted individually or in combination. They include lifestyle changes to diet and exercise, medications, and dietary supplements. Hypercholesterolemia can be treated by HMG Co-A Reductase inhibitors called as statins, Bile acid sequestrants (Resins), Fibric Acid derivatives, Nicotinic Acid or others such as Ezetimibe and Gugulipid. Usage of Statin group of drugs, which decreases the synthesis of Cholesterol by the inhibition of HMG-CoA Reductase enzyme, is the drug of choice. However, adverse effects of prolonged use of statins include rhabdomyolysis, myopathy and a possible elevation of liver enzymes which is detrimental to the individual's health. The incidence is higher with drug interactions that increase the potency and half-life of statins. There is an increased risk of neurological disorders such as headache, dizziness and paresthesia on usage of statins. Observations reveal that on higher dosage of the drug, there is an increase in the development of new-onset diabetes mellitus.[1] Rarely, experimental therapies or procedural interventions can be applied.

International guidelines have reinforced the role of pharmacological treatment to reduce cholesterol based on the risk of cardiovascular events. Despite some differences on suggested risk stratification tools and cholesterol goals, the guidelines are unanimous in recommending intensive pharmacological treatment and consequently, robust cholesterol reduction with statins in high-risk patients. By affecting blood cholesterol level, they cause an increased expression of LDL receptor gene within the hepatocyte. Simultaneously, degradation of LDL receptors is also reduced. This then leads to an increased removal of LDL from the blood. This group of drugs include the following: Simvastatin, Lovastatin, Pravastatin, Fluvastatin, Rosuvastatin, Pitavastatin and Atorvastatin. Atorvastatin has a prolonged half-life of 18-24 hours and has additional antioxidant property, with daily dosage of 10-40mg.[2]

Study Compound: Raw Garlic

It is also known as Allium sativum, belonging to family Amarylidaceae. Garlic is commonly used as a taste enhancer in Indian diets. It can be cultivated under a wide range of climatic conditions. The active compound in garlic is found to be Allicin. Crushing raw garlic triggers the formation of allicin through action of alliinase enzymes on the stable precursor alliin, and allicin inhibits cholesterol synthesis in-vitro.[6] The lipid lowering effect of garlic has been expounded upon by several studies and meta – analyses in various projects. These studies were carried out by comparing the cholesterol lowering effect of garlic as opposed to placebo in both healthy,[7] and dyslipidemic patients. A 2013 meta-analysis concluded that garlic preparations may effectively lower total cholesterol by 11–23 mg/dl and LDL cholesterol by 3–15 mg/dl in adults with high cholesterol if taken for longer than two months.[3] These studies involved the results and data of several trials conducted for a minimum duration of 2 months. The reduction was evident after one month of therapy and persisted for at least six months in these studies.[4] A double – blinded placebo controlled randomized study to determine the lipid lowering effect of garlic was conducted for a period of 8- 12 weeks on patients with hypercholesterolemia and yielded promising results. The total cholesterol levels had reduced by 7.6% and the LDL cholesterol by 11.8%. In comparison with the patients on placebo, total and cholesterol values were 11.5% and 13.8% lower respectively.[4] Studies have revealed that allicin showed a favourable effect in reducing blood cholesterol, triglycerides, and glucose levels and caused a significant decrease in lowering the hepatic cholesterol storage.[8]

A randomized clinical trial comparing the effect of raw garlic versus commercial garlic supplements such as powdered garlic supplement and aged garlic extract showed that both were equally efficacious in reducing blood cholesterol levels.[6] The active compound allicin only forms when garlic is crushed or cleaved when it is raw and loses its potency when cooked.[9] The possible mechanism of action of allicin, as determined by studies, is the formation of protein internal disulphide causing the inactivation of thiol (-SH) group enzymes such as HMG-CoA reductase and the multi-enzyme complex of fatty acid synthesis.[10] The previously conducted studies analysed lipid lowering effect of garlic as a stand-alone agent against a placebo. Hence this study was proposed to study the effects of raw garlic when taken as an add on therapy to statin treatment of dyslipidemic patients for a period of 2 months.

MATERIALS AND METHODS

Study Methodology

This Study was done as a Short-Term Student Project approved and funded by the ICMR as described in Table 1. The study was conducted after obtaining the approval from Institutional Ethics Committee. The subject's vitals were screened and blood samples were analyzed for Total Cholesterol (mg/dl). Patients with serum total cholesterol greater than 200mg/dl were enrolled after obtaining written

informed consent as per the eligibility criteria in Table 2.

The patients were randomized into Control group and Study group. The patients of Group A were given Atorvastatin while those in Group B were given garlic in addition to Atorvastatin. The enrolled patients were asked to visit on day 30 (one month) and day 60 (two months). Blood sample of the patients were obtained in a sterile manner and analyzed for Total cholesterol level (mg/dl). Patient vitals were examined during the visits. Compliance to the drug was verified and study medications were dispensed during the visits. Any adverse drug effects were asked for and documented.

RESULTS

This study was conducted to evaluate the cholesterol lowering effects of garlic as an add on therapy to statin treatment. 190 patients were screened, of which 59 were excluded from the study based on exclusion criteria. 11 patients who were eligible for the study were not willing to participate. 120 patients were enrolled in this study with 60 patients in each group. All the enrolled patients completed the study.

The results collected were analysed by the following statistical methods such as percentage, mean with standard deviation, Paired T-Test, One-Way ANOVA test and repeated measures of ANOVA.

The mean serum cholesterol level as the start of the study was 235.1mg/dl in the control group and 250.2mg/dl in the study group. Comparison of percentage reduction in serum total cholesterol levels shows that the control group has 53.3% reduction from the baseline Fig 3. Whereas the study group has 70.4% reduction from their initial values as shown in Table 3.

Comparison between the mean cholesterol level at baseline visit and final visit is represented in Figure 4. The control group has a mean cholesterol value of 235.1mg/dl at end of 1 month and 181.8mg/dl at the end of 2 months. The study group has a mean cholesterol level of 250.2mg/dl at the beginning and 179.8mg/dl at the end of 2 months.

The baseline serum cholesterol levels were compared between the control and study group and statistically analysed as shown in Table 4. There was no significant difference (p=0.06) among the two groups. Similarly, the difference in means between the control and test group at the end of 2 months shows that there is no significant difference (p = 0.65). Whereas, the reduction in cholesterol levels within the patients of the control group who received statin standard therapy has shown significant improvement.

Similarly on analysing the serum cholesterol of the patients who received both garlic and statin has shown high significant difference with a p value of 0.0001 as shown in Table 4. Repeated measures of ANOVA was used to analyse the difference in cholesterol values within the control and study group during the three visits.

This shows that the cholesterol levels have significantly reduced at the end of 1 month and 2 months in both control and study groups as shown in table 5 and 6. The above-mentioned data is also represented in Figure 5.

The subjects of the control group complained of muscle weakness, difficulty in sleeping and abdominal bloating which may be attributed to the consumption of statin drugs. The patients of the study group, in addition to muscle weakness, complained of aphthous ulcer and gastritis which may be an adverse reaction to garlic. This is represented in Table 7.

Table: 1 Study Methodology

Study design	Prospective, randomized, open labelled active controlled 2 arm parallel group
Study Population	Sample size of 120 patients. (60 patients in each group)
Study period	July – August 2017
Duration of Study	2 months
Study Centre	Department of Cardiology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu

Table: 2 Eligibilty criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Newly diagnosed Hypercholesterolemia patients with total cholesterol levels greater than 200mg/dl. Age group: 18 - 55 years Both gender Subject willing to give Written informed consent Subject is capable and willing to comply with all study procedures	Pregnant and lactating women Patients below the age of 18 Patients on anticoagulant therapy such as Warfarin Patients with severe co-morbid diseases Patients with hypercholesterolemia already on statin drug therapy H/o Hypersensitivity to any of the component's study medication Subject participated in an investigational drug or device study within 30 days prior to study screening

Table:3 Comparison of Percentage reduction in Cholesterol levels

GROUP	BEFORE INTERVENTION MEAN mg/dl	AFTER INTERVENTION MEAN mg/dl	PERCENTAGE REDUCTION
Control	235.1	181.8	53.3%
Study	250.2	179.8	70.4%

Table 4: p value determination

Group	Before intervention		After intervention		p Value
	Mean mg/dl	SD	Mean mg/dl	SD	
Control	235.1	± 25.31	181.8	± 26.50	< 0.0001
Study	250.2	± 44.58	179.8	± 26.43	< 0.0001
p value	0.06		0.65		

Table 5: Comparison of Mean Cholesterol level among study group

STUDY GROUP	BASELINE	End of I month	End of 2 months
Mean	250.2	194.5	177.5
SD	44.58	36.86	27.85
SEM	5.755	4.758	3.595
p value (compared to baseline)		0.0001	0.0001

Table 6: Comparison of Mean Cholesterol level among Control group

STUDY GROUP	BASELINE	End of I month	End of 2 months
Mean	232.8	198.8	181.8
SD	25.95	29.07	26.5
SEM	3.351	3.753	3.421
p value (compared to baseline)		0.0001	0.0001

Table 7: Adverse Drug Effects Among the Study Participants

Group	ADVERSE EFFECTS	Number of patients	Percentage
Control	Muscle weakness	9	15%
	Difficulty sleeping	4	6%
	Abdominal bloating	1	1%
Study	Muscle weakness	8	13%
	Aphthous ulcer	11	18%
	Gastritis	5	8%

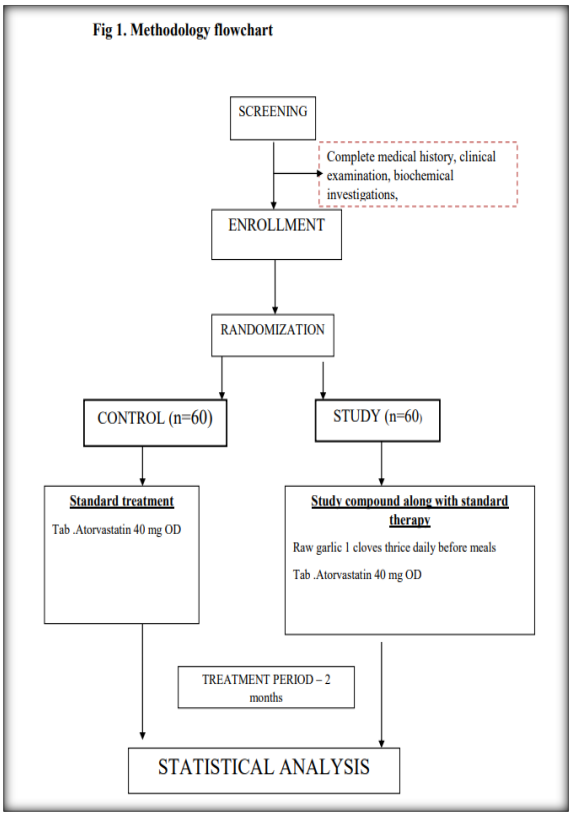

Figure 1: Methodology flowchart

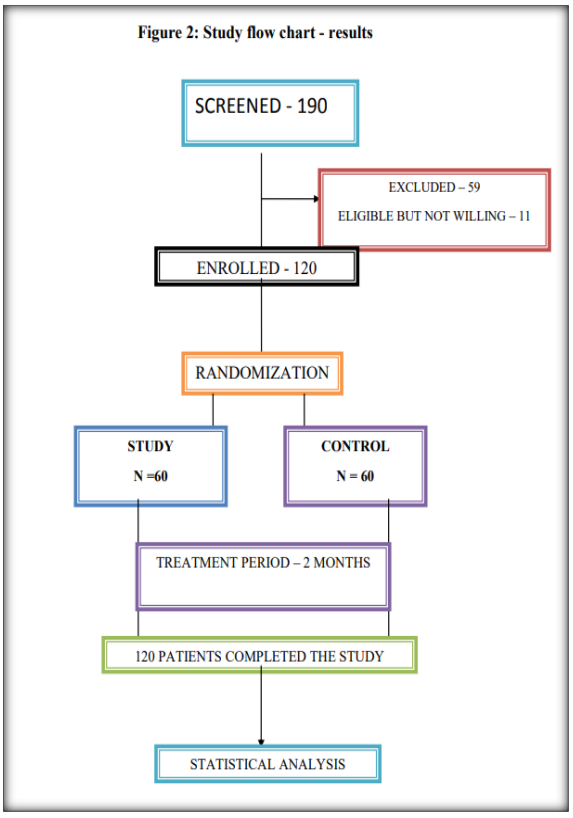

Figure 2: Study flow chart - results

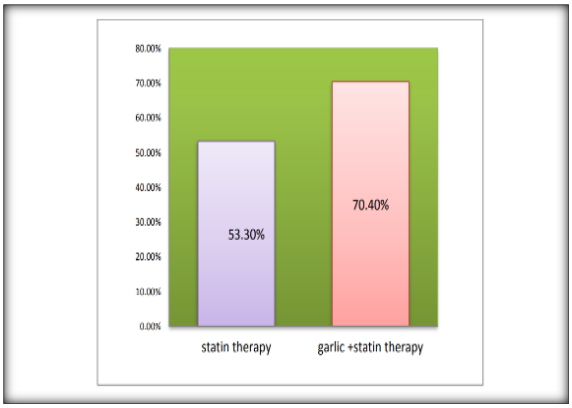

Figure 3: Comparison of percentage reduction in serum cholesterol levels

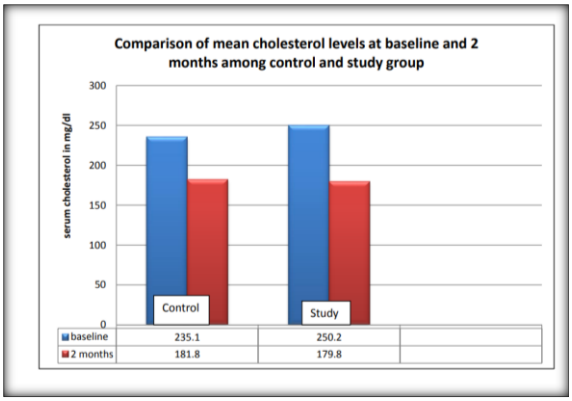

Figure 4: Comparison of mean cholesterol levels at baseline and 2 months among and study group

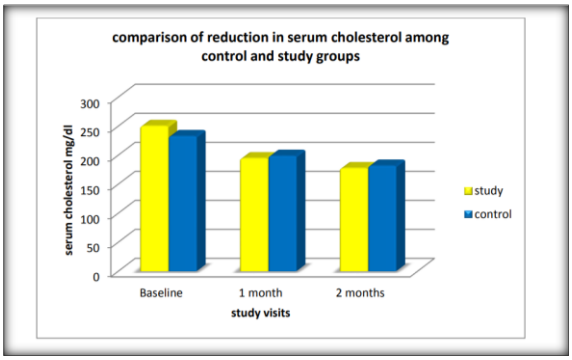

Figure 5: Comparison of reduction in serum cholesterol among control and study groups

DISCUSSION

As a result of the increasing necessity for statin prescription to dyslipidaemia patients coupled with the adverse drug reactions faced on long-term usage newer compounds including herbs and nutritional supplements are being studied for their cholesterol lowering effect.

Our study shows that Percentage of reduction in serum cholesterol level is more (70.4%) in garlic + statin group compared to statin alone (53.3%) as mentioned in Table 3 and represented in figure 4. This substantiates the results of previous study and meta-analysis comparing garlic with placebo where there is an average of 7.6% reduction in cholesterol levels with garlic alone[4]. Analysis of reduction in mean cholesterol levels during the first and second visit as compared to the baseline shows that addition of garlic has not enhanced the efficacy of statins in this study.

Further on analysing the observed results statistically, there was significant change in serum cholesterol values in both the control group and study group implying the factor that the addition of garlic to statins is non-inferior in reducing cholesterol levels. However statistical analysis of reduction in mean cholesterol levels during the first and second visit as compared to the baseline shows that addition of garlic has not enhanced the efficacy of statins. Further studies may be undertaken to study the effect of garlic in various doses in longer duration to prove potentiating effect with statins.

CONCLUSION

Percentage of Cholesterol lowering is more in the Study group compared to Control group. However, this difference is not statistically significant. Raw garlic in lower quantities may have additive benefits rather than potentiating effect with statins in reducing cholesterol levels. However, the statistically significant difference among garlic and statins can be proved in longer duration studies. Inspite of various studies proving the cholesterol lowering effect of garlic, very few have compared the efficacy of garlic with drug therapy. Therefore, this prospective, randomized, open label study has been conducted with the objective of determining the cholesterol lowering effect of garlic, when used as an adjuvant to statin therapy as compared to stand alone statin therapy.

REFERENCES

1. WHO;Raised cholesterol; http:// www. who. int/ gho/ ncd/ risk_ factors/ cholesterol_text/ en/
2. Goodman and Gilman, The Pharmacological Basis of Therapeutics; 12th Edition; McGraw Hill Publications.
3. Stevinson C, Pittler MH, Ernst E, "Garlic for treating hypercholesterolemia. A meta-analysis of randomized clinical trials". Ann Intern Med; 2000; 133(6):420-9
4. Ried K, Toben C, Fakler P, "Effect of garlic on serum lipids: an updated meta-analysis". Nutr Rev; 2013; 71(5):282-99
5. Silagy C, Neil A, "Garlic as a lipid lowering agent--a meta-analysis". J R Coll Physicians Lond. 1994; 28(1):39-45.
6. Sobenin IA, Andrianova IV, "Lipid-lowering effects of time-released garlic powder tablets in double-blinded placebo-controlled randomized study". J Atheroscler Thromb. 2008; 15(6):334-8.
7. Christopher D. Gardner; Larry D. Lawson, "Effect of Raw Garlic vs Commercial Garlic Supplements on Plasma Lipid Concentrations in Adults With Moderate Hypercholesterolemia; A Randomized Clinical Trial"; Arch Intern Med, 2007;167:346-353
8. JV Gadkari, VD Joshi, "Effect of ingestion of raw garlic on serum cholesterol level, clotting time and fibrinolytic activity in normal subjects", J Postgrad Med, 1991;37:8-31
9. Yin Lu, Zhuojin He, Xiuying Shen, et al., "Cholesterol-Lowering Effect of Allicin on Hypercholesterolemic ICR Mice," Oxidative Medicine and Cellular Longevity, vol. 2012, Article ID 489690, 6 pages, 2012. doi:10.1155/2012/489690
10. Mathew BC1, Prasad NV, Prabodh R, "Cholesterol-lowering effect of organosulphur compounds from garlic: a possible mechanism of action". Kathmandu Univ Med J (KUMJ). 2004; 2(2):100-2.