

Potential of garlic (*Allium sativum*) essence in changing blood lipid profile of the hypertension patients with hypercholesterolemia

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ABSTRACT

Background: As like hypertension, hypercholesterolemia is a major risk factor for cardiovascular disease and hypertension and its complications are one of the highest causes of death in the world.

Aims: This study aims to determine the potential of garlic essence (*Allium sativum*) mixed with honey in changing blood pressure and lipid profile of blood in the hypertension patients with hypercholesterolemia, and to compare the effectiveness with those who received Simvastatin, the most preferred pharmacological treatment of hyperlipidemia.

Methods: This research is a quasi experiment study with a Nonequivalent control group design. There were 22 hypercholesterolemia outpatients purposively selected from local health centers. The respondents were then divided equally to (a) a control group where the patients were provided with generic Simvastatin 10 mg single dose taken once in the afternoon, and (b) an intervention group where the respondents received a non-pharmacological supplement of garlic essence in 2 grams honey. The blood pressure and the blood lipid profile were examined before (Pretest) and at the Day 22 after the treatment (Posttest). The collected data was then analyzed using a T-test to define the significant mean difference between two groups, and a Cohen's effect was measured to interpret the size of changes.

Results: Either the additions of Simvastatin or the provision of garlic essence mixed with honey decreased the blood pressure (systole and diastole) and the cholesterol, triglyceride, and LDL cholesterol, but increased the HDL cholesterol. While significant difference was observed for all parameters at the intervention group, the improvement at the control group for triglyceride was not significant (p value = 0.041). Overall, by the Cohen's effect size effect, we can interpret that the changes was moderate for diastole and systole blood pressure, and also triglyceride and DLD-cholesterol; however the effect size was low for Cholesterol and HDL-cholesterol.

Conclusion: The findings show the importance of the garlic essence mixed with honey to be offered as a nutritional supplement for hypertensive patients with hypercholesterolemia.

INTRODUCTION

Hyperlipidemia is a situation where found with an increasing in cholesterol levels and / or triglycerides [1]. Cholesterol here includes: Total Cholesterol, *Low-Density Lipoprotein* (LDL-cholesterol) and *High-*

Density Lipoprotein (HDL-cholesterol); these substances are essential for the body to maintain normal function but if excessive will increase the risk of heart disease and stroke [2-4]. Hypertension is a major risk factor for various cardiovascular diseases including coronary heart disease, stroke, kidney disease, and

retinopathy. At a hypertension patients, an increasing of blood pressure was observed greater than 140/90 mmHg [5]. In most cases, hypertension is detected during a physical examination for reasons of certain diseases, so it is often called the "silent killer". Without realizing the patient has complications in vital organs such as the heart, brain or kidneys [6]. Knowing the causes or risk factors for hypertension is vital for the prevention and management of adequate hypertension in an effort to reduce the risk of cardiovascular disease [7].

Hypertension and its complications are one of the highest causes of death in the world. Vascular complications caused by hypertension can cause coronary heart disease, cardiac infarction (tissue damage), stroke, and kidney failure [8]. Likewise, hyperlipidemia is a primary risk factor for coronary heart disease and ischemic stroke. One study showed that for every decrease of LDL-cholesterol by 30 mg/dL, there would be a decrease in relative risk for coronary heart disease by 30% [9].

Management of hyperlipidemia cases is divided into two, namely non-pharmacological and pharmacological therapy. Non-pharmacologically controlling cholesterol levels can be done with *Therapeutic Lifestyle Changes* (TLC) which includes: dietary tightening, weight loss and sports activities. If TLC is not successful, a pharmacological control is needed where statins are the main choice in the treatment of hyperlipidemia [10-12]. Many natural substances that are believed to be used to control blood cholesterol levels as an alternative for the community in addressing hyperlipidemia minimal side effects [13]. Garlic (*Allium sativum*) is one of the food ingredients that are widely used every day by our society as a complementary spice and is known to have many properties including anti-hypertension and anti-cholesterol. Garlic contains *allyl methyl sulphide* (AMS) and *diallyl sulphide* (DAS) which inhibit the reaction of angiotensin II-stimulated-cycle in aortic smooth muscle cells and activate the sodium pump in the kidneys to reduce intracellular Na⁺ concentration to control blood pressure. Moreover, the lipid profile of *aliin* and *allicin* derivatives, *S-allyl cysteine sulfoxide* decreases the activity of reductase enzyme *3-hidroxy-3-methylglutaryl-CoA* in cholesterol biosynthesis.

METHODS

This research is a *quasy experiment* study with a *Nonequivalent control group design*. There were 22 hypercholesterolemia outpatients purposively selected from local health centers. Inclusion criteria in sample selection were patients with: systolic blood pressure >130 mmHg, diastolic blood pressure >85 mmHg, and total cholesterol >200 mg/dL. Exclusion criteria were patients

with: comorbid disease or pregnant women. The respondents were then divided equally to (a) a control group where the patients were provided with generic simvastatin 10 mg single dose taken once in the afternoon, and (b) an intervention group where the respondents received a non-pharmacological supplement of garlic essence in 2 grams honey. The procedures and preparations have been approved by the Health Research Ethics Committee of the Politeknik Kesehatan Kemenkes Semarang on June 21st, 2018, prior the intervention, with number 291/KEPK/Poltekkes-Smg/EC/2018.

The independent variables in the control group was the provision of 10 mg of simvastatin whereas at the intervention group the essence of garlic in 2 grams honey was introduced as the independent variable. The dependent variables measured in this present study were blood pressure systole and diastole, total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides. Simvastatin 10 mg was taken once in the afternoon while 5 mL of garlic essence in 2 grams honey was given at the intervention group twice a day at morning and evening.

The effects of the additions to blood lipid profile and the blood pressure of hypertension patients with hypercholesterol were carried out for 21 days. The blood pressure and the blood lipid profile were examined before (Pretest) and at the Day 22 after the treatment (Posttest). For the observation before and after the treatment, the blood pressure was measured using digital tensimeter, performed by the professional nurses as the enumerator while the lipid profile of the respondents was examined by the certified staffs at the CHOD-PAP method in Patra Medika Cepu laboratory. The measurement tools have been calibrated before the test with certification number 051/BP/SK/V/18 on May 10, 2018. The collected data was then analyzed using a *T-test* to define the significant mean difference between two groups, and a Cohen's effect was measured to interpret the size of changes.

RESULTS

Respondents' characteristics

The characteristics of respondents recruited in this study were displayed on Table 1. There were totally 22 respondents recruited in this study with no drop out recorded. This present study noticed that the hypertension outpatients were distributed at 4 age groups, where at the control group the most were in age range of 36-45 and 56-65 while at the intervention group the respondents were at 36 to 65 years old. Interestingly, more females were observed having hypertension. Of 11 of each group, there were 7 female respondents (63.6%) at control group, and 6 female outpatients at intervention group (54.3%). Patients with university degree level dominated the group

where half of respondents both at control and intervention group are those graduated from the university. The control group was dominated by farmers, entrepreneurs and civil servants while at the intervention group 4 of 11 respondents were civil servants.

Table 1. Frequency distribution of respondent's characteristics (N=22)

Characteristics	Control		Intervention		Total	
	N	%	N	%	N	%
Age (year)						
26-35	1	9.1	2	18.2	3	13.6
36-45	4	36.4	3	27.3	7	31.8
46-55	2	18.2	3	27.3	5	22.7
56-65	4	36.4	3	27.3	7	31.8
Gender						
Male	4	36.4	5	45.5	9	40.9
Women	7	63.6	6	54.5	13	59.1
Education						
Junior School	3	27.3	2	18.2	5	22.7
High School	3	27.3	4	36.4	7	31.8
University	5	45.5	5	45.5	10	45.5
Occupation						
Farmer	3	27.3	2	18.2	5	22.7
Entrepreneur	3	27.3	3	27.3	6	27.3
Private	2	18.2	2	18.2	4	18.2
Government	3	27.3	4	36.4	7	31.8

Effects of supplementations to blood lipid profile and the blood pressure in hypertension patients with hypercholesterolemia

Table 2 presents the univariate test for the mean difference in pre- and post- at the control and intervention groups. Either the additions of Simvastatin at control group or the provision of garlic essence mixed with honey at intervention group decreased the blood pressure (systole and diastole) and the cholesterol, triglyceride, and LDL cholesterol, but increased the HDL cholesterol. The results acknowledged that the provision of Simvastatin 10 mg to the hypertension patients until the Day 22 presents the significant effect at level of 0.05 for the blood pressure and the blood lipid profile except Triglyceride, however, the 5 mL of garlic essence in 2 grams honey given at the intervention group twice a day at morning and evening delivers significant changes to all parameters.

The provision of Simvastatin at the control group decreased the blood pressure systole and diastole until 17.64 and 3.91 mmHg, respectively, while at the intervention group the decline was relatively higher at 21.27 and 7.00 point, respectively. From the *T-test* we found that compared to the value at the control group, supplementing the garlic essence with honey will affect significant contribution to blood pressure diastole at 0.05

confidence level. This non-pharmacological supplement decreased the cholesterol and LDL-cholesterol respectively at 66.27 and 23.643 mg/dL, which slightly higher if compare to the results if administered with the pharmacological therapy with Simvastatin 10 mg at 57.72 and 14.63 point. However, we can noticed that providing Simvastatin 10 mg decreased the blood lipid triglyceride at 29.81 point, which slightly lower than the result by the supplementation of the essence garlic.

Moreover, from this study, the measurements orchestrate that the garlic essence with honey is more effective to increase the HDL-cholesterol level to 13.09 mg/dL, compared to the Simvastatin provision at 8.00 point only. Overall, by the Cohen's effect size effect, we can interpret that the change was high for blood pressure systole and diastole, compared to the blood lipid profile. However, among the blood lipid profile, highest alteration was observed for triglyceride. The results also present that the supplementation was not really effective to decrease the cholesterol level in the hypertension patients where the effect size was only at 0.1 point.

DISCUSSION

All recruited participants in this study were equally distributed into control group and intervention group, considering their age, gender, education and occupation. These characteristics are considered as the confounding factors that can affect the independent variables. The age of participants is linear with the occurrence of hypertension and dyslipidemia due to the changes in the wall of the blood vessels which can narrow it and make it more stiff [14]. A study also found a correlation of age and parity with hypertension incidence among pregnant women [15]. In gender characteristic, estrogen which is more abundant in non-menopausal women can act as the protector with its advantage effects in decreasing total cholesterol, LDL-cholesterol, and increasing HDL-cholesterol [16]. Education level of participants can be the indicator of their ability in understanding health information particularly regarding hypertension and hypercholesterol. The job of participants also can affect their hypertension and hypercholesterol status through various pressure that occur in each type of job [17, 18].

In univariate analysis, it shows that there were significant improvements in all parameter except triglyceride which was actually improved but statistically insignificant. This findings confirm that the given treatment either in intervention group or control group could improve participants' status. Nevertheless, the mean values in intervention group were higher than control group though the two groups were not compared in univariate analysis.

Table 2. Effects of the supplementation on blood pressure (systole, diastole) and blood lipid profile (cholesterol, triglyceride, LDL, HDL cholesterol) in hypertension patients at the control and intervention group

Variables	Control		Delta	Intervention		p value	Effect size
	Mean	SD		Mean	SD		
Systole (mmHg)							
Pretest	148.91	12.28	- 17.64	149.00	12.70	- 21.27	0.256
Posttest	131.27	8.17		127.73	6.75		
p value	0.001		0.001				
Diastole (mmHg)							
Pretest	86.91	49.69	- 3.91	88.55	4.32	- 7.00	0.041
Posttest	83.00	3.16		81.55	2.46		
p value	0.004		0.001				
Cholesterol (mg/dL)							
Pretest	248.91	27.49	- 57.72	255.64	27.08	- 66.27	0.466
Posttest	191.18	29.50		189.36	20.72		
p value	0.001		0.001				
Triglyceride (mg/dL)							
Pretest	152.36	55.54	- 29.81	181.76	112.80	- 25.72	0.872
Posttest	122.55	15.49		155.64	122.10		
p value	0.241		0.006				
LDL- cholesterol (mg/dL)							
Pretest	137.91	13.29	- 14.63	147.91	24.92	- 23.63	0.301
Posttest	123.27	11.98		129.27	22.85		
p value	0.001		0.017				
HDL- cholesterol (mg/dL)							
Pretest	37.64	7.92	8.00	34.09	5.07	13.09	0.242
Posttest	45.65	8.54		47.18	7.76		
p value	0.041		0.001				

This findings also can present the glimpse about the advantages of garlic essence which were given to intervention group and eventually lead them to the better improvement than control group. Simvastatin is a type of medicine used in pharmacological treatment for hypercholesterolemia and hypertension patient, while garlic is one of the natural ingredients which used in non-pharmacological treatment and proposed to be given for the hypertension patients at this present study. The mechanism of action of simvastatin itself in lowering cholesterol and LDL levels is by inhibiting the enzyme 3-hydroxy-3-methyl glutaryl-coenzyme A (HMG-CoA) reductase competitively. This drug inhibits the activity of the enzyme HMG-CoA reductase which converts Acetyl-CoA to mevalonic acid. In the process of synthesis of cholesterol in the liver, simvastatin can increase LDL receptor activity which makes the speed of LDL metabolism by the liver becomes faster and plasma LDL deposit become reduced [19]. There are several mechanisms for cholesterol synthesis that are affected by garlic. First, garlic contains saponins which act as an inhibitor of cholesterol absorption in intestines which results in a decrease in plasma cholesterol levels. Second, garlic contains water-soluble compounds, such as *S-allyl cysteine* (SAC), *S-ethyl cysteine* (SEC), and *S-propyl*

cysteine (SPC) which are the potential inhibitor for the synthesis of cholesterol, yet the mechanism is still not comprehensively understood [20].

One study found that garlic extract reduces cholesterol synthesis by 75% without evidence of cellular toxicity. This result indicates that the containing compound, *allyl-disulfide* or *allyl-sulphydryl* group are most likely responsible for inhibiting the synthesis of cholesterol and this inhibition is likely mediated in sterol 4 *alpha-methyl oxidase*. This suggests that water-soluble compounds such as SAC in old garlic extracts are less cytotoxic and more efficient at inhibiting cholesterol biosynthesis than organosulfur-fat-soluble compounds such as DAS [21]. Thus, the result also shows that intervention group which was given garlic extract had better improvement of LDL-cholesterol than control group.

Although the components of garlic have pharmacological effect in lowering blood pressure, the nature of the components of garlic that affects blood pressure is not thoroughly known. One observation study found that the treatment of allisor dose of 600 mg/day resulted in a decrease in systolic and diastolic blood pressure [22]. Another study showed that *allyl methyl sulfide* (AMS) and *diallyl sulfide* (DAS) as the compounds derived from

garlic could inhibit the reactions of *angiotensin II-stimulated-cycle* in aortic smooth muscle cells. Thus, they could be targeted as effective antioxidants in arterial remodeling in hypertensive patients. Another activity shown by garlic extract is the activation of the sodium pump in the kidneys by reducing intracellular Na + concentration so as to normalize blood pressure [23].

In bivariate test, only one (diastolic BP) out of six variables showed significant difference between control and intervention group. The intervention group made significant better improvements than control group in diastolic BP. Moreover, in the rest variables it also shows that the intervention group made better improvements than control group except in triglyceride which showed the opposite result. Additionally, effect size confirms the magnitude of the improvements despite statistical calculation. Based on Cohen's effect size reference, the present study also acknowledged that the changes was moderate for diastole and systole blood pressure, and also triglyceride and LDL-cholesterol; however the effect size was low for Cholesterol and HDL-cholesterol.

CONCLUSION

This present study concludes that either the provision of Simvastatin at the control group or the oral administration of garlic (*Allium sativum*) with honey, for 21 days supplementation, in hypertension subjects with hypercholesterolemia decreased the blood pressure (diastole, systole) and the blood lipid profile (cholesterol, LDL-cholesterol, triglyceride), but increased the HDL-cholesterol. While significant difference was observed for all parameters at the intervention group, the improvement at the control group for triglyceride was not significant at 0.05 difference level. The findings show the importance of the garlic essence mixed with honey to be offered as a nutritional supplement for hypertensive patients with hypercholesterolemia.

CONFLICT OF INTERESTS

Authors declared there is no conflict of interests involved in the study.

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