The Antilipedimic Effects of Garlic Powder in Healthy Persons

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A. Study Purpose

The purpose of this study is to evaluate the antilipedimic effects of garlic powder in tablet form in healthy persons.

B. Background

Garlic, a natural herb used by many persons over many centuries, is known scientifically as Allium sativurn. It contains about 100 biologically useful chemicals. Allicin the odiferous agent of garlic is converted by an enzyme when Garlic cloves are cut. This agent however is highly unstable and is destroyed by heat, oxygen, light, proteins or change in acidity. The break down of Allicin releases lots of sulfur-containing compounds that have a variety of pharmacological activities. These pharmacological activities are believed to affect the cardiovascular system by decreasing blood pressure, inhibition of platelet aggregation, antioxidant activity and anti atherosclerotic effects. This is very important as there is a clear association between chronic hypercholesterolemia, and Atherosclerotic Coronary Heart Disease.. Coronary Heart disease remains the #1 killer in the US and thus the reduction of cholesterol by a natural herb as garlic will prove very beneficial.

Several studies have been carried out in Germany for example, Vorberg et al.(6) reported a 21% reduction in TC and a 24% reduction in TG after 4 month treatment with standardized garlic powder 900mg/dI. Not many studies have been carried out in the US.

A meta-analysis by Silagy et al (5), indicates the need:

1 for larger Mid longer duration of randomized trials,
2 for the inclusion of dietary therapy
3 for the assessment of subjects' compliance with the treatment protocol, and
4 for studies with adequate statistical power to accurately assess the benefits of the use of garlic.

A study by Jain et al (2), at Tulane University, showed a 6% reduction in total cholesterol and a 11% reduction in LDL levels. This study looked at a total of 42 people and was carried out for a short period of time. It did not use dietary therapy and subjects' compliance was not assessed. It is also unclear whether data was analyzed in an intention to treat format.

This study is designed to evaluate the antilepidernic effects of garlic tablets in addition to dietary therapy while addressing the shortcomings listed above.

C. Hypothesis

Treatment with Garlic tablets will be associated with a 6 % reduction in total cholesterol and a 11% reduction of LDL levels.

D. Methods

a. Study desig:

This will be a randomized double blind placebo controlled trial. This trial will look at the effects of garlic tablets + Step I diet vs. a placebo + Step I diet on the reduction of total cholesterol especially LDL over a period of 20 weeks.

b. Patient selection

100 subjects between the ages of 21 - 60 yrs will be studied. These subjects will be recruited from employees and medical students at CPMC. Recruitment will be done through flyers, postings in the medical school and various departments. All subjects who complete the study will be given a chance to enter a raffle contest for a trip to Ghana. Equal numbers of men and women, persons of various ethnic groups will be attempted to be included in the study.

c. Study location

The study will take place at the Irving Center for Clinical Research.

d. Prerandomization

Subjects interested in the study will be asked to fill questionnaires about their nutritional habits, any cornorbid disease they may have, how much garlic they use in their meals and their thoughts on the study. Exclusion criteria will include persons with: Cardiovascular disease, hx of angina, past or recent myocardial infarctions, HTN, Diabetes Mellitus, familial hyperlipidemias, cirrhosis, renal failure, hx of cancer, Lung disease, hx of depressive/mental illness, hx Etoh, tobacco use, postmenaupausal women taking estrogen supplements, hx of HIV/AIDS, persons who use lots of garlic in their food and persons with rigorous excercise activity levels. Persons on antilipedimic agents will be asked to stop taking them for 6 weeks.

Subjects eligible for the study will also be asked to sign consent forms about participation in the study. Any questions that arise will be answered. They will be asked to keep their diets and exercise activity constant throughout the study. Subjects will have at baseline - a physical exam, height, weight and BMI measurements and urinalysis. Blood samples will also be collected in the morning after a 12hr fast for CBC, Chem - 20. Initial blood values will be taken as the mean of two fasting samples at I week intervals.

Subjects without comorbid disease, who have mean cholesterol levels greater than or equal to 230mg/dI, will have their fasting lipid profiles checked on two separate occasions. The mean of these values will be taken. Persons with LDL levels > 160mg/dl and TRG levels <200mg/dl will be included in the study.

Subjects who meet above criteria will have initial meetings with the Nutrition dept. of the Irving Center about the components of a Step I diet. They will be asked to complete a 7 day dietary record before being randomized into the study. This will help assess compliance to the diet and to record keeping.

e. Study drugs

The 300mg/dI garlic tablets will contain garlic powder with 0.6% of allicin and the placebo will contain 0.001% of allicin or lactose powder. These tablets will be taken orally. There are currently no known side effects of garlic.

f. Randomization

Subjects will be assigned to either the garlic tablet group or the placebo group by randomly permeated blocks within stratum of gender. Code numbers given to each subject will match the bottles of the tablets being taken. Subjects will be asked to take tablets twice a day. Persons handing out tablets will be blinded to what each subject is receiving. Persons will fill questionnaires biweekly on their dietary habits. They will answer questions about adherence to the diet, exercise habits, whether they are using any garlic in the meals, and on any adverse effects they may be experiencing. During the first month they will have biweekly telephone calls from nutritionists to assess their compliance with their diet. During the rest of the study they will be asked to mail in weekly food diaries that will be assessed by nutritionists for compliance.

Blood samples to analyze lipid profile will be collected at monthly intervals for a period of 5 months. In addition subjects will receive physical exams and measurements of weight and BMI. Tablets will be counted at each visit to measure compliance. Subjects lost to follow up or who become noncompliant with study protocol will be given telephone calls to assess their reasons.

E. Measures

Lipid profiles will be analyzed by the CPMC laboratory. Persons analyzing final data will be blinded. Statistical analyses will be done by Don McMahon, Director of CRIS of the Irving Center for Clinical Research.

F. Analyses

The primary hypothesis is that the group treated with garlic will have significantly lower serum LDL levels relative to the placebo treated group after 20 weeks of therapy. Prior considerations lead us to select 100 subjects as the total sample size that could be enrolled within the constraints of the resources of this project. Differences between the two groups will be studied using analysis of variance. Assumption of a one-way ANOVA with 80% power, type I error rate of 5% in looking at two treatment groups indicated a 0.56 within-group standardized difference would be detected between treatment groups.

This 0.56 within-group standardized difference corresponds to correlation coefficient of group membership with LDL reduction of approximately 0.29.

Adjustment for covariance with baseline LDL, age and ethnicity could improve the efficiency of the test. We recalculated the power of the test assuming a 5%, 10% or 15% reduction in the variance of LDL in an analysis of covariance with the main effect of treatment allocation and covariate adjustment for baseline LDL, age and ethnicity. Covariate adjustment achieving 5%, 10%, or 15% reduction in the variance of LDL measures, provides an increase in statistical power to 84%, 87% or 90% respectively. A one-half standardized difference reduction in LDL level associated with garlic treatment in a well-controlled trial would correspond t a 11% reduction in LDL in the study sample proposed. This is the same effect size as the study by Jain et al(2). If statistical significance is established for the effect of treatment, the two design strata of gender will be analyzed separately. The unadjusted effect size detectable with 25 subjects in each group with an 80% power and type I error rate of 5% is 0.80 standardized difference units.

The second analyses will include repeated measures of analysis of variance with data points from weeks 0, 4, 8, 12, 16, 20. This will unable as to examine the reliability of the difference in the temporal trend of LDL reduction according to level of treatment (garlic or placebo) before and after adjustment for age and ethnicity. If significant contribution to the estimate of outcome by covariate adjustment is revealed by these measurements, we will explore the association between therapeutic effect and gender. This will be done by estimating the difference in temporal trend by group separately for men and women.

G. Risks & Benefits

There will be no risks to any of the subjects involved. Subjects on the garlic tablets will benefit most in the study. However subjects in the control group will benefit from the dietary therapy in reduction of their lipids.

H. Compensation & Costs

There will be no compensation or costs to subjects.

Expected findings and interpretation:

We expect to find an 8 % reduction in the TC, a 11% reduction in LDL levels of persons taking garlic. This size effect is similar to the Jain et al study (2).

I. Significance

Garlic is a natural herb used widely by most people in the world. A clove of garlic is approximately 600mg/dI of manufactured garlic tablets. Its use in combating the atherosclerotic effects of human thromboatherosclerosis will be very beneficial as it has been shown to have no side effects.

The exact mechanism by which garlic lowers lipid levels in circulation is unclear. A study by Yeh et al (7) suggests that the cholesterol lowering action of garlic may stem from its inhibition of hepatic cholesterol synthesis. This is mainly by decreasing the activities of 3-hydroxy-3-methyl-glutaryl-CoA reductase in the liver and decreasing hepatic cholesterol 7 hydroxylase activity. Its active ingredient allin has been shown to inhibit the activity of bovine acetyl CoA synthetase (7). A study by Phelps et al (4) concluded that garlic tablets taken by persons for 2 weeks decreased the lipoprotein oxidation susceptibility that would slow down atherogeneisis.

A larger randomized study with dietary therapy like this study will contribute, in enabling the antiatherosclerotic effects of Garlic to be looked at in individuals at increased risk for heart disease. This will have wide public health consequences for prevention of atherosclerosis using a natural herb.

J. References

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